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CARDIOPULMONARY EFFECTS OF PARTIAL PULMONARY ARTERIAL OBSTRUCTION IN DOGS†

Major obstruction to pulmonary artery blood flow such as occurs in massive pulmonary embolism is usually accompanied by a sharp decline in arterial blood oxygen tension. This phenomenon has long been recognized, and over 25 years ago Mendlowitz suggested that it was due to a decrease in the permeability of the alveolar-capillary membrane to oxygen transfer.[1] Later Turino and his associates stated that the actual diffusing capacity was not affected appreciably unless the blood flow declined by over 50 per cent.[2] Searching for factors other than diffusing capacity, we chose to study the hypoxemia subsequent to diminished pulmonary blood flow by experimentally reducing the flow to a moderate degree, sufficient to produce hypoxemia but not sufficient to produce shock.

METHODS

Mongrel dogs were anesthetized with pentobarbital sodium (26 mg/kg.) and ventilated by means of a controlled mechanical respirator pump with a predetermined volume and rate (manufactured by the Palmer Company) attached to one limb of a Y-shaped tracheal cannula, the other limb being the expiratory side for collecting expired air and measuring end-tidal gas tension. A Dotter-Lucas type cardiac catheter with a balloon just proximal to the tip was inserted into the main pulmonary artery, and another cardiac catheter inserted into the right atrium. A cannula was placed in the femoral artery for obtaining arterial blood samples.

When the animal appeared to be in a steady state and the pulmonary arterial pressure and pulse rate were constant, base line control studies were recorded. Then the catheter balloon was filled with an average of 5 ml. of saline or diatrizoate sodium (Hypaque sodium), the amount being determined by a distinct decrease in pulmonary arterial mean pressure. The volume of the balloon provided a diameter of about one centimeter, sufficient to fill the pulmonary artery without distending it. The balloon was pulled back until it was just above the pulmonic valve, and the experimental studies performed between 12 and 15 minutes later or at a time when the pressure and pulse rate appeared to be stable.

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† This study was supported by U. S. Public Health Service Research Grant HE03263(07) and (08).
Received for publication 15 February 1966.

The studies performed included arterial sampling for blood gas tension and pH concomitant with expired air sampling for volume, carbon dioxide and oxygen content, and in some cases end-tidal percentages of carbon dioxide and nitrogen. Dye dilution cardiac output curves were then inscribed and pulmonary arterial pressures recorded.

Blood carbon dioxide (Pa_{CO_2}) and oxygen tensions (Pa_{O_2}) and pH were determined using Clarke and Severinghaus electrodes, a glass electrode, and a Beckman Blood Gas Analyzer. Expired air was collected in a Douglas Bag and measured in a wet-test flow meter. The gas was analyzed for carbon dioxide and oxygen concentrations using a micro-Scholander technique. End-tidal carbon dioxide and nitrogen concentrations were determined with a Beckman infra-red carbon dioxide analyzer and a Waters nitrogen analyzer respectively.

Alveolar ventilation ($\dot{V}_A$) was calculated by the method described by Comroe, and the physiological dead space (V_D physiological) using the Bohr equation substituting arterial for alveolar carbon dioxide tension.[8] Total ventilation ($\dot{V}_E$) was considered equal to expired gas volume. Alveolar oxygen tension ($P_{A_{O_2}}$) was calculated by means of the alveolar air equation.

Pressure in the pulmonary artery (P.A. pres.) was recorded on a Hathaway MBC-1 blood pressure monitoring unit with a Hathaway G-2 transducer. Cardiac output ($\dot{Q}$) was calculated from a dye dilution curve using indocyanine green dye injected into the right atrium through a pre-placed catheter and sampled from the femoral artery cannula. The dye concentration was measured by a densitometer (Gilford Instrument Company).

Resistance to blood flow through the lung was calculated in terms of resistance units according to the following equation:

$$\text{Resistance units} = \frac{\text{Pulmonary arterial mean pressure in mm.Hg}}{\text{Flow in L./min.}}$$

This equation includes resistance at the level of the left atrium.

Each animal constituted its own control in that the balloon was not inflated before reaching a "steady state" reflected by unchanging observations of physiologic functions. For additional control a group of six dogs were treated exactly as the experimental animals except that the balloon was inflated and immediately deflated with observations starting 12 to 15 minutes later.

RESULTS

Sixty experimental studies were attempted but 16 animals failed to survive the inflation of the balloon. In addition, six successful control studies were completed. Of the 44 experiments completed, 13 were discarded because following inflation of the balloon severe arrhythmias developed which made it impossible to determine a steady state. In six experiments the cardiac output either remained constant or increased and therefore they were not subject to further analysis. The remaining 25 dog studies in which both the cardiac output and pulmonary arterial mean pressure declined will be the substance of the following report. We were unable to accomplish complete studies in some experiments (see Table 1).

TABLE 1. MEAN DIFFERENCES IN CARDIOPULMONARY FUNCTION FOLLOWING PARTIAL OCCLUSION OF THE MAIN PULMONARY ARTERY IN ANESTHETIZED DOGS

	Physiologic function										
	$\dot{V}_A$ L/min.	V_D L.	$\dot{V}_E$ L/min.	R	pH	Pa_{CO_2} mmHg	$P_{A_{O_2}}$ mmHg	Pa_{O_2} mmHg	A-a mmHg	$\dot{Q}$ L/min.	Mean PA pres. mmHg
No. of experiments	23	23	23	23	17	24	21	21	21	25	25
Pre-occlusion mean	2.32	0.1224	5.000	0.82	7.335	36.70	106.9	86.1	20.8	1.80	23.6
Post-occlusion mean	2.00	0.1367	4.865	0.77	7.281	39.91	100.7	72.1	28.6	1.31	11.4
Mean differences	−0.32	+0.0143	−0.135	−0.05	−0.054	+3.21	−6.2	−14.0	+7.8	−0.49	−12.2
p value	0.2> p >0.1	0.2> p >0.1	0.2> p >0.1		0.001 >p	0.1 >p> 0.05	0.005 >p> 0.001	0.001 >p	0.01 >p> 0.005	0.001 >p	0.001 >p

NOTE: See text for interpretation of symbols. Note that alveolar and expired ventilation are reported as liters per minute whereas dead space is reported as a static volume.

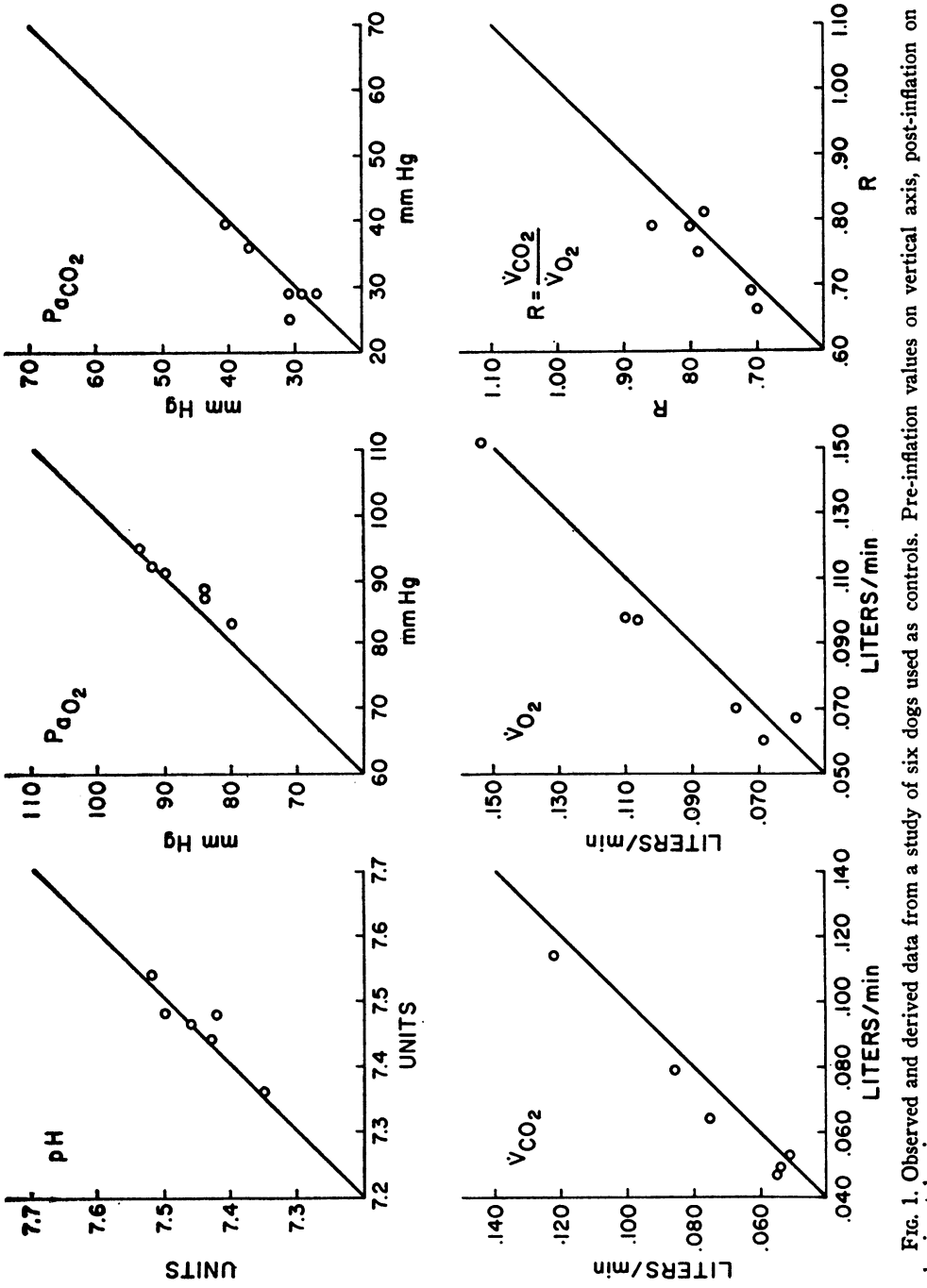

FIG. 1. Observed and derived data from a study of six dogs used as controls. Pre-inflation values on vertical axis, post-inflation on horizontal axis.

The control animals in which the balloon inflation was not maintained showed remarkable stability (Fig. 1). The observed data, pH, blood gas tension and total gas exchange, did not change significantly, and what slight changes occurred in blood gas tensions were in a direction opposite that of the experimental studies. Similarly, the derived data showed only minimal change and the mean change was over two standard deviations away from the experimental mean change for each function.

In the experimental studies there was a slight decrease in alveolar ventilation (mean decrease = —0.32 L/min. $p > 0.1$) and the physiological dead space increased slightly (mean = +0.0143 L., $p > 0.1$) but both are of doubtful statistical significance. There was also a slight drop in total ventilation (mean = —0.135 L/min., $p > 0.1$). The latter is of doubtful statistical significance and could be accounted for by failure to start collecting the expired sample at precisely the same point in the respiratory cycle. In each experiment the respiratory quotient (R) declined after inflation of the balloon, the mean values before and after being 0.82 and 0.77 respectively. The arterial pH declined significantly (mean = —0.054, $p < 0.001$). There was a consistent but slight rise in arterial blood carbon dioxide tension (Pa_{CO_2}) (mean = +3.21 mmHg, $p < 0.1$) and fall in calculated alveolar oxygen tension ($P_{A_{O_2}}$) (mean = —6.2 mmHg, $P < 0.005$), while the observed arterial blood oxygen tension (Pa_{O_2}) declined considerably more than the $P_{A_{O_2}}$ (mean = —14.0 mmHg, $p < 0.001$). The alveolar-arterial oxygen pressure gradient widened significantly following obstruction (mean = +7.8 mmHg, $p < 0.01$). In four studies the alveolar-arterial oxygen pressure gradient was calculated at two levels of oxygen breathing; room air and approximately 28 per cent (see Fig. 2). The resting gradient after inflation of the balloon rose in all four studies* and the difference between the gradients while breathing room air and while breathing 28 per cent oxygen was greater in the occlusion than in the control study in three, equal in one (see Fig. 2). In five animals mixed venous blood oxygen tension ($P_{\bar{V}_{O_2}}$) was studied. The changes were (in mmHg) —8, —5, 0, +2, —4.

In the two studies in which end-tidal carbon dioxide tension was recorded, both control and experimental records revealed a prompt rise with early plateau formation suggesting good intrapulmonary gas distribution. In four other studies end-tidal nitrogen was recorded at four and seven minutes while the animal breathed pure oxygen. Zero nitrogen concentrations at both four and seven minutes were recorded in three

* Only 1 mmHg in dog No. 4.

and a reading of 2.5 and 1.7 per cent respectively in the fourth. These data also appear to suggest that intrapulmonary gas distribution was not grossly deranged.

Total systemic blood flow declined significantly by a mean of —0.49 L/min. ($p < 0.001$) which was a 27 per cent decrease below the resting control values. The pulmonary arterial mean pressure decreased significantly by —12.2 mmHg ($p < 0.001$) or 51 per cent below the resting control values. The pulmonary arterial pressure change, relatively greater than the cardiac output change, resulted in a decrease in calculated resistance to blood flow through the lung and left atrium which correlated reasonably well ($r = 0.82$, S. E. of $r = 0.26$) with the drop in pressure, although the correlation did not become evident until the pressure had dropped by 4.6 mmHg (see Fig. 3).

DISCUSSION

The inflated balloon had a diameter of about one centimeter, which was nearly the same as the pulmonic valve that it occluded. The fact that in six

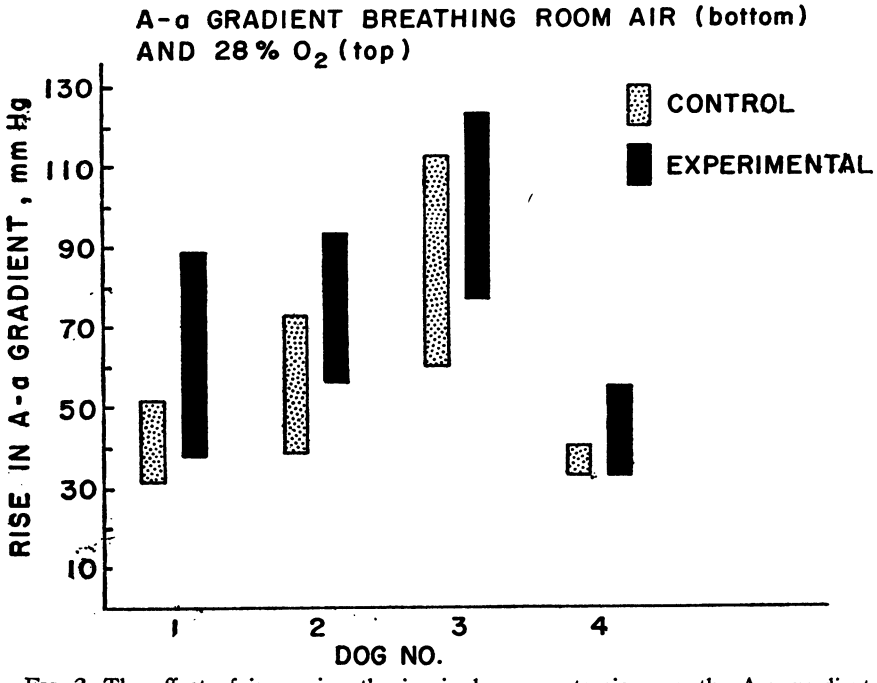

FIG. 2. The effect of increasing the inspired oxygen tensions on the A-a gradient before and after pulmonary arterial obstruction. An estimation of pulmonary A-V shunting.

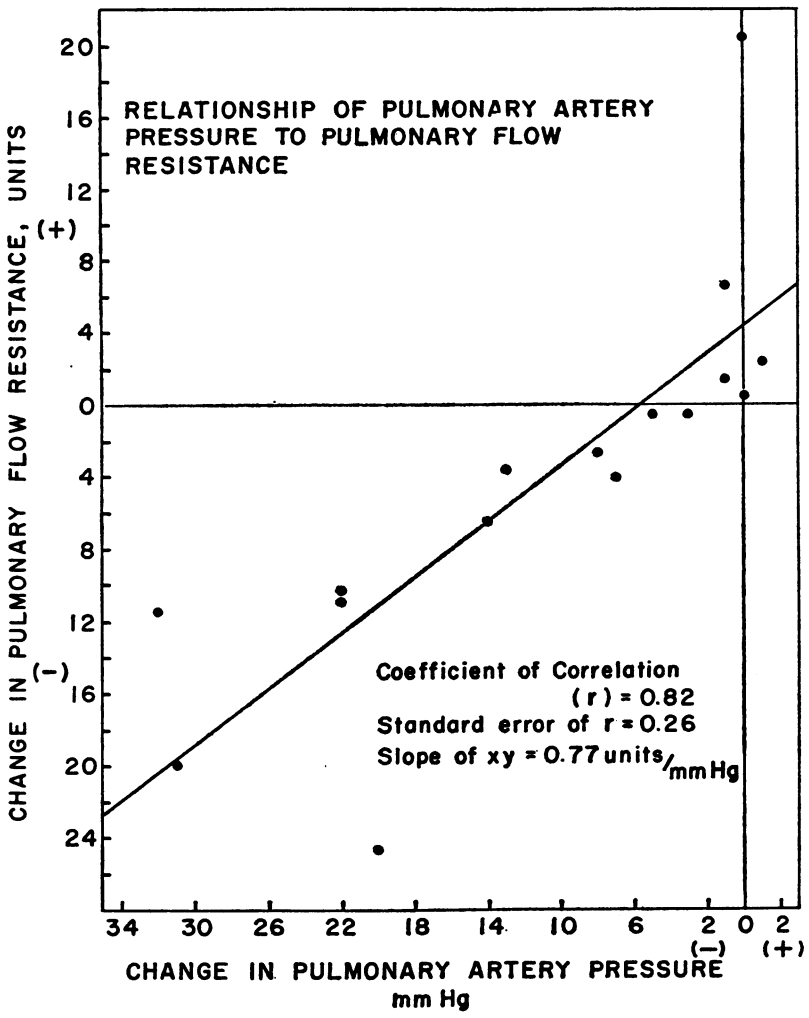

FIG. 3. The effect of diminished pulmonary arterial blood flow and pressure on resistance. Resistance was calculated for only 16 of 25 dogs due to failure to record the pressure and dye curves simultaneously in the remaining 9.

of forty-four completed studies inflation of the balloon failed to lower the cardiac output is testimony to the tremendous compensatory power of the ventricular myocardium. This remarkable ability has been pointed out by Aviado.[4] In fact the most serious consequence to dogs appears to be the arrhythmia that often supervenes following inflation of the balloon.

Although the changes in alveolar ventilation, as estimated by the alveolar ventilation equation, are of doubtful statistical significance in the present study, there appears to have been a genuine decrease as reflected by the increased arterial carbon dioxide tension. Since the alveolar ventilation determination depends upon a number of observations, each of which has inherent inaccuracies, the calculated value is likely to be less accurate than the directly observed arterial carbon dioxide tension. Some of the drop in calculated alveolar ventilation is the result of a diminished total ventilation ($\dot{V}_E$) and the cause of the latter is obscure. The respiratory pump was set to deliver a given volume at a given rate and yet there was a consistent decrease in total ventilation measured as expired volume after balloon inflation that could not be entirely accounted for by the lower respiratory quotient. It may have reflected changes in lung compliance or some sort of a systematic error in beginning the collection of expired air. At least part of the diminished alveolar ventilation in some experiments was related to an increased physiological dead space. The latter might be anticipated because, with diminished perfusion associated with a drop in cardiac output, one might expect some air spaces to retain good ventilation in the face of impaired perfusion, thus by definition becoming alveolar dead space. The physiological dead space is the sum of the anatomical and alveolar dead spaces.

We can say, therefore, that a decrease in alveolar ventilation brought about by an increase in physiological dead space may contribute somewhat to the hypoxemia of diminished pulmonary perfusion, but more prominent causes should be found in other parameters. A low alveolar oxygen tension might exaggerate a diffusion impairment, but the latter does not by itself produce significant hypoxemia.[5] A diminished capillary blood volume will reduce the available hemoglobin into which oxygen may diffuse, thereby reducing the diffusing capacity. This will not in itself, however, affect arterial oxygen tension because the hemoglobin traversing the alveolar capillaries becomes completely saturated, even though diminished in amount.

The resting control A-a gradients widened when the animal was ventilated with high oxygen tension air-mix, indicating the presence of shunts at rest, and if the mixed venous blood oxygen tension, $P_{\bar{v}_{O_2}}$, were to decline following balloon inflation, it would exaggerate the venous admixture as far as Pa_{O_2} is concerned. Some drop in $P_{\bar{v}_{O_2}}$ would be expected with a drop in $\dot{Q}$. However, the greatest change in $P_{\bar{v}_{O_2}}$ observed in five experiments was less than the mean decline of Pa_{O_2}, hence $P_{\bar{v}_{O_2}}$ could not be an important factor. Finding normal end-tidal carbon dioxide concentration curves

and normal end-tidal nitrogen concentration while breathing oxygen in several experiments, suggests that intrapulmonary gas distribution was not greatly disturbed, although minor distribution difficulties would be missed by these techniques.

We attempted to avoid distention of the pulmonary artery by adjusting the balloon diameter to the same range as that of the artery, and keeping it close to the pulmonic valve. There is a distinct possibility, however, that stretch reflexes as well as diminished blood flow and pressure may play a role in the development of hypoxemia.

We can reasonably conclude that the hypoxemia observed in our experiments is related minimally to alveolar hypoventilation, to a minor extent to impaired distribution and diffusion, and in large part to a venous admixture. The mechanism of the venous admixture is uncertain. One would suspect either direct pulmonary artery-to-vein shunts in the lung or a shunting through communications between the azygous system and the bronchial veins brought about by sudden elevation of pressure in the right side of the heart and great veins.[6]

Of pertinence to the possibility of A-V shunts in the lung was the unexpected finding of a resistance to blood flow through the lung and left atrium which decreased directly with the decrease in pulmonary arterial pressure (Fig. 3). Other studies have suggested that as the pressure rises the resistance decreases, owing to passive distention of the blood vessels.[7-9] In our experiments this principle could not be extrapolated to lower pressures for after the decrease in pressure had approached 5 mmHg, the resistance progressively declined with further decreases in pressure. The mechanism is obscure. It does not appear to be a passive phenomenon at the precapillary level for then the vessel should become smaller and the resistance greater. With low vascular pressures there may be some sort of vasodilator reflex or opening of new vascular passages that may actually be the shunts producing the venous admixture, but more likely the diminished resistance reflects a lower left atrial pressure resulting from diminished filling. The latter could, in itself, encourage right-to-left shunting at the azygous-bronchial-pulmonary vein level. Our indicator dilution curves did not suggest large shunts, but small shunts could have escaped notice.

SUMMARY

A moderate decline in cardiac output and pulmonary arterial pressure was obtained by inflation of a balloon in the main pulmonary artery of intact anesthetized dogs. The arterial oxygen tension decreased considerably and this decrease appeared to be due to several factors, including a

venous admixture and alveolar hypoventilation brought about by an increase in the physiological dead space. The obvious decrease in circulating capillary blood volume would not contribute to hypoxemia. A mild acidosis, probably metabolic as well as respiratory, lowered the arterial blood pH. An unexpected finding was a progressive decline in resistance to blood flow through the lung as the pulmonary arterial pressure declined. The latter may have been related to the opening of pulmonary arteriovenous shunts.

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