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Effects of Increased Left Ventricular Resistance Loads on Flow and Composition of Cardiac Lymph in the Dog.* (29257)

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Studies from our laboratory(1), and by others(2), have shown that the dog heart has a substantial lymph flow under normal conditions. Rates of cardiac lymph flow have been found to be increased by hypoxia(1,3), epinephrine and ephedrine(2), and by acute plasmapheresis(2).

The present study was undertaken to determine whether increased resistance to left ventricular emptying alters the flow of cardiac lymph or its composition. The resistance to emptying was produced by 1) stenosis of the aorta, 2) intravenous norepinephrine and 3) intravenous angiotensin II.

Methods. Stock dogs were anesthetized with intravenous sodium pentobarbital. The heart was then exposed through a left lateral chest incision in the 4th interspace. Positive pressure respiration was maintained with a mixture of 95% oxygen and 5% carbon dioxide *via* a tracheal catheter. A small amount of T 1824 dye (about 0.2 ml of a 1% solution) was injected into the ventricular myocardium to visualize the mediastinal lymphatic channels draining the heart.

Details of our technique of visualizing the mediastinal lymphatics draining the heart(4) and of cannulation of one of them have been described(1). After successful cannulation of a lymphatic, all other lymphatics ascending from the heart were ligated. Dressings moistened with Ringer's solution were then placed across the chest wound. An intravenous infusion of Ringer's solution (10 to 20 drops per minute) was maintained throughout each experiment, except when solutions of norepinephrine or angiotensin II were being administered.

Stenosis of the descending thoracic aorta was accomplished by tightening a screw clamp placed distal to the left brachiocephalic artery. The aortic clamp was tightened fairly rapidly, to raise the proximal diastolic arterial blood pressure between 20 and 30 mm Hg. At the end of a one-hour collection period the clamp was loosened slowly. Norepinephrine solutions were made up in a concentration of 16 μg of norepinephrine base per ml; angiotensin II solutions were made in a concentration of 2.5 μg per ml. These pressor agents were infused intravenously at a rate sufficient to raise the diastolic blood pressure 20 to 30 mm of Hg. The infusion rate to accomplish this was invariably less for angiotensin II than for norepinephrine.

Because of technical problems it was not possible to test all 3 methods of augmenting the resistance load in each animal successfully cannulated. However, in 3 dogs it was possible to compare the effects of norepinephrine with those of angiotensin II, and in 2 of them a second one-hour control period was obtained before administration of the second drug. A total of 9 dogs were successfully cannulated. In 2 of these animals 2 initial control periods were obtained.

The initial collection of lymph specimens was started after a "flush" period of 15 min-

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TABLE I. Mean Values for Composition of Cardiac Lymph.

	Hematocrits*	Proteins in g/100 cc		Chloride in meq/l		Sodium in meq/l		Potassium in meq/l	
		Lymph	Blood*	Lymph	Blood*	Lymph	Blood*	Lymph	Blood*
Initial control period (11)‡	37.1 ± 1.7	4.30 ±.23	5.94 ±.22	112.4 ± 2.0	113.7 ± 2.4	149.0 ± 2.2	147.4 ± 2.5	3.91 ±.09	3.69 ±.13
Period of increased left ventricular resistance load† (17)‡	36.1 ± 2.0	4.12 ±.22	5.60 ±.21	115.3 ± 2.6	114.8 ± 2.1	145.0 ± 2.6	145.6 ± 2.4	3.94 ±.14	3.98 ±.16
Control period after increased resistance load (6)‡	35.5 ± 3.1	3.88 ±.37	4.96 ±.37	118.1 ± 5.4	115.9 ± 2.4	149.3 ± 5.1	148.0 ± 1.1	3.76 ±.27	3.59 ±.19

* Blood samples are arterial.
† The experiments with aortic constriction, and norepinephrine and angiotensin II injections, are pooled. In each experiment the systemic arterial blood pressure was raised 20 to 30 mm Hg.
‡ All control and experimental periods were 1 hr in duration. In parentheses are number of periods included.

FIG. 1. Cardiac lymph flow during experimentally increased resistance loads compared with control value. Duration of each period was 1 hour, during which diastolic arterial pressure was increased 20 to 30 mm Hg. Figures in parenthesis represent number of dogs used in obtaining each mean value.

utes. Collections were made into centrifuge tubes, into each of which one drop of 1% heparin solution had been placed. Arterial blood pressures were recorded from the femoral or common carotid artery (the latter when aortic stenosis was to be produced) *via* a 3-way cannula connected to a Sanborn pressure transducer #276A and Sanborn twin-viso model 150. Blood specimens were obtained through the indwelling arterial cannula into heparinized syringes.

Total proteins were calculated from specific gravity determinations obtained using the Eimer and Amend falling drop apparatus(5). Hematocrits were determined with an International microcentrifuge with a capillary head and an International microcapillary reader model C. R.(6). Sodium and potassium were determined by flame photometry (7), using the Beckman model "DU" spectrophotometer with the flame attachment. A mercurimetric method was used to determine chlorides(8).

Results. The control values for rates of flow and composition of cardiac lymph summarized in Table I and Fig. 1 are comparable to the data previously reported(1). All 3 methods utilized to increase the resistance

to left ventricular outflow produced an increased cardiac lymph flow (Fig. 1), with administration of angiotensin II seemingly causing the greatest increase.

Because of the limited number of determinations made, the data on the composition of cardiac lymph obtained during the various types of resistance load increases are treated as one group; mean values are shown in Table I. Arterial hematocrits decreased with time in 7 of 8 dogs in which this parameter was analyzed.

Discussion. The control data, which agree closely with our previous findings(1), again illustrate a significant cardiac lymph flow in the sodium pentobarbital anesthetized dog. The composition of cardiac lymph was not significantly altered by increased left ventricular resistance. Rates of flow of cardiac lymph increased significantly with aortic constriction and with administration of norepinephrine or angiotensin II (Fig. 1).

The rate of formation of lymph is a function of capillary hydrostatic pressure, tissue pressure, oncotic pressure and capillary permeability(9). The data indicate that an increase in left ventricular systolic load augments the rates of flow of cardiac lymph. The fact that angiotensin II administration appeared to cause larger increases in cardiac lymph flow than aortic stenosis and norepinephrine raises the possibility that this agent either directly or indirectly alters capillary permeability. It is possible that relative myocardial ischemia occurs in the face of the increased work of the heart. Studies on the effects of angiotensin II have shown that coronary blood flow tends to remain unchanged(10) or decreases(11), in contrast to the effect of norepinephrine, which is associated with increased coronary flow(10,12).

These probing studies on cardiac lymph flow and its composition under varying hemodynamic circumstances offer a methodology of studying trans-capillary movement of protein, water and electrolytes in heart muscle. Also, because lymph arises from the interstitial space, studies of lymph composition may eventually prove to be revealing of certain aspects of myocardial metabolism.

Summary. Data on the flow and composition of cardiac lymph have been collected in 9 dogs subjected to various types of increased left ventricular resistance loads. Aortic stenosis, intravenous norepinephrine and intravenous angiotensin II significantly increased the rate of cardiac lymph flow. No significant alterations in lymph composition were found. The data demonstrate that increased resistance to left ventricular emptying causes increased lymph flow. This effect is undoubtedly a reflection of increased capillary hydrostatic pressure and/or increased capillary permeability. The suggestively greater lymph flows with the use of angiotensin II may be due to increased capillary permeability as a result of increased cardiac effort without a proportional increase in coronary blood flow.

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