Pulmonary capillary pressure and filtration coefficient in the isolated perfused lung

KERMIT A. GAAR, JR., AUBREY E. TAYLOR, L. JENNINGS OWENS, AND ARTHUR C. GUYTON
Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Mississippi

Attempts to develop a reliable method for determining pulmonary capillary pressure and arterial and venous resistances have resulted in a variety of experimental techniques. Among the most important of these, Hellems et al. (8) introduced the technique for obtaining arterial "wedge pressures" as an indication of pulmonary capillary pressure, and Agostoni and Piiper (1) reported an "osmometric" method for estimating pulmonary capillary pressure in the isolated lung. Estimation of capillary pressure in other body tissues has been the purpose of other investigators. Pappenheimer and Soto-Rivera (13) introduced the "isogravimetric" technique for determination of capillary pressure and arterial and venous resistances in the isolated hindlimb of the cat and dog. Johnson and Hanson (10), also, have used this method for similar determinations using the isolated dog intestine, and Mellander (12) and Folkow (2) have used an "isogravimetric" technique which is similar in principle to the isogravimetric technique of Pappenheimer. In the present study, we have used the isogravimetric method for determination of pulmonary capillary pressure and arterial and venous resistances in the isolated lung preparation.

The rate at which fluid transudes through the capillary membrane per unit mass of tissue, that is, the "filtration coefficient," was estimated for the pulmonary capillary membrane by Guyton and Lindsey (6) in a study in which they caused pulmonary edema in dogs by aortic constriction; this resulted in various elevated levels of left atrial pressure similar to that which occurs after acute left-sided heart failure. However, the filtration coefficient was estimated from left atrial pressure changes and not from pulmonary capillary pressure changes. Therefore, we have utilized the capillary pressure studies in these experiments to measure the capillary filtration coefficient in a more accurate way.

METHODS

Use of the isogravimetric method required a sensitive weighing device for the perfused lung. For this purpose, a beam-type balance was constructed with a lung platform at one end and a counterbalancing system at the opposite end. The lengths of the lever arms on the two sides of the fulcrum had approximately a 3:1 ratio, with the longest arm on the side of the lung platform. Use of the counterbalancing mechanism allowed increased sensitivity because only weight changes were recorded and not the entire weight of the lung and supporting system. The platform at the lung end was suspended from a wire connected to a Grass type FT-10 force-displacement transducer. The transducer was connected to a Grass model 7 polygraph for recording weight changes. The balance system was calibrated by placing gram weights on the lung platform. Sensitivity was adjusted at the polygraph so that the sensitivity at full scale deflection represented a change of 1.25 g on the lung platform.

The perfusing system was described and illustrated in a previous paper (3). Briefly, it consisted of Tygon and rubber tubing interconnecting the lung, a venous reservoir...
its height and thereby adjust the venous hydrostatic pressure to various levels. Arterial pressure could be adjusted at the perfusion pump by changing the flow rate.

The blood was oxygenated at the beginning of the experiment by inflating and deflating the lung with air. During the course of the experiment no further oxygenation was required and the lung remained collapsed. Under these conditions, alveolar pressure is zero and the lung is at minimal gas volume.

The colloid osmotic pressure of the perfusate was measured with the use of an electronic osmometer (7) in one half of the experiments.

RESULTS

Pulmonary capillary pressure. The technique for obtaining pulmonary capillary pressure can be explained by referring to Fig. 1. At the start of the measurement, the flow rate was adjusted to obtain an arterial pressure of 10–15 mm Hg. Then the venous pressure was adjusted until several isogravimetric states had been obtained. The perfusion pump was turned off for the final determination so that the isogravimetric pressure at zero flow could be obtained; the pressure thus obtained should be the same as that which existed in the capillaries at the time all of the previous measurements were made under isogravimetric conditions when flow was occurring. In order to determine the isogravimetric capillary pressure, a line was then drawn connecting the plotted points, and that point where the line intersected the venous pressure scale on the ordinate was considered to represent the isogravimetric capillary pressure for the lung. Similar results were obtained by plotting arterial pressures obtained at each isogravimetric state against the corresponding flow rate at that venous pressure (Fig. 2A). A line was then drawn connecting the plotted points, and that point where the line intersected the venous pressure scale on the ordinate was considered to represent the isogravimetric capillary pressure for the lung. Similar results were obtained by plotting arterial pressures obtained at each isogravimetric state against the corresponding flow rate at that venous pressure (Fig. 2B). Figure 3 illustrates the range of determinations of capillary pressure obtained by this method. It can be seen that the determinations were distributed approximately around a normal curve. The average of all the measurements obtained in this manner, indicative of pulmonary capillary pressure, was 7.0 mm Hg ± 1.4 mm Hg SD.

Pulmonary arterial and venous resistance. The slopes of the curves connecting the points in Fig. 2, A and B, are a measure of the pulmonary venous and arterial resistances, respectively, from the effective midpoint of the capillaries to the points where the venous and arterial pressures were monitored. We obtained in this way average values of 0.014 and 0.018 mm Hg/ml per min for the venous and arterial resistances, respectively.

Pulmonary capillary filtration coefficient. The procedure for obtaining the filtration coefficient of the pulmonary capillary membrane can be explained by referring to the
FIG. 2. A: Graphical method showing how blood flow is plotted against isogravimetric venous pressure to obtain the isogravimetric capillary pressure (where curve intersects the ordinate). Venous resistance is obtained from the slope of the curve. B: Graphical method for obtaining arterial resistance. Note that isogravimetric capillary pressure is same as that determined in A because plotted points are obtained from the same experiment.

record in Fig. 4. The flow rate was set at a low level (about 20 ml/min) and the pressures were adjusted accordingly to obtain an isogravimetric state. Then the arterial and venous pressures were simultaneously elevated 5 mm Hg and the resulting weight change recorded. It can be seen that the weight change consists of a steep rapid increase followed by a more gradual upward slope. This effect was also noted by other investigators (10, 12, 13), and it is generally concluded that the initial rapid increase in weight results from alteration of blood volume and that the gradual upward slope represents capillary filtration. A similar effect can be seen in response to lowering arterial and venous pressure 5 mm Hg (Fig. 5), except that the changes are now in the opposite direction, as expected. A higher sensitivity was used here requiring a reset of the recorder pen following the initial deflection which went off scale. The gradual slopes of the weight recordings in Figs. 4 and 5 represent the rates of fluid transudation through the pulmonary capillary membrane expressed as grams of fluid per minute. This is divided by the pressure change, 5 mm Hg, and by the weight of the lung to obtain the filtration coefficient, which is then expressed as grams per minute per mm Hg per 100 g lung tissue. The average filtration coefficient determined in this manner for the isolated lung was found to be 0.070 ± 0.010 g/min per mm Hg per 100 g.

Colloid osmotic pressure. Measurements were obtained in half of the experiments for the colloid osmotic pressure of the perfusate; the average value found was 20 mm Hg ± 1 mm Hg SD.

DISCUSSION

Pulmonary capillary pressure. To determine the isogravimetric capillary pressure in the isolated hindlimb, Pappenheimer (13) extrapolated the curve connecting the points on the graphs of Fig. 2 to zero flow. Johnson (10) remarked that this was not a feasible procedure, based on his own findings of linearity in the vascular resistance of the isolated intestine at diminished flow rates. He attributed this linearity to autoregulation of blood flow. As indicated in Fig. 2, arterial and venous resistances were almost completely linear in the isolated lung; therefore, this was not a problem with our experiments. We did not, however, have to extrapolate our curves but, instead, determined each point experimentally all the way to zero flow.

Pappenheimer found that the isogravimetric capillary pressure in the hindlimb was 1–2 mm Hg less than the colloid osmotic pressure of the blood plasma in the perfusate. He had proposed that they should be essentially equal; the difference was attributed to the presence of protein in the interstitial fluid, which, could not be determined experimentally. Johnson (10) measured a colloid...
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FIG. 4. Capillary filtration (gradual upward slope of weight change) caused by simultaneously elevating arterial and venous pressures. Sudden upward deflection of weight change is indicative of increase in blood volume. Note that blood flow increases coincidentally with change in blood volume.

osmotic pressure of 22 mm Hg in his dogs and found that the difference between it and the isogravimetric capillary pressure of the isolated intestine was about 8 mm Hg. He stated that this difference could be due to the presence of protein in the interstitial fluid and to a negative tissue pressure which had been measured in other tissues by Guyton (4, 5) using implanted hollow plastic capsules.

The average value of pulmonary capillary pressure which we have determined, 7.0 mm Hg, is about 2 mm Hg lower than that calculated by Agostoni and Piiper (1), who also used the isolated lung but with a different technique. Their value, however, was estimated on the basis of very few experiments. “Wedge pressure” measurements yield values that were first believed to represent capillary pressure. However, since this technique requires that a catheter be wedged into the pulmonary artery, which stops all flow, it can be seen from the following equation where $P_c$, $P_a$, and $P_v$ represent capillary, arterial, and venous pressures, respectively, and $R_a$ and $R_v$ represent the arterial and venous resistance, respectively,

$$P_c = P_a - \frac{P_a - P_v}{1 + R_v/R_a}$$

that if arterial resistance becomes infinitely large, as occurs when a wedged catheter stops blood flow, then the capillary pressure becomes equal to venous pressure and therefore no longer represents the true capillary pressure that previously existed in the vessel.

Pulmonary arterial and venous resistance. Agostoni and Piiper (1) found that the distribution of pulmonary vascular resistance was approximately 40% arterial and 60% venous in isolated dog lungs using an osmometric technique. We find that the distribution of this resistance is approximately 56% arterial and 44% venous. The differences in the ratio of arterial and venous resistances between our study and theirs could result from the experimental conditions, e.g., our lungs were in a collapsed state in the horizontal plane and their lungs were in an inflated state in a vertically suspended plane. However, it is apparent that the vascular resistance in the isolated dog lung is approximately equally distributed between the arterial and venous pulmonary circulation.

Pulmonary capillary filtration coefficient. According to the Starling hypothesis (14), no net transfer of fluid between the capillary and the interstitial space occurs when all the factors opposing filtration are in equilibrium with those factors which tend to cause filtration. If an imbalance between these factors does occur, then fluid will filter through the capillary membrane. In previous studies (6) we found that the rate of edema formation in the lung is directly proportional to the increase of the left atrial pressure above a certain critical pressure level. In addition, we were able to estimate the filtration coefficient for the pulmonary capillary membrane in intact animal experiments to be 0.068 g/min per mm Hg of

FIG. 5. Absorption of fluid from the tissue spaces caused by simultaneously lowering arterial and venous pressures. Sudden downward deflection (recorder pen reset after initial deflection went off scale) of weight change is due to decrease in blood volume. Note that blood flow decreases also.
left atrial pressure elevation per 100 g tissue. Thus, our findings of 0.070 using the isolated lung in the present study confirm the previous results, although, we are now able to relate this in a much better controlled experiment to elevation of capillary pressure.

In a previous study of pulmonary edema formation in the isolated lung (3), we were able to calculate the filtration coefficient of the pulmonary membrane in still another way. In these studies, the value found was 0.032 g/min per mm Hg per 100 g tissue, which was about one-half the rate found in the present experiments. However, these former values were determined in edematous lungs rather than in normal lungs, and the experimental procedure necessitated about four times as long a period of perfusion as was required in the present experiments.

In addition, a study by West et al. (15) has shown that perivascular edema produces a "cuffing" effect on the blood vessels in lungs made edematous by elevation of venous pressures. This results in occlusion of the blood vessels and would, therefore, reduce the filtration coefficient proportionally. In another study Howell et al. (9) observed that the intravascular volume of isolated lung increased when the lung was inflated which, in effect, would tend to keep the vessels expanded and counteract the vessel closure which occurs in the collapsed lung. These effects could account for the difference in filtration coefficients found in our previous pulmonary edema studies using the isolated lung (3) and the lung in the intact animal (6). For these reasons we believe the higher filtration coefficients determined in the present study on the isolated nonedematous lung and in a previous study (6) using the intact animal, to represent the true filtration coefficient for the pulmonary capillary membrane.

Filtration has been found to be nonlinearly related to arterial pressure rise in the isolated intestine by Johnson and Hanson (11). They attribute this to local autoregulation of blood flow. We found no indication of autoregulation of blood flow in the isolated lung as evidenced by the linearity of arterial and venous resistances indicated in Fig. 2. In addition, in our previous studies of pulmonary edema formation (3, 6), we have found the filtration coefficient to be constant over a wide range of elevated pressures.

REFERENCES