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The Rates of Formation of Cardiac Lymph and Pericardial Fluid After the Production of Myocardial Venous Congestion in Dogs*

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Summary

Studies in dogs show that severe myocardial venous obstruction is associated with substantial increases in the rates of cardiac lymph flow and in the formation of pericardial fluid. The pericardial effusion occurs primarily from the epicardial surface (visceral pericardium) of the heart. The hearts in these dogs show an increased water content and histological studies reveal dilated lymphatics, perivascular and interstitial edema, small hemorrhages and patchy necrosis. In dogs with less severe myocardial venous obstruction the rates of formation of cardiac lymph and pericardial effusion are proportionately less, and the histologic alterations are less pronounced. These findings resulting from myocardial venous congestion in the dog may be relevant to understanding certain aspects of congestive heart failure and pericardial effusion in man.

In 1940, *Drinker* and his co-workers (1) presented the first data on cardiac lymph flow rates in the dog. They found cardiac lymph flow to be increased by epinephrine, ephedrine and plasmaphoresis. In the same year, *Maurer* (2) described increased cardiac lymph flow with hypoxia. Our first study of cardiac lymph flow in the dog established control rates of flow which were somewhat higher than those found by *Drinker*'s group and confirmed that hypoxia increased the flow rate (3). Shortly thereafter we described increased rates of cardiac lymph flow in dogs after various types of left ventricular resistance loads (4).

Studies from this laboratory (5, 6) have shown that marked interference with myocardial venous blood and lymph drainage in the dog leads to the production of an acute pericardial effusion. These effusions, which are of substantial volume, are formed primarily from the surface of the heart itself (the visceral pericardium). In all of the organs in which it has been studied, lymph flow is increased with significant venous obstruction (7). Recently *Leeds* et al. (8) reported their findings on cardiac lymph flow after the production of moderate myocardial venous congestion (ligation of the coronary sinus) in the dog. They made no observations on pericardial fluid formation, and clearly did not achieve a high degreee of myocardial venous obstruction. Our interest centered on the possible relationship between *marked* myocardial venous congestion, the resultant rates of cardiac lymph flow, and the rates of formation of pericardial effusion. The present report is, therefore, related primarily to this latter question.

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Methods

Mongrel dogs were anesthetized with intravenous sodium pentobarbital (30 mg/kg of body weight), after which tracheal intubation was performed and respirations were maintained with room air delivered via a Harvard pump. The heart was exposed through a left lateral chest incision, usually in the fourth interspace. The superior surface of the pericardial sac was incised longitudinally, and the edges were attached to the surrounding chest musculature with silk sutures in order to make a sling of the pericardium. Clean dry gauze was then packed around the pericardial sling to prevent tissue fluids from seeping into it.

A small amount of T1824 dye (about 0.2 ml) was injected into the ventricular myocardium to visualize the lymphatic channels. All lymphatics passing cephalad from the cardiac lymph node (1, 9) were ligated. By careful dissection of the node, an entering lymph vessel draining the heart was exposed and cannulated with polythene tubing which had previously been filled with heparin solution. All other discernible lymphatics draining the heart were then ligated.

A polythene tube, positioned to drain the most dependent portion of the pericardial sac, was anchored in place with a stay suture to the chest wall, and was connected to a sigmamotor pump. The pericardial sac was then continuously drained during the experiment.

Each experiment consisted of lymph and pericardial fluid collection during a 1 hour control period and for 1 hour after cardiac venous occlusion. After the one hour control collection period, varying degrees of myocardial venous obstruction were produced. The coronary sinus was ligated where it entered the right atrium with a deeply placed ligature on an atraumatic needle. When the coronary sinus was ligated, the great vein under the left atrial appendage was also ligated. The anterior cardiac veins (10) were ligated where they entered the right atrium, each of them being tied with an individual suture. Small veins on the anterior surface of the base of the pulmonary artery were also ligated. After the venous ligations were completed, the one hour experimental period was run.

After the completion of an experiment, the animal was killed with an overdosage of intravenous sodium pentobarbital. The degree of venous obstruction, i.e., the placement of ligatures described in the experimental protocol, was verified at postmortem. The heart was examined grossly for any abnormalities. Standard blocks were taken for histology from the base of the right ventricle and from the free wall of the left ventricle. Blocks were also taken from any areas where gross abnormalities were observed. Heart water contents were determined in portions of the right and left ventricles and the interventricular septum. Care was taken to dissect the specimens free of visible fat. After gentle surface blotting of the specimens, they were placed in watch glasses and wet weights were recorded. The tissues were then finely minced with scissors and dried in an oven at constant temperature (105-110^{o}C) for at least 24 hours or until steady weight was reached (11). The difference between the wet-weight and dry-weight was expressed as percent of water content (see Table).

Histological sections were stained with hematoxylin and eosin, *Verhoff-Van Gieson* for elastic and fibrous connective tissue, and acid fuchsin (12) for evidence of early myocardial anoxia.

Results

A total of six dogs was studied. In three of them the myocardial venous obstruction was marked, with postmortem examination confirming ligation of the great cardiac vein, the coronary sinus, and the visible anterior cardiac veins (Group A). In the three other dogs studied the attempted marked venous obstruction was not accomplished; in two of these three the coronary sinus was not obstructed at all, and in the remaining dog the coronary sinus was only partially obstructed by the ligature (Group B). However, in these latter 3 animals the anterior cardiac veins and the large vein under the left atrial appendage were effectively interrupted so as to produce partial myocardial venous obstruction.

The table shows the rates of cardiac lymph flow with marked (Group A) and with moderate (Group B) myocardial venous obstruction. It is seen that the more marked

Table 1. Effects of myocardial venous obstruction on cardiac lymph flow and the formation of pericardial fluid

	Dog Number	Control Lymph Flow Rate (ml/hour)	Rate of Lymph Flow with Venous Obstruction (ml/hour)	Control Rate of Collection of Pericardial Fluid (ml/hour)	Rate of Collection of Pericardial Fluid After Venous Obstruction (ml/hour)	Dog Weight (kg)	Heart Weight (gm)	Heart Water Content (in Percent of Total Weight) Left Ventricle	Right Ventricle	Ventricular Septum
Group A. Dogs with Marked Obstruction to Myocardial Venous Blood Flow[1]	8-763	2.5	15.0	1.5	13.2	15.0	135	80.24	81.97	81.13
	8-940	1.5	17.2	2.4	24.6	16.8	126	78.03	77.27	77.23
	8-1104	2.3	7.5	0.3	11.7	15.0	130	82.26	81.10	81.26
	Mean	2.1	13.2	1.4	16.5	–	–	80.14	80.11	79.87
Group B. Dogs with Partial Obstruction to Myocardial Venous Blood Flow.[2]	8-848	1.5	4.8	0.5	3.5	13.0	118	78.07	78.06	79.51
	9-241	1.1	4.2	0.6	4.2	16.4	132	76.48	78.74	76.63
	0-388	3.5	10.0	2.0	8.0	15.8	119	77.03	79.63	77.45
	Mean	2.0	6.3	1.0	5.2	–	–	77.19	78.81	77.86

[1]Pathology: Dilated thin-walled channels, particularly subepicardial; perivascular and interstitial edema; early patchy necrosis; small hemorrhage

[2]Pathology available in only two of the three dogs. Changes similar to those found with more marked venous obstruction, but of much lesser degree.

venous obstruction in the dogs of group A was associated with a cardiac lymph flow about twice the amount observed in the dogs with only moderate venous obstruction. The rates of collection of pericardial fluid were also related to the degree of myocardial venous obstruction, with the pericardial fluid volume being over three times greater in the animals with marked venous obstruction (Group A) than with the lesser venous obstruction (Group B). The pericardial fluid which formed after venous obstruction was invariably slightly to moderately serosanguinous, as compared to the clear fluid obtained during the control collection periods.

Mean heart weight to mean dog weight ratio was essentially the same in the two dog groups studied, but the limited data are of no statistical significance. The table shows the mean heart water contents in percent of total wet weight of specimens taken from the left ventricular and right ventricular walls, and from the interventricular septum. As part of a recent study (unpublished), we did control determinations of heart water content and found the mean of 14 dogs to be 77.24 percent water (S.D. = 0.41) for the left ventricular muscle and 77.54 percent water (S.D. = 0.16) for the right ventricular muscle. *Salisbury* (11), in a similar control group of 8 dogs, found the mean left ventricular water content to be 78.3 percent of wet weight.

The pathologic findings in the three dogs in group A (marked myocardial venous obstruction) are summarized in the table. The changes were substantial in degree, with histologic evidence of edema and congestion. Gross and microscopic data were available in two of the dogs from Group B (moderate myocardial venous obstruction). Some dilated thin-walled channels were found. Occasional small hemorrhages were noted, and there appeared to be some perivascular edema, but the changes were not marked.

Discussion

The results show that venous obstruction in the ventricular myocardium causes perivascular and interstitial edema, increased cardiac lymph flow, and increased pericardial fluid formation from the surface of the heart. In a previous study (6) on pericardial effusion following the production of marked venous and lymphatic obstruction from the heart muscle, we found similar myocardial pathology.

Our data for cardiac lymph flow with moderate venous obstruction (Group B) are similar to those of *Leeds* et al. (8) and are in marked contrast to the consequence of more extensive venous obstruction (Group A) which produced a marked augmentation in the lymph flow. Though it has been stated (8) that the extensive network of lymphatics in the heart aids in the ready egress of lymph and deters the development of cardiac edema, it is clear from our data that this capacity of the cardiac lymphatic system is quite limited. Not only does interstitial edema occur with significant myocardial venous congestion, but there is an overflow to create a considerable pericardial effusion also. The pathology observed, as well as the limited data on heart water content, indicates that there was an increase in the interstitial fluid in the myocardium which was not adequately cleared in spite of the marked increases in lymph flow and pericardial fluid formation.

There is the temptation to relate these laboratory studies in dogs to certain aspects of congestive heart failure in man. To suggest, as others have done (8), that chronic venous

congestion does not occur in the myocardium in congestive heart failure, is, we believe a conclusion open to serious question. Though it is doubtful that impairment of central venous flow in clinical congestive heart failure is as severe as that produced in the experiments reported here, there is the strong possibility that elevation in central venous pressure is associated with interference to both venous and lymph outflow from the myocardium. Such alterations have been suggested as playing a role in diminishing heart muscle function in congestive heart failure (13, 14). Indeed, the evidence that myocardial interstitial edema and venous congestion do occur may be important in interpreting certain aspects of congestive heart failure and its treatment. Thus, for example, myocardial contractile function may improve when the central venous pressure is lowered because the myocardial venous blood and lymph drainage into the central venous system is enhanced.

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