# GAS EXCHANGE IN THE LUNG DEPRIVED OF PULMONARY ARTERIAL SUPPLY*

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Upon ligation of the left branch of the pulmonary artery in the dog, there is exposed to the gases in the alveoli of this side a capillary bed supplied solely by systemic arterial blood. In such a lung, blood from the bronchial arteries has been demonstrated to gain direct access to the capillaries of the alveoli through large pre-capillary anastomoses that develop with branches of the pulmonary arteries which remain patent despite the ligature at the proximal end.[7] As the collateral circulation expands, the bronchial vessels carry a flow enormously greater than the normal—equal in volume at the end of eighteen months to approximately one-third of the output of the right ventricle.[2] The burden of this flow falls solely upon the left side of the heart whose output exceeds that of the right by an amount equal to that of the collateral. The situation is analogous to that of an arterio-venous fistula—systemic artery to pulmonary vein.

Not only does this blood maintain the structural integrity of the parenchyma of the left lung, but when not fully saturated, it can also function in the absorption of oxygen. Thus a lung deprived of its pulmonary arterial supply may still possess respiratory function. The observations reported here consider some quantitative aspects of the exchange of gases between such a capillary bed and the alveoli. Two studies,[5, 12] each of a single patient, have recently appeared, but there has not been published, to our knowledge, a detailed experimental investigation.

The observations to be reported were made on dogs under sodium pentobarbital anesthesia under four conditions: (A) Both lungs supplied with room air; (B) as in A, but exchange across the carina at the tracheal bifurcation interrupted by means of a bronchospirometric cannula; (C) right lung supplied with room air, bronchospirometric cannula in place, and left lung re-breathing into a spirometer or rubber bag; (D), as in C, but right lung connected to a spirometer containing oxygen.

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## *Methods*

The animals were prepared by ligating the left pulmonary artery in each instance by a method previously described.[2] Subsequent procedures were carried out under sodium pentobarbital (35 mg/kg) anesthesia. Gases from the depths of the bronchial tree were obtained by intubation, according to a technique employed by Birath,[1] and before him by Loewy and Schrötter,[9] and by Krogh.[6] As in Birath's method, ureteral catheters (No. 6 or 8 French) were passed into the basal bronchi of each lung either under direct bronchoscopic observation or through the two halves of the tracheal divider. Gases were aspirated repeatedly, approximately 1 cc. at the end of each expiration, through the catheters into mercury-filled storage bulbs until adequate samples were collected for analysis.

The tracheal divider used for isolating the respiratory exchange of each lung is a VanAllen cannula modified for bronchospirometry.[2,13] This cannula was also used in the rebreathing experiments (conditions C and D), in which the left lung was connected to a recording spirometer or a rubber bag, as desired, while the right was in communication with room air or a supply or oxygen.

Oxygen tensions were determined by the method of Fasciolo and Chiodi,[4] employing a special type of tube which permits the rapid chilling and centrifugation of blood and subsequent harvesting of plasma without exposure to the atmosphere. It was necessary to effect rapid separation of the plasma to minimize the consumption of oxygen by the cells of the blood.

Analyses of the blood or plasma were done in the VanSlyke apparatus by standard methods, with the modifications for plasma oxygen introduced by Fasciolo and Chiodi.[4] Analyses of gases were by the Henderson-Haldane technique. In all of these procedures duplicate analyses were required to check within 0.1 vol. %.

## *Observations*

### 1. *Composition of gases in the basal bronchi.*

Determinations were made of the composition of end-expiratory gases drawn simultaneously from the deeper respiratory passages of the intact right lung and the left lung whose pulmonary artery had been ligated. Both lungs were in free communication with the outside air during this time. The samples obtained under free transcarinal exchange (condition A) are compared in Table 1 with those obtained with a tracheal divider in place (condition B). In considering the results of the analyses it must be remembered that since the animals were under sodium pentobarbital anesthesia deep enough for bronchospirometry, the arterial blood was unsaturated, averaging approximately 63% when both lungs were breathing air; in the conscious resting animals the arterial oxygen was invariably normal, and was 100% when the right lung was breathing oxygen even under the barbiturate. The reasons for the unsaturation in anesthesia with another barbiturate, sodium pentothal, have been discussed elsewhere.[10]

It is obvious from Table 1 that under both conditions the oxygen content of the basal bronchi in the intact lung is lower, and the $CO_2$ content higher, than in the left lung. When the $CO_2$ content in the left lung is low, the oxygen tends to be relatively high. Stated otherwise, the gas content of the left lung tends more to resemble room air than that of the right lung.

TABLE 1
COMPOSITION OF GASES IN BASAL BRONCHI

| | *Condition A* | | | | | | *Condition B* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Exp. #* | *Time (mo.)* | *$CO_2$ Left* | *$CO_2$ Right* | *$O_2$ Left* | *$O_2$ Right* | *Exp. #* | *Time (mo.)* | *$CO_2$ Left* | *$CO_2$ Right* | *$O_2$ Left* | *$O_2$ Right* |
| | | | | | | *Dog 52* | | | | | | |
| | 78 | ¼ | 3.1 | 5.8 | 18.1 | 14.9 | 78 | ¼ | 1.1 | 6.4 | 20.5 | 14.3 |
| | 86 | 1 | 4.1 | 6.9 | 16.9 | 10.8 | 84 | ¾ | 2.1 | 6.6 | 19.1 | 13.9 |
| | | | | | | | 89 | 1½ | 2.2 | 5.6 | 20.1 | 13.3 |
| | | | | | | | 143 | 5 | 3.2 | 5.0 | 19.2 | 11.6 |
| Mean | | | 3.6 | 6.4 | 17.5 | 12.9 | | | 2.2 | 6.1 | 19.2 | 13.3 |
| | | | | | | *Dog 11* | | | | | | |
| | 56 | 8¾ | 4.0 | 5.9 | 18.2 | 13.5 | 59 | 9 | 2.0 | 6.4 | 19.0 | 14.7 |
| | 65 | 9¾ | 6.3 | 7.2 | 15.0 | 11.9 | 67 | 10 | 5.1 | 6.8 | 16.8 | 12.2 |
| Mean | | | 5.2 | 6.6 | 16.4 | 12.7 | | | 3.6 | 6.6 | 17.9 | 13.5 |
| | | | | | | *Dog 9* | | | | | | |
| | 77 | 12¾ | 5.8 | 7.6 | 14.3 | 10.3 | 76 | 12½ | 4.4 | 5.9 | 17.7 | 12.1 |
| | 83 | 13¼ | 5.9 | 7.6 | 15.2 | 10.4 | 80 | 12¾ | 5.5 | 6.3 | 15.6 | 11.2 |
| | 85 | 13½ | 6.3 | 6.3 | 10.3 | 10.0 | 87 | 14 | 5.0 | 6.9 | 17.1 | 10.2 |
| | | | | | | | 90 | 14 | 6.2 | 6.8 | 12.9 | 10.0 |
| Mean | | | 6.0 | 7.2 | 13.3 | 10.2 | | | 5.2 | 6.5 | 15.8 | 10.9 |

**NOTE: Time is given in months after ligation of the pulmonary artery. Composition of gases is given in volumes %.**

This contrast with the gaseous contents of the right basal bronchi is even more striking when the tracheal divider is in place than when transcarinal exchange is free. Under the latter condition (A), the left lung takes in at each inspiration a relatively large portion of the tracheal and pharyngeal "dead space air," for the reason that the minute volume of gas exchange of this lung is relatively lower than that of the right. In a series of determinations on the three animals listed in Table 1 the tidal volume of the left lung ranged from 28 to 35% of the total exchange. This "dead space air" at the end of expiration is more representative of the contents of the alveoli of the right lung.

In all of the samples from the side of ligation the $CO_2$ tends to approximate much more closely than the $O_2$ the respective levels from the normal right side. Roh and his co-workers point out that the probable mechanism involves not only the twenty to thirty times greater diffusibility of $CO_2$ in comparison with $O_2$, but also the high dissociation gradient for the carbonate.[12]

The sooner after ligation of the pulmonary artery the samples from the left side are obtained, the closer the similarity to room air, especially under

TABLE 2

$pO_2$ OF GASES IN BASAL BRONCHI AND SYSTEMIC ARTERIAL BLOOD

| | | *Time* | *$pO_2$, mm. Hg.* | | |
|---|---|---|---|---|---|
| *Dog* | *Exp.* | *(mo.)* | *Right lung* | *Left lung* | *Blood* |
| 52 | 86* | 1 | 76 | 119 | 41 |
| 52 | 89† | 1½ | 95 | 144 | 30 |
| 9 | 87* | 14 | 74 | 123 | 22 |

* Transcarinal exchange unimpeded (condition A).
† Through bronchospirometric cannula (condition B).

condition B (tracheal divider in place). Thus, in the earlier weeks after ligation, the quantity of $CO_2$ leaving and the oxygen entering the relatively small volume of bronchial arterial blood then perfusing the capillaries of the left lung is insignificant in comparison with the volume of gases exchanged at each breath. Evidence for this is found in the fact that the $pO_2$ of the systemic arterial blood is lower than that of the contents of the left basal bronchi. The arterial $pO_2$ is lower, by some 35 to 65 mm. Hg, than that even of the right lung (Table 2). It is the latter datum which suggests that systemic venous blood is traversing poorly ventilated alveoli and is being contributed relatively unchanged to the general stream entering the left auricle. Later (dogs 9 and 11), the gases from the two sides tend to be more closely similar in composition.

2. *The lung as a tonometer.*

When the lung with a capillary bed supplied solely by systemic arterial blood was placed into communication with a spirometer or bag containing air, its function as a tonometer could be studied. Observations were made under these conditions: (a) when the relatively normal right lung was open to air (condition C), and (b) when this lung was supplied with oxygen (condition D).

*A. Condition C:* While the right lung was breathing freely from the room, the left was connected through its cannula either with a rubber bag or with a spirometer containing respectively 750 cc. and approximately 2000 cc. of air. The sequence of events during the earlier phases of such an experiment can be demonstrated graphically by projecting selected points from the spirometric tracing as ordinates on a graph and by indicating the composition of the gases at intervals. This has been done in Figures 1 and 2 for the data of Experiment 80 which may be used as an example. It is apparent that there is at first an increase in the total volume of the gaseous contents of the spirometer, accounted for chiefly by the excess of $CO_2$ and $N_2$ transferred into the spirometer over the oxygen absorbed during the same interval. After the first thirty minutes the concentration of $N_2$ and $CO_2$ remains relatively constant, while $O_2$ absorption continues with the result that the contents of the spirometer decrease in volume below that at the start of the experiment. In this particular instance, at the end of an hour, 195 cc. of $O_2$ has been absorbed from the spirometer while 29 cc. of $CO_2$ and 31 cc. of $N_2$ were transferred into it; this resulted in a decrease of 135 cc. in the total volume of the contents of the spirometer.

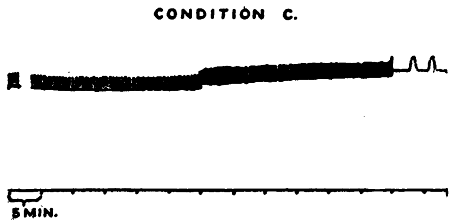


FIG. 1. Photograph of tracing of spirometer connected to the operated left lung while the right lung is breathing air. A fall in the curve indicates a rise in the volume of gases contained in the spirometer, and vice versa. The factors responsible for these changes are indicated in Figure 2. The sudden rise in the level of the tracing near the mid-portion of the curve results from withdrawal of a sample for analysis. At the right tracings during two respiratory cycles are shown with the kymograph at high speed.

The composition of the gases in the spirometer is recorded in Table 3. In the present experiment the percentage of oxygen at the end of an hour appears to be low in comparison with that of normal "alveolar air," but actually its tension is 82 mm. Hg, much higher than that of the arterial blood in any of the animals studied under similar circumstances of anesthesia (Table 2). Obviously equilibrium has not been attained at the end of one hour. Inspection of the data shows that this must also be true for the other experiments recorded in Table 3.

*B. Condition D:* When the right lung is given $O_2$ rather than air to respire under similar circumstances, $O_2$ enters the left spirometer, more rapidly during the first thirty minutes as shown in Figures 3 and 4 constructed from the data of Experiment 80. $CO_2$ values are not indicated since this gas has been absorbed from the system by soda-lime scrubbers in the expiratory line of each spirometer. Even at the end of two hours in this experiment, the process of oxygen transfer has not ceased. It will further be noted from Figure 4 that $N_2$ is being absorbed from the left spirometer presumably to enter the right spirometer which contains nearly pure $O_2$ at the start. The rate of $O_2$ transfer into the left spirometer exceeds that of $N_2$ absorption, as a consequence of which the total volume of the gases is increased. At the end of two hours, the $O_2$ may reach a concentration of 39.8% and a tension of 286 mm. Hg (Table 4, Experiment 80, condition D). Figure 4 shows that during this interval the spirometer gained 445 cc. of oxygen (at ambient temperature and pressure), while losing 298 cc. of $N_2$; thus, the total gain in volume was 147 cc. The results of the various determinations are comparable in Dogs #9 and #11 both of which were tested more than eight months after ligation of the pulmonary artery. During

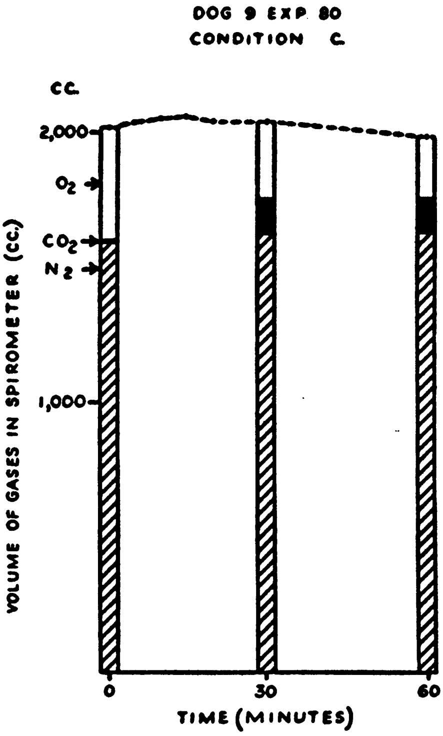


FIG. 2. Points from the tracing shown in Figure 1 have been used to indicate the total volume; in addition, the composition of gas samples obtained at three points is indicated. It is obvious that the early rise in total volume results from the excess of $CO_2$ and $N_2$ transferred into the spirometer over the $O_2$ absorbed, a condition that is reversed later. Numerical data are given in Table 3.

the first six weeks (Dog #52) the rise of $O_2$ appears to be much slower, but more quantitative data are needed to substantiate this point. The difference does not appear to be associated with the mean tidal volume as this is actually greater in Dog #52 than in either of the others (94 cc. for Dog #52, 93 cc. for Dog #11, and 79 cc. for Dog #9).

A comparison of the oxygen tensions in the arterial blood and in the contents of the left spirometer at the end of two hours is available for Dog #52, Experiments 86 and 89, one and one and one-half months after ligation of the left pulmonary artery respectively. In Experiment 86 the

TABLE 3

LUNG AS A TONOMETER: CONDITION C

| *Dog* | *Exp.* | *Time (mos.)* | *Interval (min.)* | *$CO_2$ vol. %* | *$O_2$ vol. %* | *Container* | *Vol. at start, cc.* |
|---|---|---|---|---|---|---|---|
| | 56 | 8¾ | 60 | 6.3 | 11.6 | Bag | 750 |
| | | | 75 | 6.9 | 11.7 | | |
| 11 | 59 | 9 | 60 | 5.9 | 11.0 | Bag | 750 |
| | | | 75 | 6.8 | 10.7 | | |
| | 62 | 9¼ | 60 | 7.7 | 10.6 | Bag | 750 |
| | | | 75 | 7.3 | 10.2 | | |
| 9 | 80 | 12¾ | 30 | 6.4 | 13.9 | Spirometer | 2017 |
| | | | 60 | 6.5 | 11.4 | | |

arterial oxygen tension was 391, while the $pO_2$ in the left lung was 171, and in Experiment 89, the respective $pO_2$ values were 405 and 189. In view of the low final percentages of oxygen reached at the end of two hours (Table 4), these large gradients are not surprising. Even at the end of 12¾ months in Dog #9, however, the oxygen tension in the left lung was only 286 mm. Hg when the oxygen percentage was 39.7, the highest recorded at the end of two hours in any of the present observations. Although data on the arterial $pO_2$ are not available in this instance, it is probable that a gradient of at least 100 mm. Hg existed.

### *Discussion*

Common to all of these observations are the large differences between the alveolar and arterial $pO_2$ values, much greater than those which exist normally, at least in man.[3,8] In the case of the "normal" right lung these can be accounted for by the sodium pentobarbital anesthesia with the consequent poor ventilation of many alveoli which results in failure of oxygenation of considerable quantities of venous blood. Desaturation of the systemic arterial blood under another barbiturate has been demonstrated by Penrod and Hegnauer.[10]

More difficult to explain is the disequilibrium on the left side, where the $pO_2$ of rebreathed air is higher at the end of an hour than the arterial $pO_2$ when the normal lung is breathing air, and lower than arterial $pO_2$ when the right lung is breathing oxygen. These differences cannot be accounted for on the basis of shunting of blood. Among the factors that may be concerned, however, are (i) the relatively small flow through the lung whose pulmonary artery has been ligated; (ii) inadequate turnover of gases in the left spirometer or rebreathing bag; (iii) decreased permeability of the alveolar membranes[8,11] after ligation of the pulmonary artery.

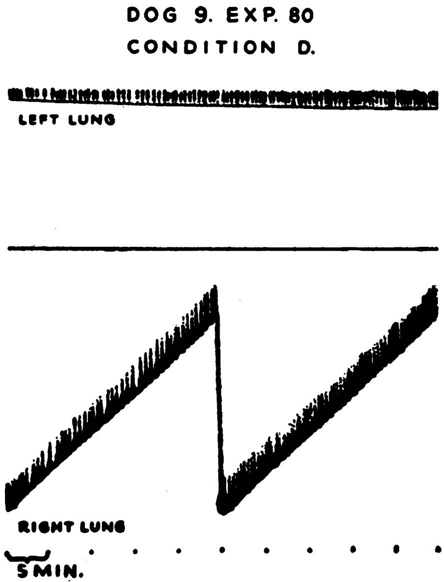


FIG. 3. Photograph of bronchospirometric tracing during the first fifty minutes while the left lung is rebreathing from the spirometer and the right is respiring oxygen. The fall in the upper tracing indicates a rise in the total volume. Alignment of portions of this curve with a straightedge shows that this increase is more rapid at first.

Concerning the first factor, data are available from previous observations on the bronchial arterial flow made on these animals under sodium pentobarbital anesthesia. During the first six weeks the expected flow through the alveoli of the left lung is usually less than 250 cc/min/$M^2$.[2] Thus the slow circulation is probably of importance so soon after ligation. After the eighth month, however, flows of more than 500 cc/min/$M^2$ are to be expected.

Concerning the second factor, the tidal volumes of the left lung of the three dogs, as averaged in each instance from a large series of observations

TABLE 4

LUNG AS A TONOMETER: CONDITION D

| Dog | Exp. | Time (mos.) | Interval (min.) | $CO_2$ vol. % | $O_2$ vol. % | Container | Vol. at start, cc. |
|---|---|---|---|---|---|---|---|
| 52 | 86 | 1 | 30 | 0.0 | 21.9 | Spirometer | 2000 |
| | | | 126 | | 24.2 | | |
| | 89 | 1½ | 38 | | 23.0 | Spirometer | 2000 |
| | | | 127 | | 26.6 | | |
| 11 | 59 | 9 | 60 | 8.5 | 24.4 | Bag | 750 |
| | | | 75 | 9.7 | 26.1 | | |
| | 62 | 9¼ | 60 | 11.3 | 33.6 | Bag | 750 |
| | | | 75 | 10.9 | 36.1 | | |
| | 64 | 9½ | 15 | 8.3 | 24.1 | Bag | 750 |
| | | | 30 | 8.5 | 26.8 | | |
| | | | 120 | 7.5 | 36.0 | | |
| | | | 180 | 7.9 | 36.4 | | |
| | 65 | 9¾ | 15 | 5.7 | 23.1 | Bag | 750 |
| | | | 30 | 7.1 | 25.8 | | |
| | | | 60 | 7.2 | 31.2 | | |
| | | | 120 | 6.9 | 37.9 | | |
| | 68 | 10 | 30 | 7.1 | 23.4 | Spirometer | 2000 |
| | | | 60 | 9.0 | 26.1 | | |
| | | | 120 | 11.3 | 29.2 | | |
| | 69 | 10¼ | 30 | 9.4 | 22.4 | Spirometer | 2000 |
| | | | 120 | 9.9 | 27.2 | | |
| 9 | 75 | 12¼ | 30 | 0.0 | 24.2 | Spirometer | 2000 |
| | | | 60 | 0.0 | 26.6 | | |
| | | | 90 | 0.0 | 28.5 | | |
| | 76 | 12½ | 30 | 0.0 | 35.1 | Spirometer | 2000 |
| | | | 60 | 0.0 | 37.4 | | |
| | 80 | 12¾ | 30 | .07 | 33.8 | Spirometer | 2000 |
| | | | 60 | .04 | 36.6 | | |
| | | | 120 | .04 | 39.7 | | |
| | 85 | 13½ | 30 | 0.1 | 30.3 | Spirometer | 2000 |
| | | | 60 | 0.1 | 33.0 | | |
| | | | 120 | 0.1 | 37.2 | | |
| | 87 | 14 | 30 | 0.02 | 25.6 | Spirometer | 2000 |
| | | | 111 | 0.00 | 33.1 | | |
| | 90 | 14 | 152 | 0.0 | 33.9 | Spirometer | 2000 |

in many experiments, range from 76.6 to 82.4 cc. Thus, with a respiratory rate of 10, a volume corresponding to the entire contents of the spirometer should have been exchanged at least twenty times in an hour, and in the case of the rubber bag at least fifty times.

These considerations suggest that the alveoli of the lung with ligated pulmonary artery may not be as permeable to the passage of oxygen as those of the normal lung. No obvious histological differences have been observed, however.

*Summary and conclusions*

Under sodium pentobarbital anesthesia, the gases in the basal bronchi of a lung whose main pulmonary artery has been ligated as long as fifty weeks previously have a higher oxygen and lower $CO_2$ content than those in an intact lung. The difference is less striking the greater the interval after ligation; at all times the $CO_2$ shows proportionately less deviation than the $O_2$.

There is evidence from bronchial intubation experiments of considerable transcarinal exchange.

With a bronchospirometric cannula in place and the lung of the ligated side rebreathing, gaseous equilibrium with the systemic arterial blood in the latter is not attained on the operated side, even at the end of two hours, since there is evidence that oxygen transfer has not ceased.

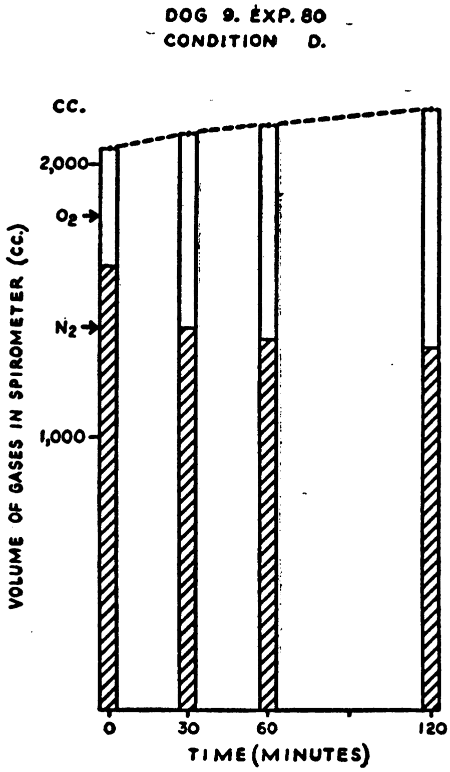


FIG. 4. Volumetric data from the upper tracing of Figure 3 are indicated here in relation to the composition of the gases. Percentage figures are given in Table 4. The rates of transfer of both $O_2$ and $N_2$, especially of the latter, are more rapid at first.

These observations suggest, with due allowance for the effect of barbiturate anesthesia and decreased tidal volume of the operated lung, that the permeability of the alveolar membranes to gases may be impaired after ligation of the pulmonary artery.

## References


1 Birath, G.: Simultaneous samples of alveolar air from each lung and parts thereof. Am. Rev. Tuberc., 1947, *55,* 444.

2 Bloomer, W. E., Harrison, W., Lindskog, G. E., and Liebow, A. A.: Respiratory function and blood flow in the bronchial artery after ligation of the pulmonary artery. Am. J. Physiol., 1949, *157,* 317.

3 Comroe, J. H. and Dripps, R. D.: The oxygen tension of arterial blood and alveolar air in normal human subjects. Am. J. Physiol., 1944, *142,* 700.

4 Fasciolo, J. C. and Chiodi, H.: Arterial oxygen pressure during pure $O_2$ breathing. Am. J. Physiol., 1946, *147,* 54.

5 Janton, O. H., Redondo, H. P., and Scott, J. C.: Pulmonary gas exchange following ligation of a pulmonary artery in man. Fed. Proc., Balt., 1948, *7,* 61.

6 Krogh, A. and Krogh M.: On the tension of gases in the arterial blood. Skand. Arch. Physiol., Berl., 1910, *23,* 179.

7 Liebow, A. A., Hales, M. R., Bloomer, W. E., Harrison, W., and Lindskog, G. E.: Studies on the lung after ligation of the pulmonary artery. II. Anatomical changes. Am. J. Path. (In press.)

8 Lilienthal, J. L., Jr., Riley, R. L., Proemmel, D. D., and Franke, R. E.: An experimental analysis in man of the oxygen pressure gradient from alveolar air to arterial blood during rest and exercise at sea level and at altitude. Am. J. Physiol., 1946, *147,* 199.

9 Loewy, A. and Schrötter, H.: Untersuchungen über die Blutcirculation beim Menschen. Zschr. exp. Path., 1905, *1,* 197.

10 Penrod, K. E. and Hegnauer, A. H.: Effect of pentothal sodium on blood gas transport. Am. J. Physiol., 1948, *153,* 81.

11 Riley, R. L., Lilienthal, Jr., J. L., Proemmel, D. D., and Franke, R. E.: On the determination of the physiologically effective pressures of oxygen and carbon dioxide in alveolar air. Am. J. Physiol., 1946, *147,* 191.

12 Roh, C. E., Greene, D. G., Himmelstein, A., and Humphreys, G. H.: Cardiopulmonary function studies on a patient with ligation of the left pulmonary artery. Am. J. Med., 1949, *6,* 795.

13 VanAllen, C. M.: A dilatable bronchial cannula. Yale J. Biol., 1930, *2,* 295.