JOURNAL OF APPLIED PHYSIOLOGY
Vol. 28, No. 5, May 1970. *Printed in U.S.A.*

Effects of transpulmonary and vascular pressures on pulmonary blood volume in isolated lung

DAVID Y. ROSENZWEIG, J. M. B. HUGHES, AND JON B. GLAZIER
Respiratory Research Group, Royal Postgraduate Medical School, London, W 12, England

ROSENZWEIG, DAVID Y., J. M. B. HUGHES, AND JON B. GLAZIER. *Effects of transpulmonary and vascular pressures on pulmonary blood volume in isolated lung.* J. Appl. Physiol. 28(5): 553–560. 1970.—By repeatedly weighing the isolated perfused greyhound lung, we studied changes in pulmonary blood volume resulting from variations in vascular and transpulmonary pressures. Lung weight increased linearly when arterial pressure was raised over the 0–25 cm H_2O range, but the rate of change was greatest at moderate inflation corresponding to 5–10 cm H_2O transpulmonary pressure (Ptp). The response to changing venous pressure was similar. At constant vascular pressures, changes in Ptp produced different weight changes according to the relation between vascular and alveolar pressure. When vascular pressures exceeded alveolar pressure, the greatest weight change occurred at low Ptp, but when vascular pressures were less than alveolar pressure, greater weight gain occurred at high Ptp. We attempted to separate these changes on inflation into arterial or venous components by occluding either of their cannulas in order to prevent vascular filling, but found that the occluded side communicated with the opposite side via extra-alveolar vessels even when alveolar pressure exceeded vascular pressure by 10 cm H_2O or more. India ink injections showed that a site of these arteriovenous communications may be vessels at alveolar septal junctions.

vascular compliance; extra-alveolar vessles; corner vessels

RECENT WORK has emphasized that the mechanical properties of pulmonary blood vessels are important in determining the vascular resistance and distribution of blood flow in the lung. For example, gravity (3,29,30) and lung volume (2,14) both markedly affect the distribution of flow in normal subjects and isolated lungs. Although many studies have emphasized the particular roles of arteries, capillaries, and veins (6,7,9,11,18,32), others have shown that the pulmonary vasculature consists essentially of two compartments whose volumes change oppositely as the lung is inflated (13,22,24,27). This concept of alveolar and extra-alveolar vessels (17) is a functional one and no precise anatomic sites have been proposed for where the two compartments join. There is evidence that the pressure surrounding extra-alveolar vessels is less than that around alveolar ones (22), but the precise value of this perivascular pressure and its relation to transpulmonary pressure (Ptp) is uncertain. These and other problems such as whether extra-alveolar vessels extend to capillaries under some circumstances such as high distending transpulmonary pressures, and whether measurements of vascular volumes made under static conditions are comparable to those made during blood flow have prompted this study.

We have devised a method for repeatedly weighing the isolated perfused lung to measure changes in lung weight which occur rapidly and reversibly in response to altered vascular or transpulmonary pressure and presumably reflect intravascular volume changes. Slower irreversible weight changes indicating extravascular edema formation can also be measured with this method, but this paper deals exclusively with intravascular volumes.

We have used this method to examine several aspects of vascular mechanics. Some of these, such as compliance, have been studied by other means, but several others are uniquely suitable for this technique. First, previous measurements of pulmonary blood volume have been made either under static, no-flow conditions or when blood flow is established, but to what extent these two states are comparable is not known. Since the lung weight can be determined equally as well during blood flow as in its absence, these two conditions can be directly compared. Second, we have examined vascular volume patterns during inflation of the lung with negative pleural pressure (vascular pressure constant in relation to alveolar pressure) at several vascular pressures in order to measure extra-alveolar vessel volumes and, indirectly, alveolar vessel volumes. Finally, we have found that at high transpulmonary pressures arteriovenous communications exist even when the alveolar vessels are collapsed. This effect has been examined further by selectively filling these communicating vessels with India ink, and we have found that they may be the "corner" vessels at alveolar septal junctions.

METHODS

The left lungs from 24 greyhounds were studied in the following manner: after anesthesia with pentobarbital, heparin, 20 mg/kg, was given intravenously and the dog killed by exsanguination. The left lung was removed, and cannulas were placed in the bronchus, pulmonary artery, and left atrial cuff. The preparation was placed horizontally in a Perspex box and the perfusion and ventilation circuits attached. The greyhound lung which is long and flat has the advantage when placed horizontally, of being a rather large lung in terms of air or blood volume, but one of minimal height. The details of this apparatus have been described previously (30) and will only be summarized here.

The lung was inflated by negative pleural pressure and perfused through the arterial cannula with a roller pump while venous outflow went into a reservoir. An anesthetized mongrel dog completed the perfusion circuit, accepting the blood in the venous reservoir and priming the pump on the arterial side. Circulation through this dog served to prolong the integrity of the lung preparation. The principal modification was the positioning of the box on a balance (Gallenkamp model 7, rotating weight balance) and ensuring that all connections were freely flexible by using segments of Penrose drain or soft gum-rubber tubing so that the balance would swing freely. In addition the interior of the box was coated with liquid soap and a drain was placed in the bottom of the box in order to prevent any accumulation of blood, condensation, or other fluid in the box which would otherwise produce an artifactual weight gain during the experiment. Figure 1 shows a sketch of the box and balance.

Arterial and venous pressures (Pa, Pv) were measured with saline manometers or with an electronic pressure transducer. The reference zero for these pressures was the bottom of the lung. Box or pleural pressure was measured by a water manometer. Alveolar pressure (PA) was assumed to be atmospheric under static conditions. Blood flow ($\dot{Q}$) was measured by collecting timed samples of venous blood in a graduated cylinder. Blood flow, venous pressure, and box pressure could be independently varied and arterial pressure could be varied by altering the output of the blood flow pump. The effect of changes of each of these variables on lung weight (WL) was examined.

Although each preparation gained weight irreversibly over the course of the day, this gain was nearly always small (<20 g over 2–3 hr). The procedures described below, however, involved large weight changes (40–70 g) which were reversible within 1 min of the termination of the maneuver, and thus presumably reflected changes of intravascular blood volume rather than extravascular accumulation of edema or other fluid.

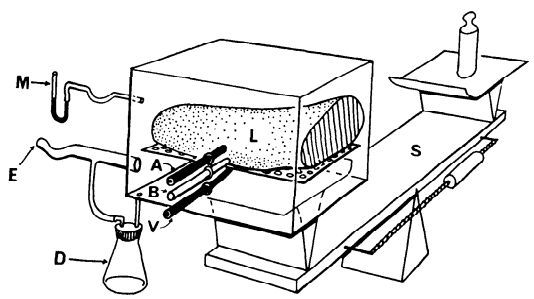

FIG. 1. Sketch of box-balance apparatus. Abbreviations: A, B, V, cannulas for pulmonary artery, bronchus, and left atrial cuff; D, drain tube; E, air extractor line; L, lung; M, water manometer; S, balance.

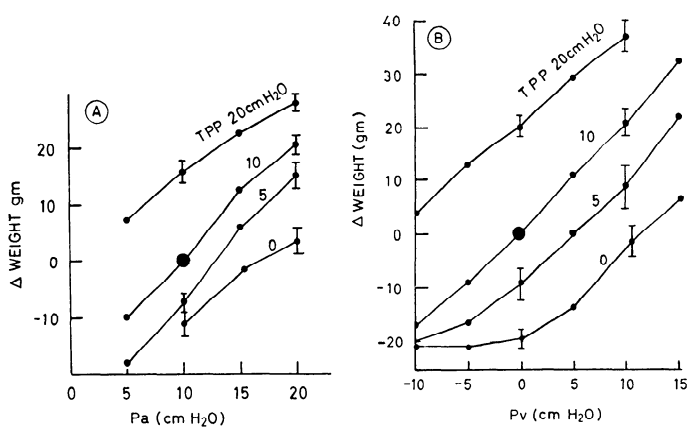

FIG. 2. *A:* weight/arterial pressure relationship at several different TPP (transpulmonary pressure) (eight preparations, means ± SD at selected points). A standard reference point at TPP: 10, Pa: 10 cm H_2O is used for purposes of comparison. *B:* same as *A* for venous pressure. Reference point of TPP: 10, Pv: 0 cm H_2O used.

PROCEDURES AND RESULTS

Several procedures were carried out on each lung preparation. In order to avoid confusion and repetition, each procedure and its result will be considered consecutively.

Effects of changing vascular pressure at constant transpulmonary pressure. If Pv is set sufficiently low (−10 cm H_2O), arterial pressure (and blood flow) could be manipulated independently, and stepwise changes from 0 to 25 cm H_2O were examined. Also with Pa sufficiently high (+25 cm H_2O), venous pressure was varied from −15 to +25 cm H_2O. Most of these measurements were made at Ptp of 10 cm H_2O inflation, but additional measurements were made in several lungs at Ptp of 0, 5, and 20 cm H_2O of inflation. A standard volume history consisting of inflation to 24 cm H_2O, followed by deflation to 0, then reinflation to the desired level was done in each case. Finally in three preparations blood flow was reversed—perfused from vein to artery—and the entire sequence repeated. The results are summarized in Fig. 2*A* which shows that the arterial pressure-lung weight relationship are nearly linear over a wide range of transpulmonary pressures. The venous pressure-lung weight results in Fig. 2*B* show a similar linear plot except at the lower distending pressures (Ptp 5 and 0 cm H_2O) and when the venous pressure is low (0 to −10 cm saline); under these conditions the veins would tend to be empty of blood and cause the slope to flatten. The slopes are greatest at moderate lung inflation and somewhat less at Ptp of 0 and 20 cm H_2O. The maximum slopes are nearly the same for ΔWL/ΔPa and ΔWL/ΔPv, being 2.1 and 2.0 g/cm H_2O, respectively. On subsequent stepwise lowering of pressure no hysteresis was observed, the weight/pressure points being nearly exactly the same. In the reverse flow procedures the ΔWL/ΔP was unchanged from that in forward flow at similar vascular pressures.

Effects of changing transpulmonary pressure. At constant vascular pressures the lung was inflated by increasing Ptp in steps from 0 to 30 cm H_2O, then deflated in steps. The relationship of WL to Ptp was examined at several vascular pressures, and inflation volume and blood flow were also measured simultaneously. In addition to a series at various pressures and flows where Pa > Pv, another series was performed under no-flow conditions where Pa = Pv. Figure 3 illustrates a typical series from one preparation. Figure 3*A* shows a family of curves representing the WL/Ptp relationship on inflation and subsequent deflation at various vascular pressures under blood flow conditions. Figure 3*B* shows the same relationship under no-flow conditions, while Fig. 3*C* shows the same procedure (*B*) but relating weight to lung volume. Several points are noteworthy.

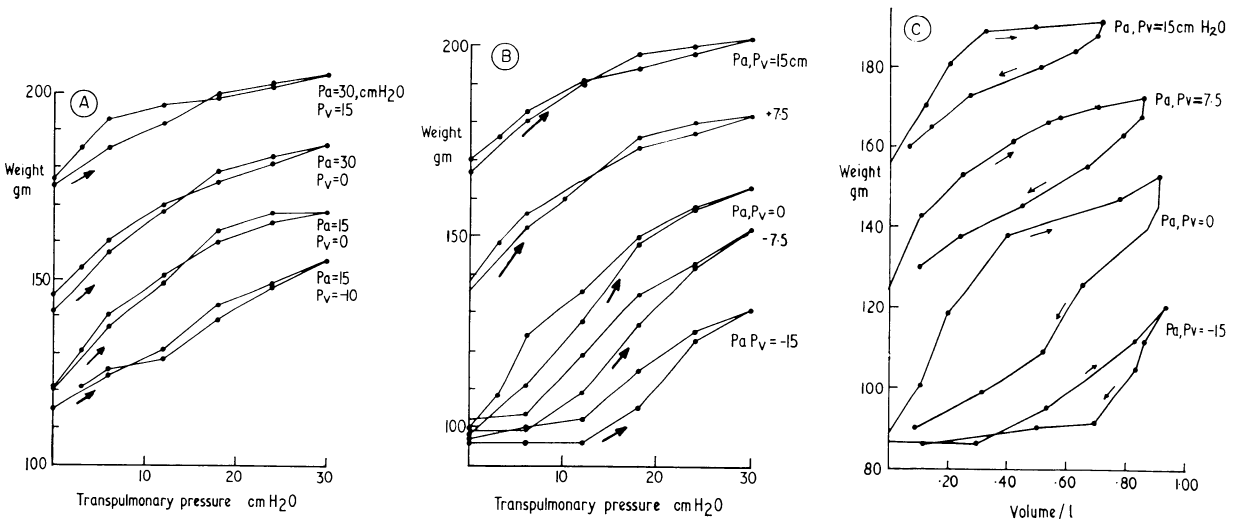

FIG. 3. *A:* lung weight related to transpulmonary pressure at several constant vascular pressures during blood flow (one preparation). Inflation proceeds on lower limb, but little hysteresis is seen on deflation. *B:* weight related to transpulmonary pressure during static or no-flow conditions at several vascular pressures (same preparation). *C:* same condition as *B*, but weight vs. lung volume is shown.

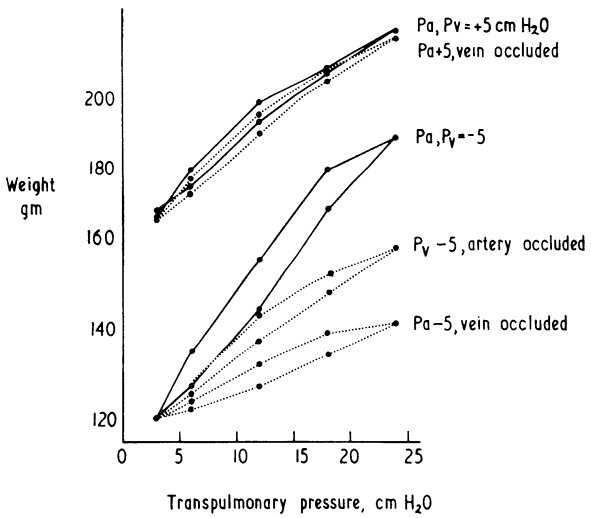

FIG. 4. Comparison of weight changes occurring during lung inflation with similar changes after occlusion of either arterial or venous cannula. Two sets of conditions; one where vascular pressures are set equal but below bottom of lung, other equal and above (one preparation).

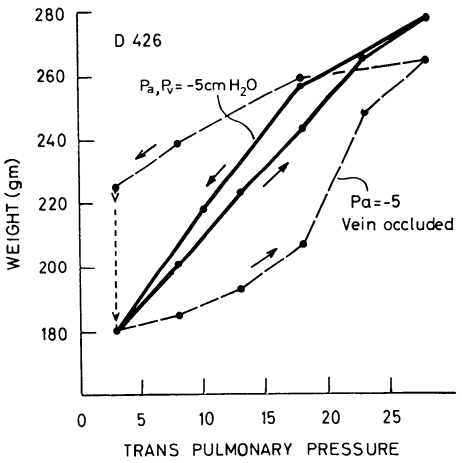

FIG. 5. Effect of venous occlusion. Different preparation but same maneuver as previous figure. Pressures set below bottom of lung. At higher levels of inflation weight approaches that in unoccluded state and on deflation much of this weight gain remains even when deflation is completed, but original weight reappears when occlusion is removed (one preparation).

First, as the lung is inflated, its weight always increases, the only exception being when both vascular and transpulmonary pressures are low (*B*), then it remains the same. Similarly on deflation the weight always decreases. Second, when inflation and deflation are compared, WL follows Ptp much more closely (*A* and *B*) than it does lung volume (*C*), suggesting that Ptp is the principal determinant of this weight change. Third, there is a progressive deformation of these curves from concave up through linear to concave down as vascular pressures are progressively increased (*A* and *B*). A closely related point is that overall weight change is greatest at vascular pressures near zero and is somewhat less when these are either higher or lower (*B*). Finally, the WL/Ptp curves under blood flow conditions (*A*) are somewhat similar in shape to those under no-flow conditions (*B*), but in general the slopes and total weight change at flow are somewhat less at comparable pressures.

As a reasonable explanation for the last point we considered that the blood flow curves represented a mean value between two no-flow curves. For example, $\Delta W_L/\Delta Ptp$ (at Pa = +15, Pv = 0) = ½ [$\Delta W_L/\Delta Ptp$ (at Pa = Pv = 15) + $\Delta W_L/\Delta Ptp$ (at Pa = Pv = 0)]. Indeed a reasonably close relationship of this type appears if the data is averaged in this way, suggesting that flow conditions are identical to no-flow conditions if a correction for the different vascular pressures is made. For example, if the topmost and third curve of Fig. 3*B* are averaged, its shape is nearly superimposable on the third curve of Fig. 3*A*. However, instead of presuming that the arterial and venous contributions to this weight change were equal as in the equation above, we attempted to separate these two components by the following procedure.

Effects of occlusion of either arterial or venous cannula. If vascular pressures are equal and set below alveolar pressure, then either the arterial or venous cannula occluded, any change in weight which occurs as the lung is inflated should be accounted for by expansion of the opposite unoccluded venous or arterial tree, since the occluded side maintains constant volume, being sealed on the distal side by pulmonary capillaries (alveolar vessels) which remain collapsed. Obviously if vascular pressures are initially above alveolar pressures the alveolar vessels will remain open and the weight change with occlusion will be identical to that without occlusion. Indeed, in the first procedure of this sort, this is exactly what happened (Fig. 4). With low pressure and occlusion, arteries accounted for rather less weight change than veins and the sum of the changes was that before occlusion. At high vascular pressure occlusion resulted in no change from the original curve. However, a different, unexpected result occurred in the next preparation and in six of eight subsequent ones. Figure 5 shows a typical example of this latter result: as lung inflation proceeds at Ptp between 13 and 18 cm H_2O the weight does not quickly stabilize but gradually over 30–60 sec approaches the weight found in the unoccluded procedure and, on further inflation, this type of response continues. On deflation this weight gain is only partially reversible, but if the occlusion is removed at end deflation the original weight is quickly resumed. This behavior suggests that certain arteriovenous connections are opened as inflation proceeds, blood is transferred to the no longer sealed opposite vascular tree, and this blood is trapped there on subsequent deflation. In order to explore this further, pressure was recorded from the occluded side using an electrical pressure transducer. Figure 6 shows such a pressure tracing as the lung is inflated by steps. As inflation proceeds the pressure becomes more negative, paralleling or very slightly lower than pleural pressure, but at 18 cm H_2O Ptp this pressure is no longer stable and rises toward the original value (where pressure on the unoccluded side remains). This equilibration resembles an exponential decay function. On further inflation the pressure change is less stable and rises more rapidly.

This procedure was repeated at four vascular pressures in 5-cm H_2O intervals between -10 and $+5$ cm H_2O. At pressures higher than -5 cm H_2O, instability occurred at lower inflation pressures, but a point of instability was found at Ptp between 20 and 25 cm H_2O, even when vascular pressure was -10 cm H_2O.

Finally, we have attempted to identify the site of these arteriovenous connections by repeating the venous occlusion procedure after injecting 10 ml of India ink into the arterial cannula. Vascular pressures are again kept low (-10 cm H_2O) to avoid filling alveolar vessels with ink. After deflation and removal of the occlusion, ink was visible draining from the venous side. Following this procedure the lung color was a mottled grey, certain areas showing no ink present, but sections taken from areas of average ink staining showed a characteristic appearance (Fig. 7). Figure 7*A*, a 25-μ section, shows a web of ink filling but very little ink in the alveolar septal wall faces. This web can be appreciated to be at septal junctions on serial focusing through the original section. Figure 7*B* is a thin section (6 μ) showing the pattern of filling when alveolar walls are seen on end only. Again most of the ink is seen at junctions; Fig. 7*C* and *D* are higher magnifications of the 6-μ sections. The size range of these filled vessels was 10–20 μ.

Many septal junctions were, however, free of ink. It is possible that some of these were without vessels in this locus, since no red cells were present there either, but others showed red cells present without ink. Other areas as large as subsegments were grossly and microscopically ink free, and these areas as well as the ink-stained areas were present throughout the entire vertical thickness of the lung. We considered that inadequate mixing could account for this

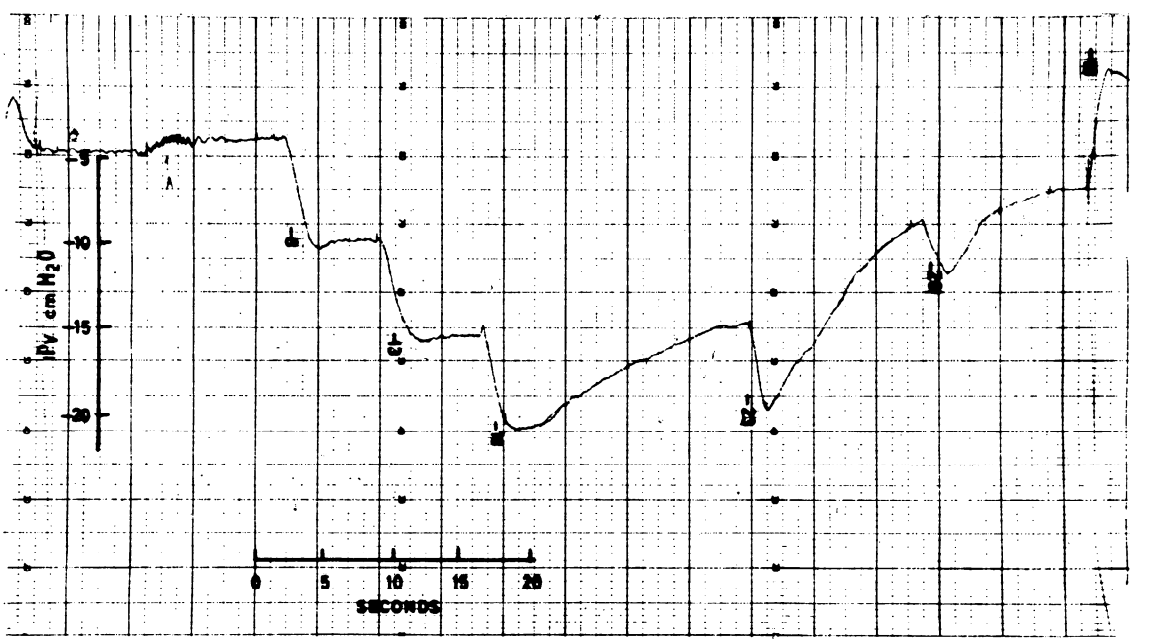

FIG. 6. Continuous recording of pressure within occluded vein. Same procedure as in Fig. 5. Figures on tracing are transpulmonary pressure.

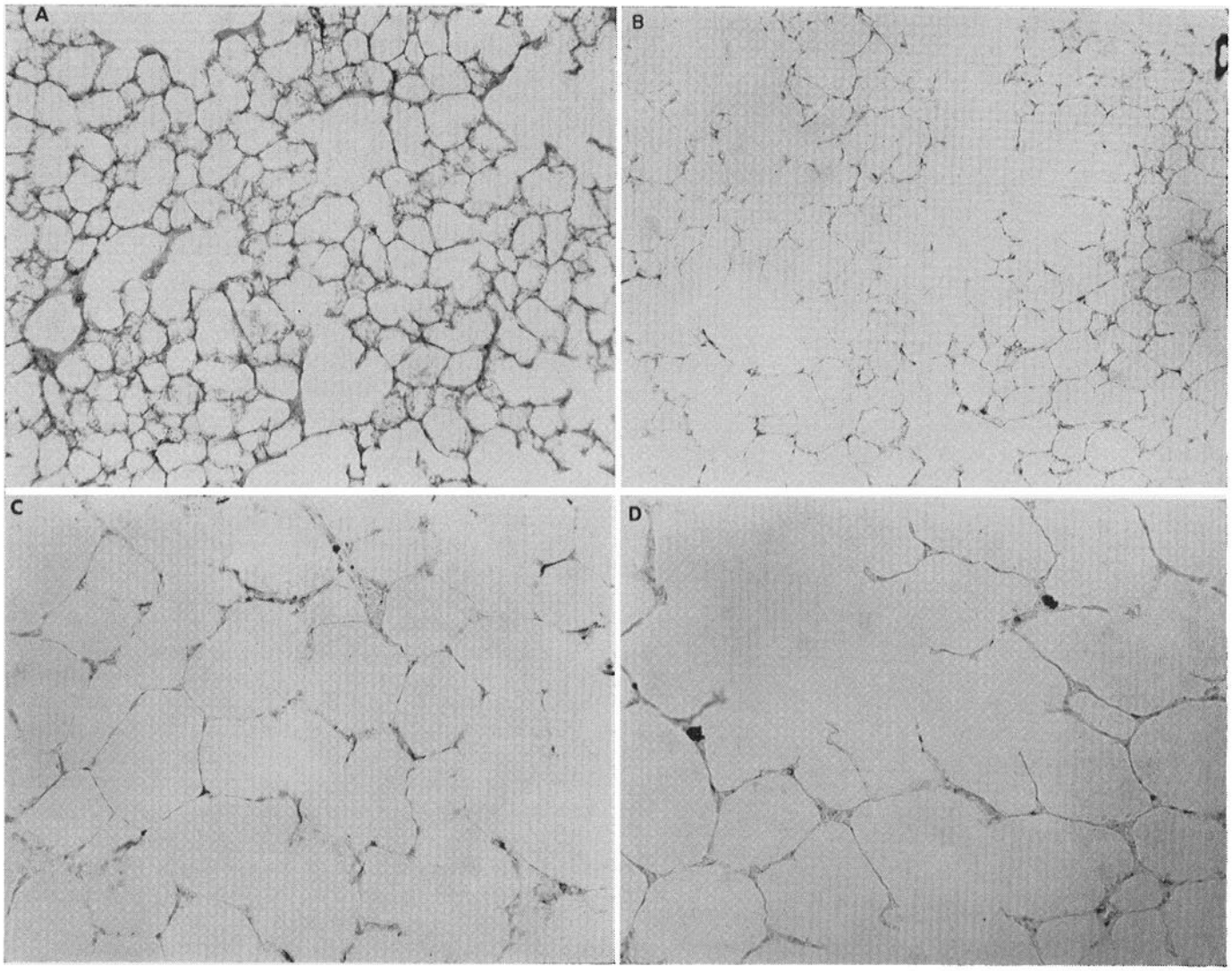

FIG. 7. Photomicrographs of lung after India ink introduced into pulmonary artery with venous occlusion and pulmonary artery pressure–10 cm H_2O. Eosin stain. *A:* thick (25 μ) section showing a network of ink deposition, but virtually no ink in alveolar septal walls seen en face. Site of this network at septal junctions could be appreciated by serially focusing through section. × 87. *B:* thin (6 μ) section in which most of the ink deposition at or near septal junctions is noted. × 87. *C* and *D:* higher magnification of moderately inked areas. × 212.

patchy appearance, so we used two methods to homogenize the ink dispersion. After injection of the ink with vascular pressures low, but without occlusion, the lung was moderately inflated one or two times. This drew the ink mixture farther into the arterial extra-alveolar compartment. The cannula was then occluded and the lung fully inflated and deflated as before. Second we removed the occlusion after deflation, replaced it, then repeated the procedure in order to draw more ink through the lung. This intensified the staining but did not appreciably change its distribution, nor did the microscopic appearance of the stained areas show a more uniform dispersion of the ink-filled vessels. Thus we doubt that mixing can account for this distribution, but rather that it is due to intrinsic differences in the vessels themselves or the pressures surrounding them.

DISCUSSION

The alteration of weight in response to vascular pressure changes in the first procedure is a measure of compliance, but if so, then we must ask compliance of what? We cannot say that either arteries or veins are the sole vascular compartment involved since the capillary bed is also changing. There is little doubt that the pulmonary capillary bed is distensible (6, 8,10). The limit to which capillary compliance would affect these measurements is probably related to the relative size of the pulmonary capillary bed (7,11, 32), a reasonable estimate being 10–12% of the pulmonary blood volume or about 20–25% of either the arterial or venous volume. However, the pulmonary capillaries are important resistive vessels of the pulmonary circulation (1, 8,10) so that the arterial or venous pressure is not transmitted throughout their length. Assuming this pressure is only "seen" by half the length of the capillary and only this portion distends, then again the figure 10–12% emerges as an overestimate of arterial or venous compliance due to capillary filling. The reverse flow procedure was an attempt to clarify this point. If a difference in compliance was seen this might represent a different fraction of capillaries being

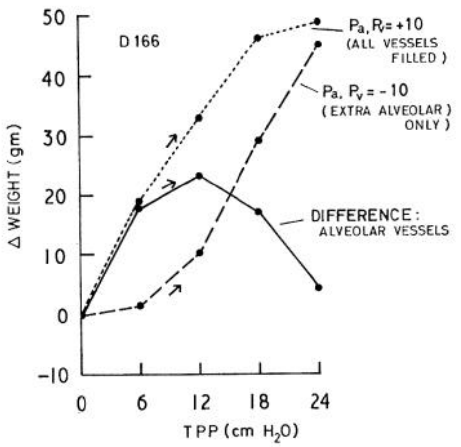

FIG. 8. Pattern of weight change on inflation when all vessels are filled and when only extra-alveolar vessels are filled. Difference reflects change in volume of alveolar vessels.

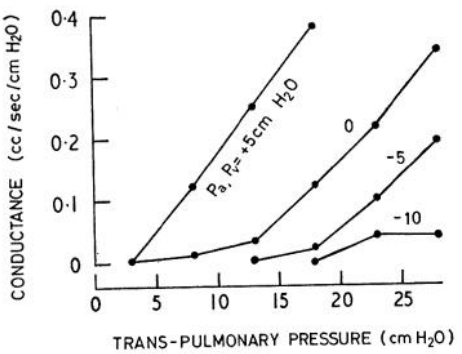

FIG. 9. Conductance of A-V connections seen in occlusion experiment at several vascular pressures, as calculated from rate of pressure equalization and compliance of unoccluded side.

filled, and the smaller of the two compliances would more closely follow only arteries or veins. Unfortunately the lack of any difference was inconclusive in this respect although it is compatible with capillaries equally filled from either end. Because of this we prefer to label these slopes compliance of the arterial or venous side rather than strictly arterial or venous compliance, which would imply an anatomic entity.

It is somewhat difficult to compare these measurements to those of vascular compliances in other species. The greyhound has an enormous lung for its size (110–160 g left lung after exsanguination with body weight 21–27 kg) so that estimates based on body weight would not be comparable. If such comparisons are made, these measurements, considering maximum $\Delta W_L/\Delta P$ slopes only, are somewhat higher than reported values in rabbits (7), cats (9), and man (18, 32) done with differing techniques, but if a correction is made for average lung weight of these species the differences are minimized.

The linearity of compliance in these pressure ranges is expected. No attempt was made to find the limits of weight change at higher pressures which might be expected to occur at 40 cm H_2O or above (10, 24). The lack of any hysteresis is, however, one point where these data differ from previous studies (9, 26, 28). However, the pressure range examined in the present study is not as high as in those where hysteresis has been clearly found. Perhaps there is not sufficient stress to observe the "stress relaxation" effect.

The dependence of vascular compliance on transpulmonary pressure has been previously noted (8, 15, 20). This can most easily be explained if one considers the absolute lung weight rather than weight-pressure relationships at the various inflation volumes. Absolute weight reflects the state of overall vascular filling which is determined principally by transmural pressures. The reduced vascular compliance at very high or very low lung inflations must then represent the extremes of vascular distention or closure as determined by such transmural pressures.

The relationship of vascular volumes to lung inflation has been extensively described before both with positive and negative pressure inflation (13, 16, 22, 24, 27). The results of the present study are consistent, but are unique in being able to compare volumes during steady flow with those at no flow, whereas previous studies with direct volume measurement have been limited to the no flow state. Since the relationships during blood flow, where vascular pressures are unequal, essentially reflect those at no flow, where vascular pressures are equal, then the conclusions drawn from previous studies at static vascular volumes can be extrapolated to conditions of blood flow.

One important point is the changing shape of the weight/Ptp curve at different vascular pressures. In comparison to the data of Howell et al. (13) in which the vessels were filled with kerosene, thus excluding the alveolar vessels, the shape of our no flow curves is very similar. This is not surprising since in the present study vascular pressures are kept constant relative to alveolar pressure, and inflation would principally affect extra-alveolar vessels. However, when vascular pressures are below the bottom of the lung the alveolar vessels are emptied, but when such pressures are well above the bottom of the lung both alveolar and extra-alveolar vessels are filled. Thus by subtracting the curve under the former conditions from the latter (Fig. 8) the volume of the alveolar compartment can be calculated, and is shown to be at a maximum at moderate lung inflation. This argument

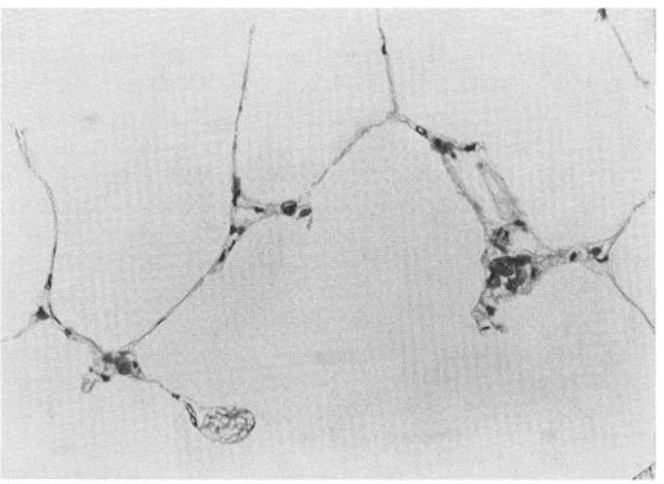

FIG. 10. Frozen greyhound lung where erythrocytes are found only in corner vessels. Transpulmonary pressure 18 cm H_2O, Pa–15, Pv–32. × 300.

must be qualified in that vascular compliance must be reasonably constant throughout the range of study. Since this is the case except at both low vascular and transpulmonary pressures, then we can still say that alveolar vessels become smaller at high Ptp, but at Ptp below 10 cm H_2O no conclusions can be reached.

In the occlusion procedure the pressure equalization in an exponential manner which occurs above certain transpulmonary pressures (Fig. 6) is analogous to the discharge of a capacitor. Using this analogy, and assuming the compliance measurements previously obtained, the resistance (or its reciprocal, conductance) can be calculated from the formula $(Pa - Pv)_t = (Pa - Pv)_0 e^{-t/RC}$ where the binomials represent pressure gradient at time (0, t), R = resistance, C = compliance, and conductance = 1/R. Figure 9 shows the results of such calculations for four lungs. We interpret this figure as follows: the tendency of conductance to rise at most vascular pressures in the occlusion procedure reflects the recruitment of alveolar vessels (capillaries) as the lung is inflated, even with vascular pressures as low as -5 cm H_2O. This results from surface forces which are capable of opening capillaries by lowering pericapillary pressure. But at -10 cm H_2O the role of surface forces is overcome, the limit for such forces being approximately 6 cm H_2O (5, 15, 20), and therefore flow only occurs here through extra-alveolar arteriovenous connections. Variations in surface forces could produce pericapillary pressures as low as -10 cm H_2O, but it must be remembered that vascular pressures are referred to the bottom of the lung and lung depth is at least 8 cm. Despite this, ink staining was observed throughout the entire thickness so that a hydrostatic gradient considerably in excess of 10 cm was overcome. Although the conductance of these vessels is small relative to overall vascular conductance, it is not negligible, being approximately 10% of conductance calculated in a conventional way.[1]

Another explanation is possible: that as pressure on the occluded side gets sufficiently low, blood is simply pulled through the collapsed vessels. However, these pressures are clearly in sluice-gate conditions (4, 23) the behavior of which is independent of downstream pressure, making this explanation an unlikely one.

Although the corner vessels are selectively ink filled, we have not rigorously demonstrated them as arteriovenous connections. Larger arteries and veins also contained ink. Nevertheless, arteriovenous transport did occur under conditions when the alveolar vessels were collapsed or severely compressed, and the corner vessels were the most peripheral vessels showing filling. It is known that corner vessels may be exposed to pressure other than alveolar pressure (10, 22) but a procedure which selectively fills these vessels by utilizing alveolar-extra-alveolar differences has not been described. Glazier et al. (10) were aware of these vessels and excluded them from their study of septal capillaries. The procedure in the present study essentially reflects conditions high in zone 1 (30), and the picture of the ink-stained lung closely parallels the conditions seen by Glazier et al. (10) (Fig. 10).

These vessels are not shunts in terms of capability for gas exchange. Their small size and location speaks for an active role in gas exchange. They are shunts in that they may represent a pathway of relatively low resistance; but a preferable description would be extra-alveolar capillaries and pre- or postcapillaries. Shunts of a more familiar type have been described before in dog lungs (19, 21, 25), but such vessels with diameters of 100–200 μ are clearly different than the ones presently demonstrated.

It has been recently speculated that the pulmonary edema of high altitude may result from excessive permeability of extra-alveolar vessels (31). If vessels as small as these (10–20 μ) are exposed to extra-alveolar pressure, then these could well be a site of edema formation.

The authors express their appreciation to Mrs. R. Stevenson, Mr. G. Kingaby, Mr. M. Dickens, and Mr. D. Woodland for their valuable technical assistance throughout this series of experiments, and to Dr. J. B. West for his continuing advice and encouragement.

This study was supported, in part, by Public Health Service Training Grant 5 T01 HE 05538-07.

D. Y. Rosenzweig is a Special Fellow, National Heart Institute. His present address: Dept. of Medicine, Marquette School of Medicine, 8700 West Wisconsin Ave., Milwaukee, Wis. 53226.

J. B. Glazier is an Advanced Research Fellow, American Heart Association.

Received for publication 28 February 1969.

REFERENCES

1. Agostoni, E., and J. Piiper. Capillary pressure and distribution of vascular resistance in isolated lung. *Am. J. Physiol.* 202: 1033–1036, 1962.
2. Anthonisen, N. R., and J. Milic-Emili. Distribution of pulmonary perfusion in erect man. *J. Appl. Physiol.* 21: 760–766, 1966.
3. Ball, W. C., P. B. Stewart, L. G. S. Newsham, and D. V. Bates. Regional pulmonary function studied with ^{133}xenon. *J. Clin. Invest.* 41: 519–531, 1962.
4. Bannister, J., and R. W. Torrance. The effect of tracheal pressure on flow: pressure relation in the vascular bed of isolated lungs. *Quart. J. Exptl. Physiol.* 45: 352–367, 1960.
5. Bruderman, I., K. Somers, W. K. Hamilton, W. H. Tooley, and J. Butler. Effect of surface tension on the circulation in the excised lungs of dogs. *J. Appl. Physiol.* 19: 707–712, 1964.
6. Daly, W. J., S. T. Giammona, and J. C. Ross. The pressure volume relationship of the normal pulmonary capillary bed. *J. Clin. Invest.* 44: 1261–1269, 1965.
7. Engleberg, J., and A. B. DuBois. Mechanics of the pulmonary circulation in isolated rabbit lungs. *Am. J. Physiol.* 196: 401–414, 1959.
8. Fishman, A. P. Dynamics of the pulmonary circulation. In: *Handbook of Physiology. Circulation.* Washington, D. C.: Am. Physiol. Soc., 1963, sect. 2, vol. II, chapt. 48, p. 1667–1743.
9. Frank, N. R., E. P. Radford, Jr., and J. L. Whittenberger. Static volume-pressure interrelation of the lungs and pulmonary blood vessels in excised cat lungs. *J. Appl. Physiol.* 14: 167–173, 1959.
10. Glazier, J. B., J. M. B. Hughes, J. E. Maloney, D. Y. Rosenzweig, and J. B. West. Effect of vascular pressures on pulmonary capillary morphology. *Clin. Res.* 16: 370, 1968.
11. Green, H. D. Circulatory system, physical principles. In: *Medical Physics*, edited by O. Glasser. Chicago: Year Book, 1955, vol. II, p. 228–251.
12. *Handbook of Respiration*, edited by D. S. Dittmer and R. M. Grebe. Philadelphia: Saunders, 1958.
13. Howell, J. B. L., S. Permutt, D. F. Proctor, and R. L. Riley.

[1] Conductance, $\dot{Q}/(Pa-Pa)$, measured during steady-state zone 2 (30) blood flow procedures, when Pa = 15, Pa = 0, Ptp = 10, and Pv = -10 cm H_2O, averaged 0.43 ml/sec per cm H_2O for these four lungs. Conductance during the occlusion procedures at vascular pressures of -10 cm H_2O did not exceed 0.04 ml/sec per cm H_2O.

Effects of inflation of the lung on different parts of the pulmonary vascular bed. *J. Appl. Physiol.* 16: 71–76, 1961.
14. Hughes, J. M. B., J. B. Glazier, J. E. Maloney, and J. B. West. Effect of lung volume on the distribution of pulmonary blood flow in man. *Respiration Physiol.* 4: 58–72, 1968.
15. Lloyd, T. C., Jr., and G. W. Wright. Pulmonary vascular resistance and vascular transmural gradient. *J. Appl. Physiol.* 15: 241–245, 1960.
16. Macklin, C. Evidence of increase in the capacity of the pulmonary arteries and veins of dogs, cats, and rabbits during inflation of the freshly excised lung. *Rev. Can. Biol.* 5: 199–232, 1946.
17. Mead, J., and J. L. Whittenberger. Lung inflation and hemodynamics. In: *Handbook of Physiology. Respiration.* Washington, D. C.: Am. Physiol. Soc., 1964, sect. 3, vol. 1, chapt. 18, p. 477–486.
18. Milnor, W. R., A. D. Jose, and C. J. McGaff. Pulmonary vascular volume, compliance and resistance in man. *Circulation* 22: 130–137, 1960.
19. Niden, A. H., and D. M. Aviado. Effects of pulmonary embolism on the pulmonary circulation with special reference to arteriovenous shunts in the dog. *Circulation Res.* 4: 67–73, 1956.
20. Pain, M. C. F., and J. B. West. Effects of volume history of the isolated lung on distribution of blood flow. *J. Appl. Physiol.* 21: 1545–1550, 1966.
21. Parker, B. M., D. C. Andresen, and J. R. Smith. Observation on arteriovenous communication in lungs of dogs. *Proc. Soc. Exptl. Biol. Med.* 98: 306–308, 1958.
22. Permutt, S. Effects of interstitial pressure of the lung on pulmonary circulation. *Med. Thorac.* 22: 118–131, 1965.
23. Permutt, S., B. Bromberger-Barnea, and H. N. Bane. Alveolar pressure, pulmonary venous pressure, and the vascular waterfall. *Med. Thorac.* 19: 239–260, 1962.
24. Permutt, S., J. B. L. Howell, D. F. Proctor, and R. L. Riley. Effects of lung inflation on static pressure volume characteristics of pulmonary vessels. *J. Appl. Physiol.* 16: 64–70, 1961.
25. Rahn, H., R. C. Stroud, and C. E. Tobin. Visualization of arteriovenous shunts by cine fluorography in the lungs of normal dogs. *Proc. Soc. Exptl. Biol. Med.* 80: 239–241, 1952.
26. Remington, J. W. Extensibility behaviour and hysteresis phenomenon in smooth muscle tissue. In: *Tissue Elasticity*, edited by J. W. Remington, Washington, D. C.: Am. Physiol. Soc., 1957.
27. Riley, R. L. Effects of lung inflation on the pulmonary vascular bed. In: *Pulmonary Circulation*, edited by W. R. Adams and I. Veith. New York: Grune & Stratton, 1959, p. 147.
28. Sarnoff, S. J., and E. Berglund. Pressure volume characteristics and stress, relaxation in the pulmonary vascular bed of the dog. *Am. J. Physiol.* 171: 238 244, 1952.
29. West, J. B., and C. T. Dollery. Distribution of blood flow and ventilation-perfusion ratio in the lung measured with radioactive CO_2. *J. Appl. Physiol.* 15: 405–410, 1960.
30. West, J. B., C. T. Dollery, and A. Naimark. Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. *J. Appl. Physiol.* 19: 713–724, 1964.
31. Whayne, T. F., Jr., and J. W. Severinghaus. Experimental hypoxic pulmonary edema in the rat. *J. Appl. Physiol.* 25: 729–732, 1968.
32. Yu, P. N., G. W. Murphy, B. F. Schreiner, Jr., and D. H. Janes. Distensibility characteristics of the human pulmonary capillary bed. *Circulation* 35: 710–723, 1967.