THE object of this investigation was to measure simultaneous changes in blood pressure and blood flow in the pulmonary circulation of the intact dog. Observations were made during standing and running at different rates on a treadmill. A further group of dogs subjected recently to ligation and division of the left pulmonary artery was studied also. This permitted an extension of the observations in the presence of unusually high blood flow through a single lung.

The pulmonary and left-heart blood volumes were measured simultaneously in an attempt to assess changes in the volume of blood in the lungs.

Methods
Preparation of Animals

Ten mongrel dogs weighing 14 to 20.1 Kg. were taught to run on a horizontal treadmill at different speeds. Six dogs (nos. 1 to 6) were intact; and 4 (nos. 7 to 10) had been subjected to ligation and division of the left pulmonary artery 3 to 6 weeks previously. Two intact dogs were studied twice and one with a ligated and divided pulmonary artery (hereinafter referred to as "ligated pulmonary artery") was studied 3 times, making a total of 14 experiments.

The dogs were trained to lie quietly supine while catheters were inserted under local procaine anesthesia with fluoroscopic and manometric guidance. A 40-cm. catheter (dead space, 0.4 ml.) was inserted via the common carotid artery into the left ventricle, and then the tip was withdrawn until it lay just above the aortic valve. Two 80-cm. catheters were inserted into an external jugular vein. One was advanced so that its tip lay in the pulmonary trunk just above the pulmonary valve, and the other was wedged into a distal pulmonary artery.

Measurement of Pressure

Statham strain-gage transducers were used to measure aortic, pulmonary-artery (PA), and pulmonary-artery wedge (PAW) pressures. The zero reference point was midway between the dorsal and ventral aspects of the thorax when the dog was standing. In the process of recording, the pressures were electrically damped to minimize motion artifact and to produce mean values. At the beginning and end of each period of exercise the pressures were recorded undamped to confirm the positions of the catheter tips. Owing to changes in the dog's position during exercise, absolute PA and PAW pressures could not be measured accurately. However, simultaneous recording of PA and PAW pressures made the difference between these pressures (PA minus PAW pressure) independent of such changes.

Measurement of Output and Volume

Cardiac output was measured by the indicator-dilution method of Hamilton and associates.1 Indocyanine green (cardiogreen) dye* was used as the indicator in concentrations of 1.25 to 2.5 mg/ml, the doses on different occasions varying from 1 to 3 mg. Injection of dye was made into the pulmonary artery via the catheter by a pneumatic syringe capable of delivering 1 ml. of dye solution in 0.1 second. A linear potentiometer linked to the syringe piston recorded the instant and magnitude of each injection.

Arterial blood was sampled continuously from the aortic catheter. Vacuum suction at flow rates of 100 to 130 ml. per minute drew it through a densitometer,† and the dilution curves were recorded on a photokymograph or a multichannel oscillographic recorder.

*Kindly supplied by Hynson, Westcott & Dunning, Inc., Baltimore, Md.
†This densitometer, developed in the Section of Engineering, Mayo Clinic, is similar to Model XC-100A manufactured by the Waters Corporation, Rochester, Minn., but has a slightly larger internal diameter to permit higher sampling rates.
The volume of blood in the lungs and left heart chambers was calculated as the product of the cardiac output and mean transit time (MTT) of indicator between the injection and sampling sites. The MTT of the recorded curve, however, was equal to the sum of the MTT between injection and sampling sites and the MTT of the sampling system. The latter was derived using the apparatus described by Fox and co-workers; at a sampling rate of 120 ml per minute it was 0.40 second. Subtraction of this MTT from that of the recorded curve gave the corrected MTT for the lungs and left heart chambers.

In the first 5 experiments of the series, a Wood cuvette oximeter was used instead of a densitometer, and sampling was accomplished through a longer catheter (dead space, 1.05 ml.) at slow rates (20 to 30 ml/min.). The dynamic response of this sampling-recording system is unsuitable for measurement of time components, and in these 5 experiments (dogs 1, 2, 3, and 7) only the data for pressure and flow were obtained.

In 2 of the intact dogs (5 and 6), measurements were made of only the cardiac output and the pulmonary and left-heart blood volume. The surface area of the dogs was calculated from Meeh’s formula:

\[ \text{Surface area (cm}^2\) = 11.2 \times \text{weight (Gm.})^{2/3} \]

Plan of Experiments

The first recordings were made with the dog standing at rest on the treadmill. Additional recordings were made while the dog was running on the treadmill at a speed that had been maintained for 2 minutes. The speed of running was increased by increments of 2 or 4 km./hr. up to a maximum of 10 to 14 km./hr. At speeds up to 8 km./hr. there were no rest periods between runs. At higher speeds, periods of rest alternated with exercise.

Before each period of exercise the PA catheter was filled with dye and attached to the pneumatic syringe. The catheters in the aorta and the PAW position were connected to their strain-gage transducers. The aortic catheter was connected by a 3-way stopcock to the densitometer also. After 2 minutes of exercise the stopcock on the aortic catheter was opened to the densitometer and sampling was begun. After the injection of dye via the PA catheter, this catheter was disconnected from the syringe and connected to its strain-gage transducer to obtain pressure records simultaneously with or just after injection of the dilution curve. On completion of the curve the stopcock on the aortic catheter was opened to its transducer, permitting simultaneous pressures to be recorded from all 3 sites. Sampling was accomplished in not more than 20 seconds, and the blood was reinfused after the pressure records were completed.

Calibration curves were constructed for each experiment by drawing known concentrations of cardiogreen dye in the dog’s own blood through the densitometer or oximeter and recording the deflections produced.

From 4 dogs, samples of arterial and mixed venous (PA) blood were obtained at rest and during exercise for determination of the oxygen content and capacity by the method of Van Slyke and Neill.

Results

Intact Dogs

The effects of graded exercise on dog 4 are illustrated in figure 1 (left). The cardiac output at rest was 3.6 L/min. It increased steadily as exercise became more severe up to 8.7 L/min. at 14 km./hr. Arterial blood was 99 per cent saturated with oxygen during rest and 98 per cent saturated during running at 12 km./hr. The oxygen saturation of mixed venous blood fell sharply from 79.5 per cent at rest to 51.5 per cent at 4 km./hr., and more gradually to 36 per cent at 12 and 14 km./hr. Oxygen consumption was calculated indirectly from the cardiac output and the oxygen content of blood samples; it increased from 130 ml./min. at rest to 900 ml./min. at 14 km./hr., a sevenfold increase. The difference between PA and PAW pressures increased...
only slightly from rest to severe exercise. Hence there was a steady fall in calculated pulmonary vascular resistance through the range of activity. The volume of blood in the lungs and left heart chambers was 240 ml. during rest and 240 ml. during severe exercise; at intermediate grades of activity the volume showed only slight variations from this figure, probably within the range of experimental error.

The results in all 6 intact dogs are shown in figures 2 and 3 (left panels). The cardiac index varied from 3.4 to 4.8 (mean 4.2) L. while the dogs were standing at rest. At 4 km./hr. it averaged 5.9 L., an increase of 40 per cent over the resting value; and at 8 km./hr. it averaged 8.3 L., an increase of almost 100 per cent. Further increases occurred at 10 to 14 km./hr. Since the dogs differed in size and capacity for exercise, however, running at a particular speed cannot be regarded as an equally severe test for each of them.

The difference between PA and PAW pressures among the 4 intact dogs in which they were measured ranged from 8.5 to 14 mm. Hg during rest. It increased only slightly through the range of exercise, and thus there was a progressive fall in calculated pulmonary vascular resistance.

The mean transit time of indicator from the pulmonary to the aortic valve was measured in 4 experiments on 3 intact dogs. It decreased with increase in cardiac output. The net effect in 3 experiments was no significant change in calculated pulmonary and left-heart blood volume throughout the range of activity in which measurements were made. In the other experiment (dog 5), the volume was 18 per cent greater during running at 14 km./hr. than during standing at rest.

**Dogs with Ligation of LPA**

Complete data from dog 10 are given in figure 1 (right). Pulmonary blood flow increased progressively from 4.3 L./min. during standing at rest to 10.6 running at 13 km./hr. The oxygen saturation of arterial blood was 95 per cent both during standing and severe exercise; saturation of venous blood fell progressively from 63 per cent to 33 per cent. Oxygen consumption was calculated as 250 ml./min. during standing and as 1,300 ml./min. during running at 13 km./hr., a 5-fold increase. The PA minus PAW pressure increased from 10 to 15 mm. Hg. This slight change was disproportionate to the increase in cardiac output, and therefore the calculated pulmonary vascular resistance gradually fell. The blood volume of the lungs and left heart chambers was unchanged up to 8 km./hr.; at higher speeds it increased about 10 per cent.

The data for the other 3 dogs in this group were in general similar and are shown in figures 2 and 3 (right panels). The cardiac index in 6 experiments on the 4 dogs was 3.1 to 5.9 (mean 4.5) L during standing at rest. At 4 km./hr. it averaged 7.6 L and at 8 km./hr. 10.0 L, the increments amounting to about 70 and 120 per cent over the resting value, respectively. Further marked increase occurred up to 14 km./hr. Similar results were obtained in each of the 3 experiments on dog 8. Among the whole group there was little change in pulmonary and left-heart blood volume throughout the range of activity in which the measurements were made; at the higher speeds the volume was about 5 to 20 per cent greater than at rest. The PA minus PAW pressure during standing at rest was similar to that in the group of normal dogs, ranging from 8 to 18 mm. Hg. In 3 dogs this
difference of pressure increased only moderately, even with severe exercise; and in consequence the calculated pulmonary vascular resistance fell progressively. In dog 9, however, increases in cardiac output were accompanied by corresponding increases in pressure.

Discussion

Technics of Measurement

Pressure

It was not possible to measure directly the left atrial pressure during exercise. However, in man the pulmonary wedge pressure is considered to reflect left atrial pressure. In the present experiments the assumption was made that this is true for the dog also, and that the PA minus PAW pressure indicated the pressure difference across the lung vessels.

Output

The indicator-dilution method has the advantage that steady-state conditions are necessary only for the 5 to 15 seconds between injection of indicator and completion of the curve. In the direct Fick method, gas must be collected over several minutes, and the oxygen saturation of single arterial and venous blood samples may not be representative of those over the entire period of gas collection. In both groups of dogs, pulse rates, blood pressures and cardiac output reached plateaus within 1½ minutes of the start of each run.

Volume

Accurate measurement of the blood volume of a vascular compartment necessitates a densitometer and recording galvanometer with a
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rapid dynamic response and a sampling system with a small dead space and rapid flow rate. This is especially important during exercise. Subtraction of the MTT of the entire detecting system from that of the recorded curve at identical sampling rates gives the “true” MTT between injection and sampling sites.9 The blood volume measured was that of the lungs and the left heart chambers. Reasons for not attempting to measure the blood volume of the lungs alone have been presented elsewhere.10, 11

Changes With Exercise
Pulmonary Pressures and Flow

The cardiac index at rest, averaging 4.2 L. for the intact dogs and 4.5 L. for those with ligated left pulmonary arteries, was similar to values obtained for normal dogs by other workers.12-14 Several dogs were excited following manipulation of the catheters, so that some of the values obtained during standing cannot be regarded as basal. The cardiac index increased by 2½ to 3½ times during the most severe exercise, and the dogs with ligated left pulmonary arteries achieved as high levels of cardiac output as did the intact dogs (fig. 2). The difference between PA and PAW pressures in the intact dogs varied from 8.5 to 14 mm. Hg at rest. Since this increased only slightly through the entire range of activity, a continued fall in the calculated pulmonary vascular resistance occurred in all. This is of interest in view of conflicting data for pulmonary pressure-flow relations in man.15-19

The left pulmonary artery was ligated and divided in 4 dogs in order to increase the blood flow through a single lung. These dogs were studied soon after operation to minimize any complicating effects from the development of bronchopulmonary anastomoses. Exercise produced as marked an increase in cardiac output in them as in the intact animals. These dogs were also similar to the normals in respect to PA minus PAW pressures at rest, and, with one exception, to the change in PA minus PAW pressure and consequent decline of calculated pulmonary vascular resistance with increase of exertion. For example, in dog 10 the PA minus PAW pressure increased from 10 to 15 mm. Hg and the cardiac output increased from 4.3 to 10.6 L./min. between rest and running at 12 km./hr. Assuming that the vascular beds of the right and left lungs are comparable, the flow of 10.6 L./min. would be equivalent to a cardiac output of about 21 L./min. through the lungs of an intact dog. This may be compared with the situation that exists in some patients with uncomplicated atrial septal defect, in that the pulmonary blood flow may be as much as 5 times the normal resting level with little increase in the pressure difference between the pulmonary artery and the left atrium. In dog 9 the PA minus PAW pressure increased commensurately with the increase in cardiac output. Thus in only 1 of the 8 dogs was there an indication that the pulmonary vessels were approaching the limits of distensibility. Courmand and Lategola21 have suggested from studies on the lungs of man and the dog that when a critical level of flow is reached the pulmonary vessels behave as a system of rigid tubes. Our studies have not demonstrated this phenomenon in 4 intact dogs or in 3 of the dogs with ligated left pulmonary arteries. Thus the pulmonary vascular bed of the normal dog is capable of accommodating easily any flow likely to be presented to it, with only a modest increase in pressure difference across the pulmonary vessels.

Lung and Left-Heart Blood Volume

With the most severe exercise this was from 0 to 20 per cent greater than at rest. Since the calculation was dependent on accurate measurement of small time intervals it can be regarded as an approximation only. There is evidence that in the dog during exercise the left ventricular diameter during diastole is similar to, and during systole slightly smaller than, that at rest.22, 23 Thus, while it is likely that pulmonary blood volume increases during exercise, the increase is small; and our data do not support the view expressed by Sjöstrand24 that the lungs function as a large reservoir for blood during exercise in order to ensure a ready reserve of blood for the left atrium.
**Summary**

The effect of exercise on the pulmonary circulation was studied in a group of 6 intact dogs and in a second group of 4 subjected to ligation and division of the left pulmonary artery. Observations were made with the dogs standing and running on a horizontal treadmill up to the maximal speed they could maintain for periods of at least 2 minutes, usually 12 or 14 km./hr.

Continuous records were made of the difference in pressure between the main pulmonary artery (PA) and a pulmonary-artery wedge (PAW) position. Cardiac output was determined by the indicator-dilution method, with injection of indocyanine (cardiogreen) dye into the main pulmonary artery and continuous sampling from the root of the aorta. The mean transit time of indicator between the pulmonary and aortic valves was obtained from the dilution curves, a correction being made for the transit time through the sampling apparatus. From these measurements the blood volume of the lungs and left heart chambers was derived.

In the intact dogs, cardiac output increased approximately threefold from rest to severe exercise. There was an increase of only 12 per cent to 50 per cent in PA minus PAW pressure. Thus a continued fall occurred in pulmonary vascular resistance. The blood volume of the lungs and left heart chambers of 3 intact dogs was measured. In 2 it did not change through the range of activity, and in the third the increase with maximal exercise was 18 per cent.

The dogs with ligated left pulmonary artery also showed a threefold increase in output with severe exercise. Since the entire output passed through a single lung, the effect on the pulmonary vessels was comparable to that of a sixfold increase in output in a normal dog. Despite such large flows, in 3 of 4 dogs the difference between PA and PAW pressure rose only 37 per cent to 50 per cent. The volume of blood in the lungs and left heart was unchanged between rest and 8 km./hr., and at higher speeds showed a 0 per cent to about 20 per cent increase.

**Acknowledgment**

We wish to thank Dr. D. E. Donald of the Section of Surgical Research for performing the operation for ligation and division of the left pulmonary artery. We are indebted to Dr. A. D. Jose for helpful discussion of the theoretical requirements of the sampling system. Our thanks are due also to Miss Lucille Cronin, Mrs. Jean Frank, Mr. W. F. Sutterer, Mr. W. A. Mecker, and Mr. Julius Zarin for technical assistance.

**References**

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Flow, Pressure, and Volume Relationships in the Pulmonary Circulation During Exercise in Normal Dogs and Dogs with Divided Left Pulmonary Artery

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doi: 10.1161/01.RES.9.1.53

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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