Right Duct Lymph Flow in Experimental Heart Failure Following Acute Elevation of Left Atrial Pressure

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ABSTRACT
We measured the pulmonary lymph flow in dogs with mild congestive failure before and after acute elevation of the left atrial pressure to 40 cm of water. The creation of an aortocava fistula and the administration of desoxycorticosterone trimethylacetate and a salt enriched diet in 6 dogs produced mild pulmonary edema and partial expansion of the pulmonary lymphatics 10 to 12 days postoperatively. Elevation of the left atrial pressure to 40 cm of water under pentobarbital anesthesia led to an immediate increase in right duct flow in the "mild failure" dogs, in contrast to a delayed flow in normal dogs. The average peak flows in the 10- to 12-day dogs after increasing the left atrial pressure were higher than the peak flows observed in normal dogs. In addition, the mild failure dogs survived twice as long as normal dogs after acute elevation of the left atrial pressure. These results suggest that an animal with an expanded pulmonary lymph system is better able to withstand the stress of acute elevation of left atrial pressure than a normal animal. The pulmonary lymph system may serve as an important compensatory mechanism in the prevention of fulminating pulmonary edema.

ADDITIONAL KEY WORDS lymphatic system (pulmonary) arteriovenous anastomosis edema desoxycorticosterone arteriovenous fistula lymph (pulmonary) pulmonary circulation pulmonary edema anesthetized dogs

Following the production of chronic pulmonary edema in dogs by our technique (1), the right duct lymphatics that drain the lung became markedly enlarged and a very large increase in right duct lymph flow occurred. Since only a limited augmentation in lymph flow occurred in acute pulmonary edema produced by elevating left atrial pressure to 40 cm of water (2), we suspected that a gradually developing expansion of the lymph system may play a role as a compensatory mechanism in chronic pulmonary edema, by facilitating the removal of critical accumulations of fluid from the lungs.

The present experiment was designed to study pulmonary lymph flow and the course of events subsequent to acute elevation of the left atrial pressure in dogs with mild chronic pulmonary edema, whose lymphatics, presumably, have had a chance to partially expand, and in normal dogs subjected to the same acute elevation of left atrial pressure. It has been demonstrated that 10 days after initiation of procedures inducing chronic heart failure in the dog (3), right duct lymph flow began to increase significantly and presumably lymphatic expansion was well underway. Accordingly, the right duct lymph flow was recorded (4) before and after elevation of left atrial pressure at 40 cm of water by inflating a balloon (2) in the left atrium of...
dogs that had been developing "failure" for 10 to 12 days.

**Methods**

Ten dogs not included in the experimental group were required for preliminary studies owing to the complexity of using three separate experimental techniques in each animal (i.e. production of chronic congestive failure, recording of right duct flow and acute elevation of left atrial pressure). The experimental group was composed of 6 dogs initially weighing between 14.1 and 21.5 kg.

Chronic heart failure was produced by creating under pentobarbital anesthesia given intravenously (29 mg/kg), a side-to-side aorticocaval anastomosis (7 to 10 mm in length) approximately 2 to 3 cm below the renal vessels. It has been observed clinically and experimentally that heart failure is variable and delayed in association with arteriovenous fistula (5,7). In order to control the onset of failure we have employed (1,3) desoxycorticosterone trimethylacetate (25 mg administered subcutaneously twice weekly) and approximately 6 g of salt per day mixed with food. The pattern of failure in experimental animals with aorticocaval fistula and the administration of hormone and salt has been described (3). In experiment 24, the dog did not appear well following the surgical procedure and the steroid was withheld.

Lymph from the lungs was collected by an improved technique (4) wherein the right external jugular vein was isolated and utilized as a fistula to drain right duct lymph. The animals were anesthetized with sodium pentobarbital administered intravenously (approximately 33 mg/kg). Respirations were maintained with an intermittent positive pressure respirator. Two to three milliliters of Evans blue dye (2% solution) given intratracheally was used to visualize the right duct lymphatics. Right duct lymph was collected and its volume measured at 15 min intervals.

Acute elevation of left atrial pressure was produced as follows. A left thoracotomy was made; a Foley catheter with its lumen tied off and a small bore plastic tube were inserted through the left atrial appendage into the left atrium. The other end of the plastic tube was attached to a water manometer for recording left atrial pressure. The Foley balloon was inflated until left atrial pressure was approximately 40 cm of water and the pressure was maintained until the animals died. Pulmonary edema was estimated by the gross appearance of the lungs, the percent fluid in small lung biopsies obtained before inflating the left atrial balloon and that in samples obtained terminally (2), and the ratio of the wet lung weight to body weight (LW/BW) (8). The heart weight-body weight ratio (9) was also measured.

**Results**

All animals exhibited mild congestive failure by the 10th day, manifested by slight to moderate limb edema. In addition, the left atrial pressures ranged between 10 and 16.5 cm of water and the lungs appeared more moist and darker red than normal lungs. In four of the dogs, the percent fluid in the lung biopsy before inflation of the left atrial balloon was greater than the upper limit of normal (78%).

Following inflation of the left atrial balloon, the average right duct lymph flow increased from 1.4 to 4.25 ml in the first 15 min (Table 1). The average peak flow was 6.9 ml/15 min; its time of appearance was variable (Fig. 1). In general, the immediate and subsequent "postinflation" lymph flows were well above the preinflation levels (Fig. 1). However, in experiment 28, the balloon broke at 15 min and thereafter technical difficulties with the replacement prevented adequate maintenance and registration of the left atrial pressure.

As each experiment progressed, the gross pulmonary edema became more manifest with the appearance of a dark red color on the surface of the lung. The lymph at times would become bloody and then clear again in the same collection period. The hearts generally dilated and most of the animals died in ventricular fibrillation from 70 to 280 min (average, 172 min) after inflation of the left atrial balloon. Terminally, the percent fluid in the biopsy was increased over the preinflation level in each experiment and the ratio of the lung weight to body weight was above the upper limit of normal (.014). The heart weight-body weight ratio remained normal (not greater than 0.009). Generally, 50 to 200 ml of frothy tracheal fluid was obtained from these animals during the course of the experiments and there was some excess pericardial (20 to 100 ml) and occasionally pleural fluid (15 to 30 ml).
Discussion

It has been shown that our method of producing congestive failure (aorticocaval fistula, desoxycorticosterone trimethylacetate and a salt enriched diet) can lead to cardiomegaly and overt pulmonary edema after 21 days (3). At the earlier stage used in these experiments, i.e. 10 to 12 days, mild congestive failure and pulmonary edema or congestion were present as manifested by an increase in right duct lymph flow, a mild elevation of the left atrial pressure and a slight increase in the fluid content of lung biopsies. At this early stage, before the onset of cardiomegaly, high left atrial pressures, high lymph flows and the presence of profuse alveolar transudate, it is difficult to know whether mild failure or simple fluid retention secondary to salt loading is present. However, it appears that at 10 to 12 days postoperatively, the chain of events is established that will progress to overt congestive failure and that it is proper to call this an early stage of congestive failure.

These studies demonstrate that elevation of the left atrial blood pressure to 40 cm of water in dogs with mild chronic congestive failure resulted in a threefold increase in right duct flow in the first 15-min period. In previous studies in which the left atrial pressure was similarly elevated in normal dogs, it took approximately 38 min for the right duct flow to begin to increase (2). The peak right duct flow in dogs with mild failure was five times the preinflation flow and two times the peak flow in normal dogs with acutely elevated left atrial pressures (2). Thus, these experiments show that when dogs with mild preexistent heart failure (left atrial pressure elevated to 10 to 16.5 cm of water and increased percent of pulmonary tissue fluid) are subjected to acute elevation of left atrial pressure by a balloon, the response of the lymph system was more rapid and the increase in lymph flow was greater than that in normal dogs subjected to the same acute elevation of left atrial pressure.

Furthermore, the normal dogs died with massive pulmonary edema approximately 60 to 90 min after inflation of the balloon (2).
while the “mild failure” dogs lived approximately twice as long. Thus the animals with mild congestive failure have apparently developed one or more compensatory mechanisms which decrease the deleterious effects of an abrupt elevation of pulmonary venous pressure. The greater pulmonary lymph flow in the dogs with mild failure as compared with that of previously normal dogs suggests that there had been an expansion of the volume of the lymph system. It is suggested that this mechanism may function importantly in the prevention of alveolar flooding.

Clinically, this experimental situation may be comparable to patients with mitral stenosis in mild chronic failure who frequently demonstrate a surprising tolerance to elevated left atrial pressures (10, 11), in contrast to patients with hypertension or coronary artery disease not initially in failure who suddenly develop an abnormal left atrial pressure and severe overt pulmonary edema. The former patients rarely have fulminating attacks of acute pulmonary edema, but generally have milder episodes of nocturnal dyspnea and persistent pulmonary vascular congestion. We suggest that patients with chronic elevation of the left atrial pressure may have ample time to expand and adapt their lymph system and so develop some protection against alveolar flooding, whereas patients with acute elevation of the left atrial pressure may not have sufficient time to expand the lymphatic system, and accordingly, may more readily develop fulminating pulmonary edema.

References
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