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EVALUATION OF THE ROLE OF A MYOCARDIAL DEPRESSANT FACTOR IN SHOCK

L. B. Hinshaw, L. T. Archer, M. R. Black, R. C. Elkins

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13. ABSTRACT

The purpose of the present study was to evaluate the role of a myocardial depressant factor (MDF) in shock. Experiments were carried out in dogs subjected to either splanchnic arterial occlusion (SAO) shock or endotoxin shock after pancreatectomy. An isolated heart monitored substances in blood released during SAO shock or was subjected to endotoxin shock during a 4-5 hour period. Afterload and cardiac output of the isolated heart were controlled or maintained constant. Results demonstrated normal myocardial performance of the test heart receiving blood from the splanchnic region after release of occlusion clamps during early and late phases of SAO shock. Hearts were observed to fail in animals acutely pancreatectomized and administered endotoxin while pancreatectomized controls exhibited normal myocardial performance. Pancreatectomy did not lessen the degree of heart failure after endotoxin. These findings fail to lend support for the MDF hypothesis but suggest a role of peripheral vascular factors in the pathogenesis of SAO shock and ascribe to as yet unknown mechanisms the precipitation of myocardial failure in endotoxin shock.

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The relative importance of the heart in contributing to the pathogenesis of shock is not well defined. At present, there are no available experimental data to evaluate the separate contributions of peripheral and cardiac factors in the intermediate or preterminal phases of shock. Our laboratories have developed several experimental canine heart models for use in the evaluation of myocardial performance in shock (7-13). Subsequent reports utilizing these models in the early and intermediate phases of endotoxin shock have provided evidence that the myocardium is not directly poisoned by endotoxin (12) and is very resistant to its adverse hemodynamic actions, surviving periods of marked hypotension for 3 hours without revealing adverse performance characteristics (8). Our studies have also yielded indirect evidence for the absence of circulating myocardial toxic or depressant factors in the blood of shocked animals in the intermediate or terminal stages of shock (7,9,10). We have documented the development of significant heart failure within 4-6 hours following administration of endotoxin, although the mechanism of failure is not known (11,13). In these studies, heart failure was manifested by elevated left ventricular end diastolic pressures, depressed myocardial contractility (decreased dP/dt and power), decreased efficiency, and mitochondrial edema and disruption (4), which were observed 5-9 hours after an LD_{50-90} endotoxin. These facets of myocardial dysfunction and structural damage were partially or totally

reversed or prevented by early administration of digoxin (13). The probability of a substantial role of the heart in shock is further suggested by reports of clinical septic shock which have included descriptions of myocardial dysfunction or failure (18,22).

Evidence for the presence of a circulating toxin or depressant substance in shock has been previously described by Cannon (2), Shorr and colleagues (21,21), and more recently by Lefer, Glenn, and others (4,5,14-18,23), with the introduction of the term "myocardial depressant factor" (MDF). The critical significance of circulating toxic factors cannot be overemphasized because of their possible overwhelming actions on both the peripheral vascular bed and the myocardium. Pathophysiological manifestations of such factors might well include depressions of both aortic pressure and cardiac output, thus providing a logical rationale for the pathogenesis of shock. Lefer, Glenn and others (5,6,15,17) have reported that plasma MDF activity is inversely related to splanchnic blood flow in endotoxin shock and that a 2-hour occlusion yields high plasma MDF activity. They have further shown that occlusion of pancreatic arteries alone or subjecting the pancreas to ischemia or hypoxia results in MDF activities comparable to those in shock. Finally, they have demonstrated that pancreatectomy before occlusion of the splanchnic arteries, or prior to induction of hemorrhagic shock, almost completely abolishes MDF production (15,17).

The purpose of the present study was to evaluate the possible role of a circulating myocardial depressant factor in two forms of shock

produced by splanchnic arterial occlusion or E. coli endotoxin after pancreatectomy. Findings do not support the view that a myocardial depressant factor performs a significant role in the pathogenesis of shock. There was no evidence for its release from visceral splanchnic sites in SAO shock or from the pancreas after endotoxin.

METHODS

Experiments were conducted on adult mongrel dogs intravenously anesthetized with 30 mg/kg pentobarbital sodium. A total of 21 experiments was carried out in which each study was composed of a small heart donor animal and a large support dog providing blood continuously for an isolated working heart preparation. This procedure has been described in previous reports from this laboratory (8-11).

Two types of experiments were conducted to evaluate the role of the splanchnic region in contributing to the possible release of a circulating factor toxic to the myocardium:

Splanchnic arterial occlusion experiments (N = 7)

The purpose of these experiments was to determine if toxic factors might be released from the ischemic splanchnic region and return through the venous system to depress the myocardium. Basically, the procedure consisted of isolating a heart and supporting it with blood exchanged with a heparinized "support animal", as previously reported (8,10,11). The test system included both lungs, left atrium,

left ventricle, and aortic arch. The right ventricle was bypassed following cannulation or the pulmonary artery. Functional analyses were carried out on the isolated left ventricle as it was influenced by blood circulating from the support animal subjected to shock elicited by splanchnic arterial occlusion. Previous studies utilized a similar procedure (5). Central venous blood from the support animal was supplied to the test heart with lungs ventilated, via a pump set at a constant flow rate (76 cc/kg/min, based on weight of the dog supplying the isolated heart). The tip of the cannula supplying blood to the isolated heart was placed in the central veins of the support animal, between the hepatic vein confluence with the cava and the right atrium. Coronary venous return and aortic outflow of the test heart were separately collected, measured volumetrically and returned to the support animal as previously described (8,10). Aortic pressure (afterload), cardiac output (pulmonary blood flow) and blood temperature were maintained constant in the working heart preparation. The adequacy of this test system has been documented in earlier studies (10). Coronary arterial and venous PO_2, PCO_2 and pH were estimated by an Instrumentation Laboratories blood analyzer while myocardial O_2 and CO_2 arterial and venous blood contents were measured by a Van Slyke manometric blood analyzer. Cardiac power in gram-meters/sec and left ventricular dP/dt in mm Hg/sec were calculated as previously reported (8,10). Splanchnic arterial occlusion was carried out by atraumatic clamping of the celiac, superior and inferior mesenteric arteries at their origins, for a 2-hour period in the support

animal. Myocardial performance, hemodynamics and oxidative metabolism of the test heart were documented during the pre-occlusion period, twice during occlusion, and at several periods following release of occlusion in the support dog and monitored ordinarily until death of the animal (20-90 min post-occlusion).

Endotoxin administration following acute pancreatectomy (N = 14)

These experiments were carried out to determine if the presence of the pancreas is essential for the elicitation of myocardial failure after endotoxin injection. Previous reports (11,13) demonstrated heart dysfunction 5 hours after endotoxin, as revealed from work performance stresses carried out on an isolated heart preparation. The reports of Lefer and Glenn (6,15,17) have clearly implicated the pancreas as the chief site of MDF production and release in shock. The aim of the studies outlined below was to determine if heart failure after endotoxin could be abolished or diminished by acute removal of the pancreas prior to an LD_{70} injection of endotoxin. Control studies without endotoxin were carried out to determine levels of myocardial performance 5-7 hours following acute pancreatectomy.

The basic surgical procedure for this series of experiments was to conduct a laparotomy in a small adult dog via a midline incision under pentobarbital anesthesia. The pancreas was removed together with a small section of adjoining duodenum and the spleen by sectioning tissue between doubly tied ligatures without loss of blood. The abdominal incision was then closed and secured with clamps, animals were positioned on their left sides and placed on regulated heating pads, and rectal temperature probes and arterial and venous catheters

were secured. Following a 15-30 minute equilibration period, endotoxin was intravenously administered to 7 of 14 animals. Hearts were removed and transferred to the intact-dog perfusion system described above in the splanchnic arterial occlusion (SAO) experimental group, except that oxygenated (arterial) blood was removed from the support animal and the isolated lungs were not ventilated. Mean systemic blood pressures, monitored in all animals, remained in the normotensive range in control animals and fell to varying levels of hypotension in endotoxin-injected animals during the 3-4 hour period preceding heart transfer. All hearts were subjected to afterload stresses as performed in the previously described SAO experiments.

Statistics were carried out by means of a modified Student t test.

RESULTS

Splanchnic arterial occlusion SAO) experiments.

Table I illustrates the effect of splanchnic arterial occlusion on mean systemic arterial pressure and heart rate of the intact dog. It can be seen that pronounced hypotension was elicited by release of splanchnic occlusion, while heart rate changes were variable. Figure 1a and 1b are two typical myocardial responses to 2 hours of SAO. The persistent finding demonstrated by both figures is that release of 2 hours of occlusion of blood flow to the splanchnic region did not result in any demostrable myocardial failure or depression of function in the test heart. On the contrary, even during pre-terminal periods in the animal, the myocardium performed normally at elevated

afterloads of 100 and 150 mm Hg when intraventricular systolic pressure often exceeded 200 mm Hg; left ventricular end diastolic pressure (LVEDP) remained below control values at all periods following release of occlusion; dP/dt was elevated; cardiac power equaled or exceeded control values; and myocardial oxygen uptake remained relatively similar to control values at each afterload. Two unsuspected findings were noted after release of the occlusions: coronary blood flow increased markedly while heart rate fell below the pre-occlusion value. There was no evidence for a depression of myocardial performance unless it could be construed that coronary flow was inefficiently or non-economically elevated. All animals became severly hypotensive within 5 minutes following restoration of splanchnic blood flow.

Figures 2a and 2b further describe the effects of SAO shock on the heart at 100 mm Hg afterload and fixed cardiac output of 76 cc/kg/min. Mean values of performance parameters from all experiments clearly show that myocardial performance is unimpaired following release of occlusion: LVEDP, dP/dt, and cardiac power are maintained similar to pre-occlusion values ($p > 0.05$) while coronary resistance markedly fell ($p < 0.05$) in comparison to pre-occlusion values, and hearts performed normally even up to the death of the animals.

Table II summarizes the effect of SAO shock on oxidative metabolism of the heart at a maintained afterload of 100 mm Hg and constant cardiac output of 76 cc/kg/min. Coronary flow increased significantly ($p < 0.05$) and oxygen delivery to the myocardium was elevated ($p < 0.05$) during the post-occlusion period. Oxygen uptake and carbon dioxide production

were elevated on the average above pre-occlusion values following release of the clamps. Significant elevations of coronary venous O_2 content occurred ($p < 0.01$) but since coronary blood flows were markedly elevated ($p < 0.05$), O_2 uptake was well maintained during the period of SAO shock. Gradual decreases in pH were observed during SAO shock. When afterload was increased to 150 mm Hg there were large changes in most parameters, as shown in Table III. Of special note is the observation that myocardial performance of the test heart was notably good during the period of rapidly developing hypotensive shock in the animal: LVEDP and heart rate were in the normal range, while dP/dt was elevated on the average though not statistically altered from control values ($p > 0.05$). Increased coronary blood flow ($p < 0.05$) resulting from coronary vasodilation, together with well maintained coronary arterial oxygen content, would provide an augmented oxygen delivery rate to the myocardial tissue of the test heart during SAO shock.

Endotoxin administration following acute pancreatectomy.

The second series of experiments was carried out to evaluate the role of the pancreas in the elicitation of heart failure in endotoxin shock. No differences were observed between myocardial performances of pancreatectomized dogs in the present experiments and animals with intact pancreata in previous studies from this laboratory (11,13), none of which received endotoxin. This observation clearly demonstrated that 4-6 hours of acute pancreatectomy exerted no detrimental action it-

self on the myocardium. However, endotoxin administered to pancreatectomized animals, whose hearts were evaluated 4-6 hours later, demonstrated the same degree of myocardial failure as reported earlier by this laboratory (11,13). Figure 3 presents raw and derived data from one control and two experimental heart preparations. The control heart at the left side of the figure reveals a normal response to varied afterloads as previously reported (10,11,13) even though it was obtained from an animal pancreatectomized 5 hours earlier. On the other hand, the two experimental heart preparations in Figure 3, obtained from animals given endotoxin 4-5 hours previously and after pancreatectomy, exhibited notable degrees of heart failure. Myocardial dysfunction was characterized by abnormally elevated LVEDP values and relatively depressed dP/dt and cardiac power quantities at matched afterloads and cardiac outputs. The experimental heart (#2), in the right column, exhibited a severe degree of heart failure in that both output and afterload could not be increased above the subnormal levels shown in the figure without precipitating rapid overdistension and profound failure.

Figures 4a and 4b provide means, plus and minus one standard deviation, of various performance and hemodynamic parameters of control, non-shocked hears (N = 7). However, because of the extreme variability of failure of the endotoxin-treated hearts, individual values of the 7 experimental hearts are separately displayed. Two hearts could not function at an afterload of 100 mm Hg even at a reduced cardiac output. The heart indicated by the open square (□) could not support a normal

cardiac output. It can be seen that only one of the shocked hearts could sustain a normal LVEDP at 150 mm Hg and that very high LVEDP values were evident even at low afterloads. Values of dP/dt tended to be depressed at 150 mm Hg although only 3 hearts could tolerate an afterload of this magnitude, without precipitous overdistension and extreme failure in contrast to the controls, each of which performed within normal limits at all afterloads. Heart rates and coronary resistances were relatively scattered and not significantly modified from normal hearts. Two of 3 hearts able to survive the 150 mm Hg afterload (Figure 4a) demonstrated subnormal power quantities and this was evident since individual LVEDP values were abnormally high.

Table IVa and IVb array polled data of certain metabolic parameters in hearts obtained from endotoxin-shocked and control pancreatectomized animals at 100 and 150 mm Hg afterloads. No significant differences in coronary arterial and venous oxygen or carbon dioxide partial pressures or contents were observed in the control and experimental groups, and no alterations in myocardial arterial or venous pH values were discernible in hearts able to perfrom against the higher afterloads. Table V summarizes findings of coronary blood flow, myocardial oxygen supply in accounting for myocardial failure after endotoxin.

DISCUSSION

The purpose of the present study was to evaluate the possible role of a circulating myocardial depressant factor in shock produced separately

by splanchnic arterial occlusion (SAO) and endotoxin. Each stress was applied in a lethal fashion, SAO shock characterized by precipitously developing systemic hypotension followed by early death, and an LD_{70} E. coli endotoxin shock eliciting sustained hypotension, acidosis, and heart failure after 4-5 hours. Research in this laboratory, though clearly demonstrating heart failure after endotoxin, has failed to reveal the mechanism. We have excluded a direct myocardial toxic action of endotoxin (12) and have demonstrated that the blood of endotoxin-shocked animals, in the intermediate or pre-terminal stages, does not possess a circulating myocardial toxic factor of significant importance (7-9,10). Nevertheless, a myocardial depressant substance, termed "MDF", has been described to perform a critically important role in the elicitation of myocardial dysfunction in several forms of shock, including those elicited by splanchnic arterial occlusion and endotoxin (14-17,23).

In the course of attempting to harmonize the findings of this laboratory (7-13) with those of others (5,6,14-18,23), it became increasingly recognized that at least two critical experiments should be carried out: (a) splanchnic arterial occlusion and (b) pancreatectomized animals administered endotoxin. The former would be essential in that this form of shock, involving 2 hours of arterial occlusion of three major splanchnic vessels, has been shown to be a sufficient stimulus to release a maximum concentration of MDF after release of the occlusion (15). The latter pancreatectomy experiment would be of critical importance because the pancreas has been implicated as being the major, if not the only,

source of MDF in shock (16,17). If heart failure was due in large part to MDF released from the ischemic splanchnic region, SAO experiments should yield a significant measure of myocardial dysfunction in the test heart. If pancreatectomy was carried out and shown by itself not to adversely affect myocardial performance, injection of endotoxin would be expected not to result in heart failure in the absence of the pancreas, according to Lefer and Glenn (5,6,17).

Unfortunately, results from our experiments as carried out in the present study, have failed to harmonize our previous findings (7-13) with those of others (5,6,14-18,23). We obtained no evidence whatsoever to support the view that a myocardial depressant factor performs a significant role in the pathogenesis of SAO shock or endotoxin shock post-pancreatectomy. There was no indication of myocardial depressant factors circulating in the blood released from abdominal visceral sites after release of splanchnic arterial occlusion or following lethal injections of endotoxin. Experiments carried out in this laboratory to evaluate the MDF hypothesis incorporated the rigid control of afterload and cardiac output in order to more clearly recognize and interpret changes in myocardial performance at the separate afterloads.

In SAO shock, as carried out in the present study, myocardial contractility in a test heart receiving blood directly from the previously ischemic splanchnic region, at constant afterload and cardia output, was normal in all respects: LVEDP was low or lower than normal, dP/dt and cardiac power were at control pre-occlusion levels or higher, while

heart rate changes were variable. These findings persisted even in the face of severe systemic hypotension and up to the point o f death in the intact animal. It is possible that a myocardial excitatory factor might also be elaborated following relase of the clamps, which would counteract or negate the myocardial effects of a depressant substance. It should be pointed out that since the tip of the cannula carrying blood to the isolated heart is placed downstream from the confluences of the hepatic veins and inferior vena cava, the isolated heart is ampling precisely the same blood as the intact heart. Since both arterial and venous inflows to the liver were obstructed during the occlusion period, it is likely that the liver would have been rendered incapable of detoxigying agents released from the ischemic splanchnic region (19). Further, it would appear that since the mean aortic pressure of the dog falls dramatically to shock levels after release of the occlusion, the precipitation of shock must have been due to peripheral vascular rather than direct cardiac factors in view of the normal performance of the test heart. The marked increase in coronary blood flow observed in the SAO experiments might have been elicited by catecholamine release; however, the absence of tachycardia in the test heart appears to negate this possibility. In addition, heart rates of the intact animals were not significantly modified in SAO shock. Results from this first set of experiments would suggest that systemic hypotension in the intact animal was caused by peripheral pooling of blood, which yielded a greatly depressed venous return and cardiac output. This

view is supported by the findings of Chiu and others (3) and Wilson and Ebert (25), but other possibilities are raised by Selkurt (19) and Williams (24).

Pancreatectomy experiments, carried out in the present study, failed to interfere with the elicitation of myocardial failure in endotoxin shock as previously reported (11,13). Precisely the same degree of heart failure after enodtoxoin was observed in the acutely pancreatectomized animal, as previously reported in animals with intact pancreata (11,13): LVEDP was notably elevated at lower afterloads and only half of the hearts could tolerate a normally high afterload (150 mm Hg) without the precipitation of total myocardial destruction, and dP/dt and cardiac power were relatively depressed, particularly at the higher afterload of 150 mm Hg. Finally, these experiments have failed to identify the critical factors instrumental in the pathogenesis of cardiac dysfunction in endotoxin shock. Explanations have been posed by Cann and others which appear to invoke abnormal emphasis on sympathetic drive and rate (1). Findings from cases of human septic shock have documented myocardial failure (18,22), underscoring the need for a clearer understanding of its mechanism in order to provide effective therapy (13).

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FIGURE LEGENDS

Figure 1a. Effect of splanchnic arterial occlusion on myocardial performance, hemodynamics and metabolism (typical experiment; constant cardiac output; afterload, 100 mm Hg; LVEDP = left ventricular end diastolic pressure).

Figure 1b. Effect of splanchnic arterial occlusion on myocardial performance and hemodynamics (typical experiment; constant cardiac output; afterload, 150 mm Hg: LVEDP = left ventricular end diastolic pressure).

Figure 2a. Effect of splanchnic arterial occlusion on myocardial performance (mean ± SE, 7 experiments; afterload, 100 mm Hg; LVEDP = left ventricular end diastolic pressure).

Figure 2b. Effect of splanchnic arterial occlusion on myocardial performance and hemodynamics (mean ± SE, 7 experiments; afterload, 100 mm Hg; power, work/sec = gm·meters/sec).

Figure 3. Effect of endotoxin after pancreatectomy (and splenectomy) on myocardial performance, hemodynamics and metabolism (1 control and 2 experimental preparations).

Control: post-pancreatectomy (6 hours); no endotoxin administered.

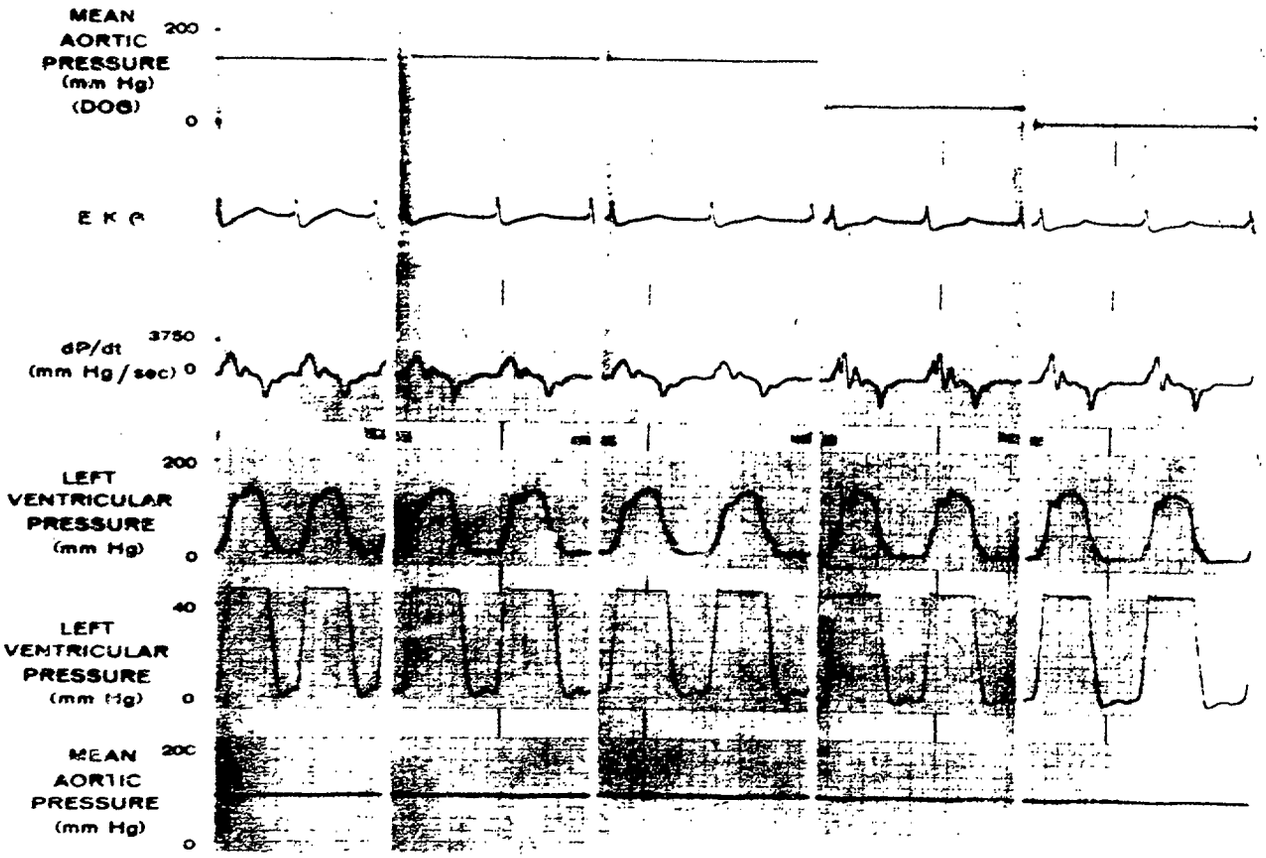
Experimental #1: post-pancreatectomy (6 hours); post-endotoxin (5 hours).

Experimental #2: post-pancreatectomy (5-1/2 hours); post-endotoxin (4-1/2 hours).

(Afterload and cardiac output could not be elevated because of severe degree of heart failure).

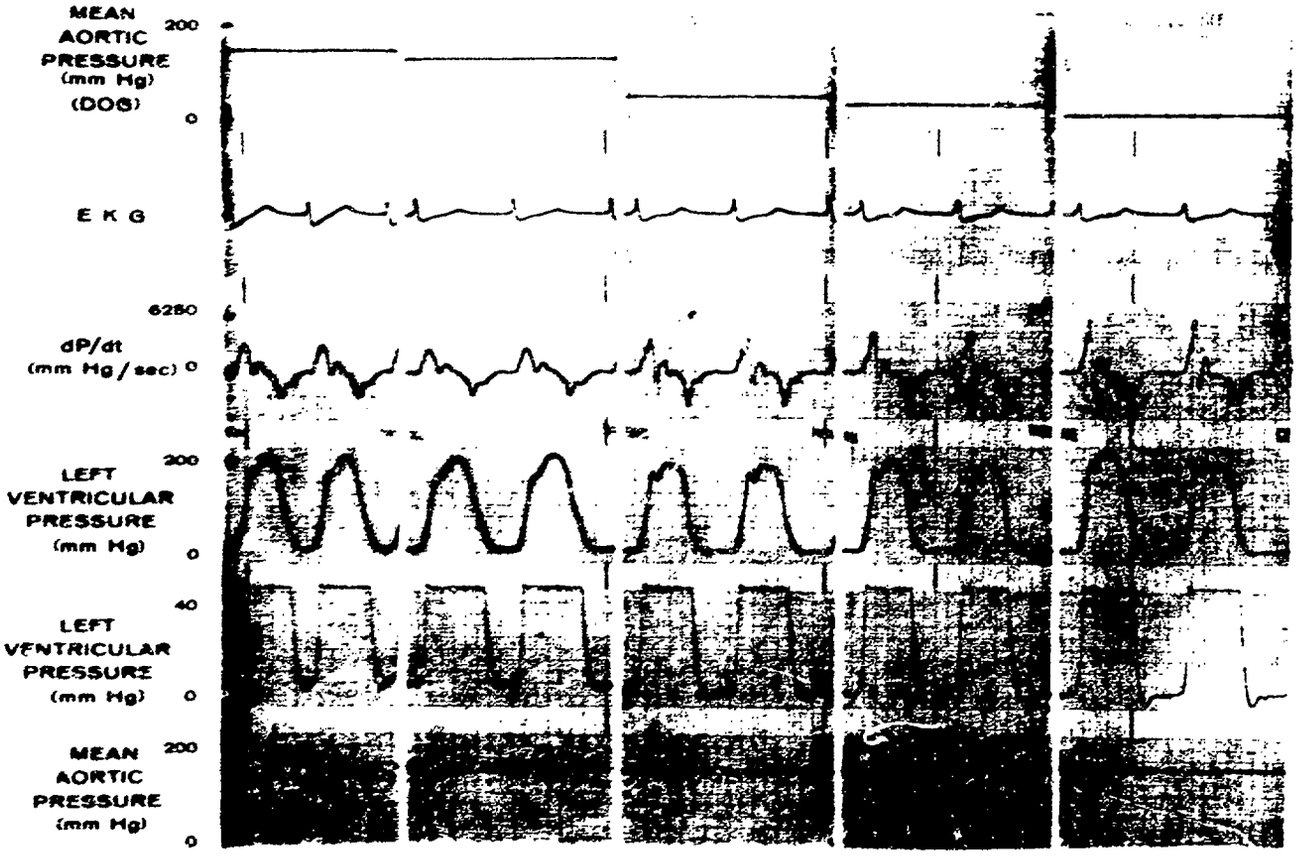
Figure 4a. Effect of endotoxin administration in acutely pancreatectomized animals on myocardial performance (14 experiments). (Performance responses evaluated at 100 and 150 mm Hg afterload in all controls and experimentals except the latter in which severe degree of heart failure prevented attainment of afterload.)
Control hearts (N = 7); acute pancreatectomy without endotoxin. Mean = dashed (- - - - - - - - -) line; ± SE = solid (————————) line.
Experimental hearts (N = 7); acute pancreatectomy followed by endotoxin. Individual hearts represented by separate symbols.

Figure 4b. Effect of endotoxin in acutely pancreatectomized animals on coronary vascular resistance, cardiac power (work/sec) and heart rate, at variable afterloads (14 experiments). (Refer to Figure 4a for further explanation).



TIME	Pre Occlusion		+60 min During Occlusion	+120 min During Occlusion		+36 min Post Occlusion	+60 min Post Occlusion
MEAN AORTIC PRESSURE (mm Hg)	100		100	100		100	100
LVEDP (mm Hg)	+3.0	Vessels Occluded	+2.0	+3.0	Occlusion Opened	+1.5	+1.5
CORONARY FLOW (cc/min)	52		40	40		96	84
CARDIAC OUTPUT (cc/min)	502		490	490		486	494
HEART RATE (beats/min)	180		158	144		150	144
dP/dt (mm Hg/sec)	2475		2041	1937		2440	3229
POWER (work/sec)	11.0		10.9	10.8		10.9	11.0
O_2 UPTAKE (cc/min)	5.7		4.2	4.8		5.0	5.7

FIGURE 1a



TIME	Pre Occlusion	Vessels Occluded	+125 min During Occlusion	Occlusion Opened	+15 min Post Occlusion	+40 min Post Occlusion	+70 min Post Occlusion
MEAN AORTIC PRESSURE (mm Hg)	150		150		150	150	150
LVEDP (mm Hg)	+6.0		+4.0		+2.0	+1.5	+2.5
CORONARY FLOW (cc/min)	72		68		156	168	136
CARDIAC OUTPUT (cc/min)	492		488		486	498	496
HEART RATE (beats/min)	186		150		150	186	138
dP/dt (mm Hg/sec)	3543		2859		3731	5102	5625
POWER (work/sec)	[illegible]		18.1		16.3	16.8	16.6

FIGURE 1b

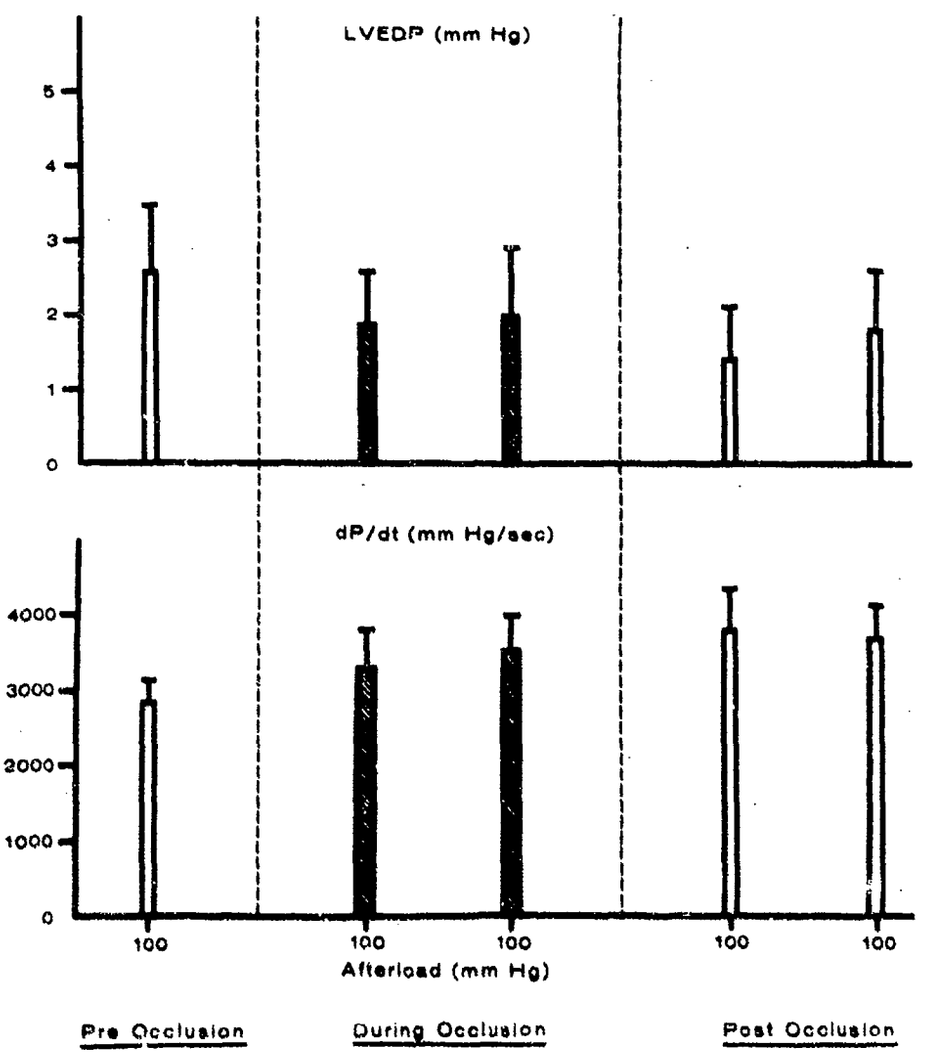

LVEDP (mm Hg)
5
4
3
2
1
0
dP/dt (mm Hg/sec)
4000
3000
2000
1000
0
100
100
100
100
100
Afterload (mm Hg)
Pre Occlusion
During Occlusion
Post Occlusion

FIGURE 2a

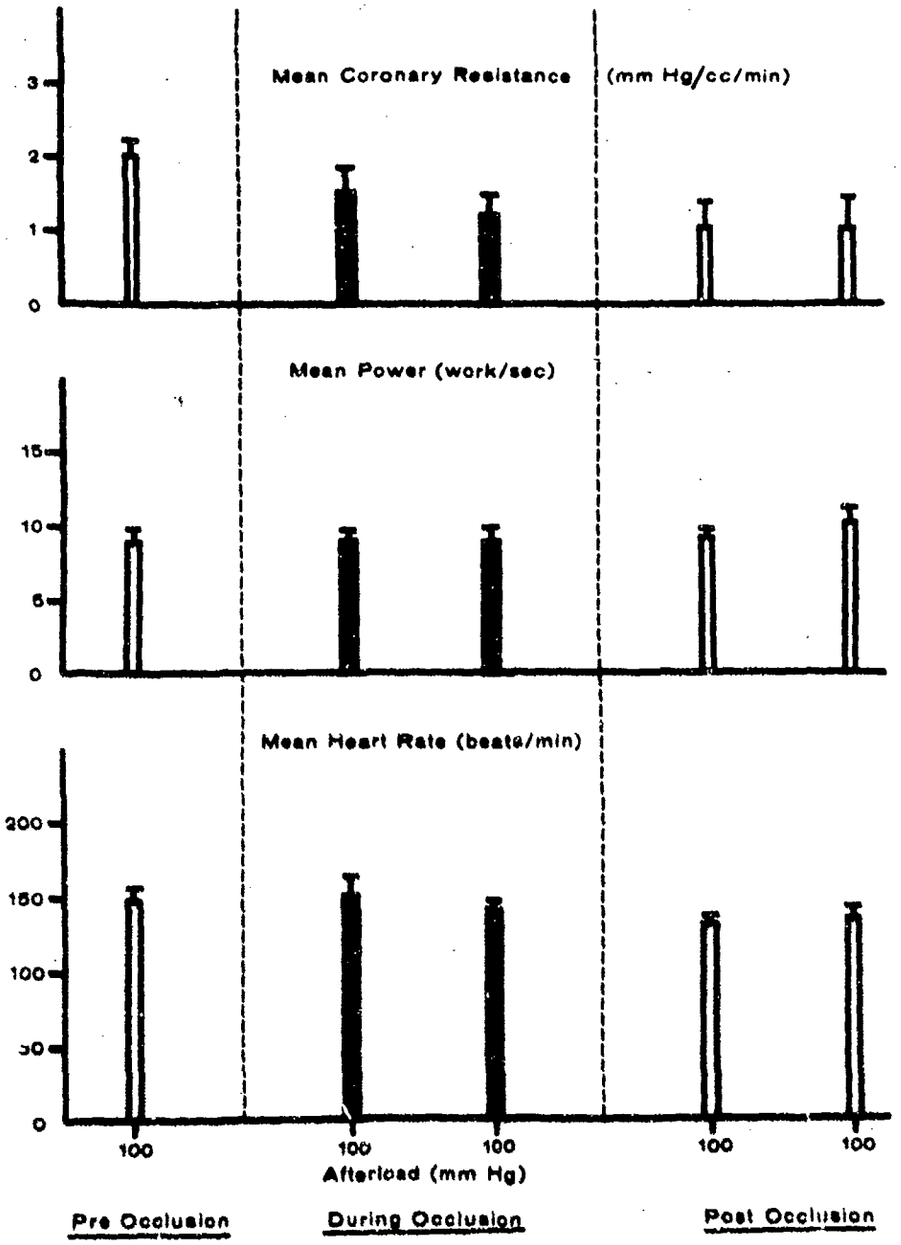
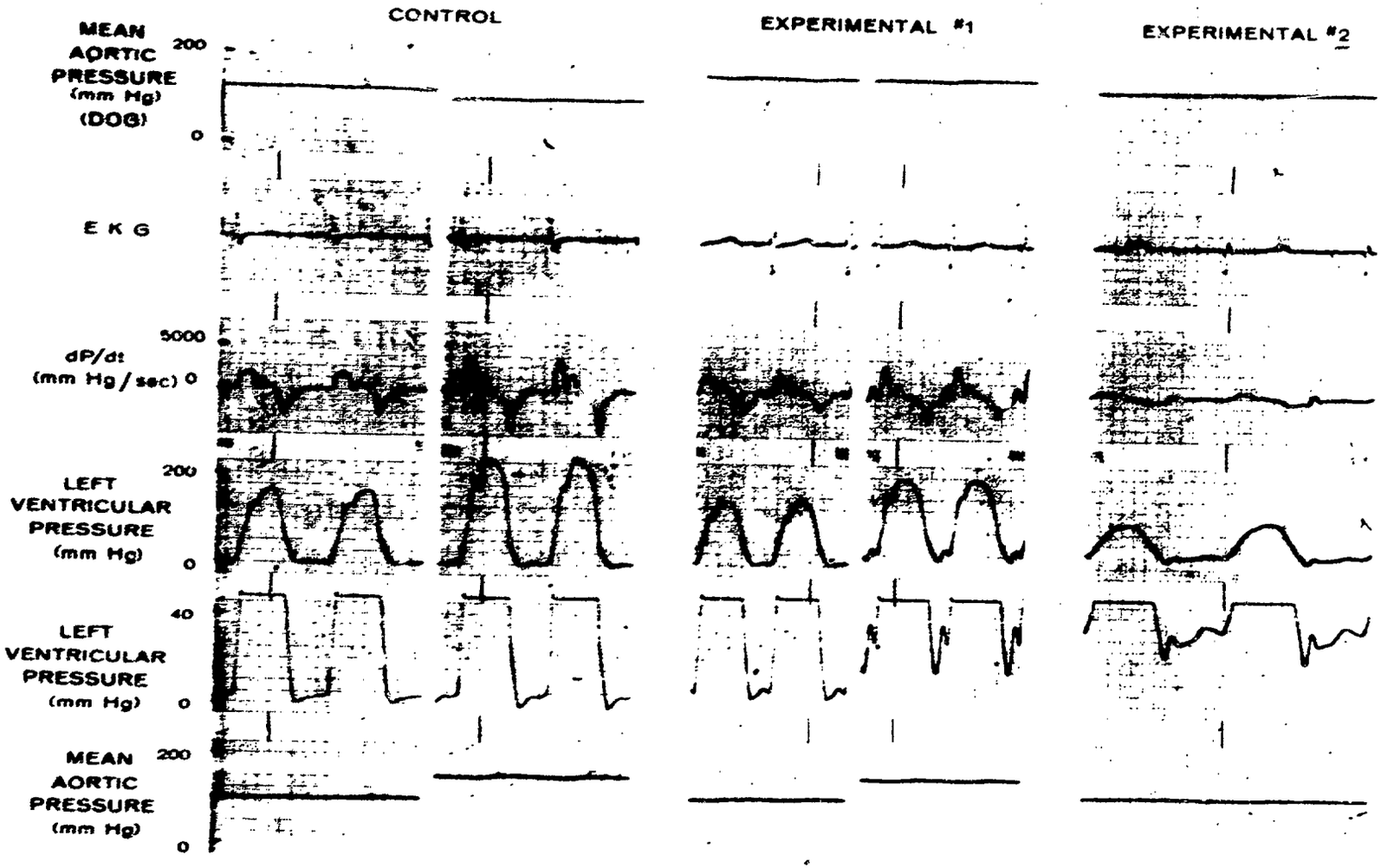

Mean Coronary Resistance (mm Hg/cc/min)
3
2
1
0
Mean Power (work/sec)
15
10
5
0
Mean Heart Rate (beats/min)
200
150
100
50
0
100
100
100
100
100
Afterload (mm Hg)
Pre Occlusion
During Occlusion
Post Occlusion

FIGURE 2b



MEAN AORTIC PRESSURE (mm Hg)	100	150	100	150	100
LVEDP (mm Hg)	+3.5	+4.5	+6.0	+29.0	+34.0
CORONARY FLOW (cc / min)	60	168	80	100	72
CARDIAC OUTPUT (cc / min)	570	588	390	390	78
HEART RATE (beats / min)	150	162	192	198	102
dP / dt (mm Hg / sec)	2041	4545	2173	3846	713
POWER (work / sec)	12.5	19.4	10.7	15.1	1.12
O_2 UPTAKE (cc / min)	5.7	7.9	4.2	7.6	–

FIGURE 3

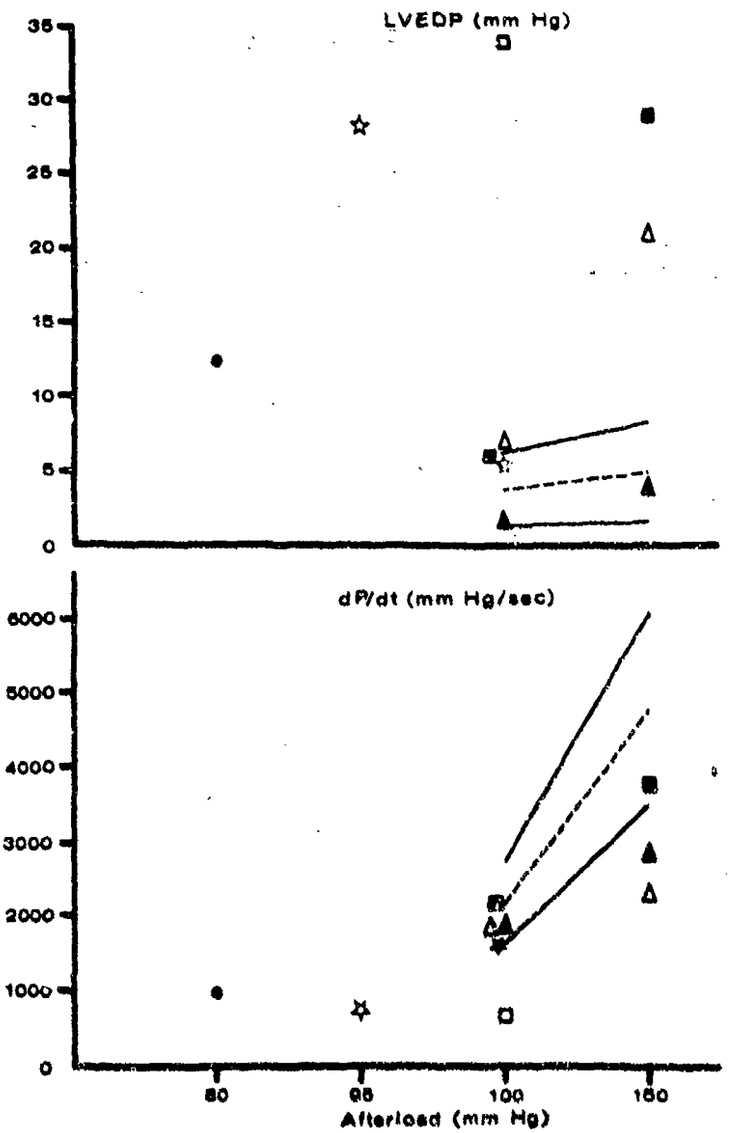

LVEDP (mm Hg)
35
30
25
20
15
10
5
0
dP/dt (mm Hg/sec)
6000
5000
4000
3000
2000
1000
0
80
90
100
150
Afterload (mm Hg)

FIGURE 4a

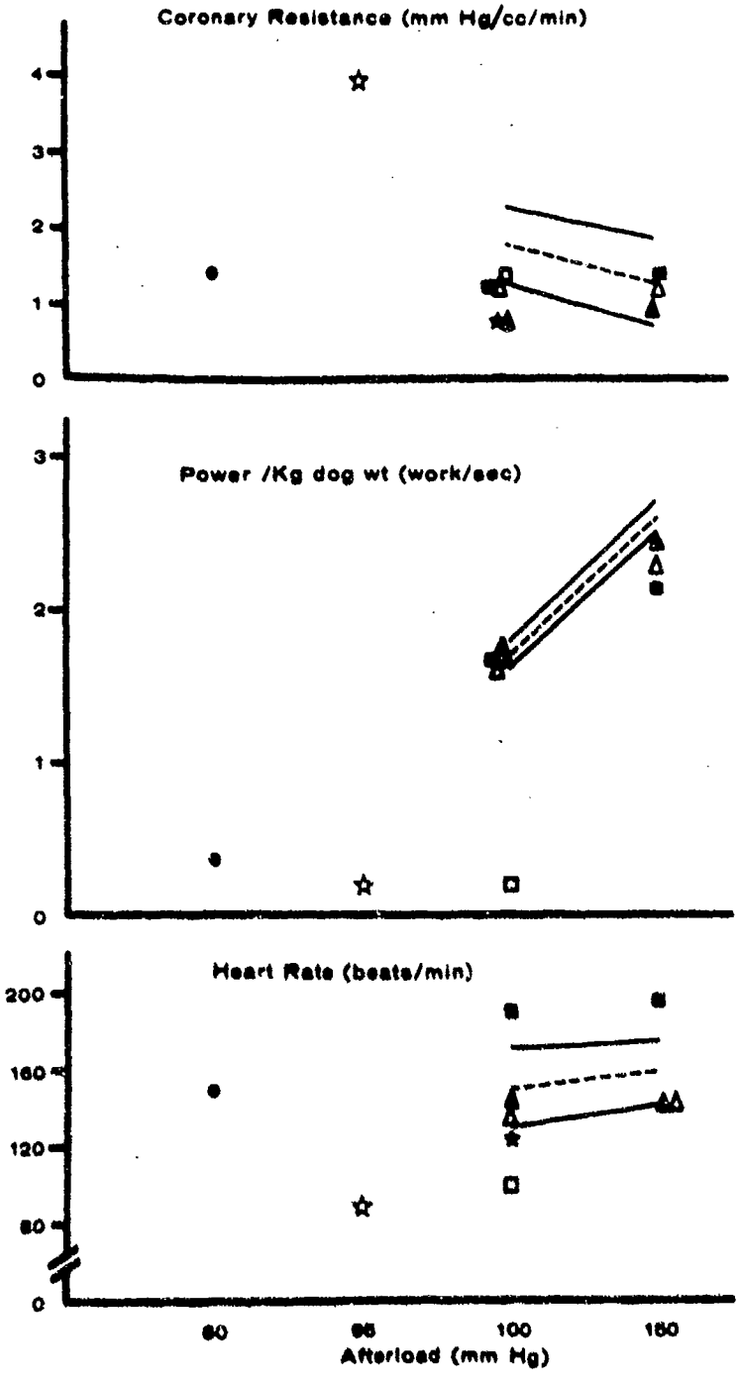

Coronary Resistance (mm Hg/cc/min)
4
3
2
1
0
Power /Kg dog wt (work/sec)
3
2
1
0
Heart Rate (beats/min)
200
160
120
80
0
60
85
100
150
Afterload (mm Hg)

FIGURE 4b

TABLE I. Effect of Splanchnic Arterial Occlusion on Mean Aortic Pressure and Heart Rate of Intact (Support) Animals (N = 7; Mean ± SE)

	Pre-Occlusion	During Occlusion		Post-Occlusion	
		60 min	120 min	0–20 min	20–90 min
Mean Aortic Pressure (mm Hg)	108 (± 7)	106 (± 12)	98 (± 12)	47 (± 9)	47 (± 13)
Mean Heart Rate	157 (± 11)	146 (± 14)	163 (± 10)	157 (± 7)	142 (± 29)

TABLE II. Effect of Splanchnic Arterial Occlusion on Oxidative Metabolism of the Heart* (Mean ± SE; 100 mm Hg Afterload)

	Pre-Occlusion	During Occlusion		Post-Occlusion	
	(N = 7)	(N = 7)	(N = 7)	(N = 7)	(N = 5)
		60 min	120 min	0-20 min	20-90 min
Mean O_2 Content (A)	17.3(±1.3)	17.0(±1.2)	15.7(±1.8)	14.4(±1.3)	15.2(±2.3)
Mean O_2 Content (V)	8.6(±1.6)	9.0(±1.4)	9.6(±1.4)	9.4(±1.0)	9.0(±1.7)
Coronary Flow (cc/min 100 gms left ventricle)	157(±29)	243(±53)	316(±63)	353(±63)	341(±95)
O_2 Delivery to Myocardium (cc/min/100 gms left ventricle)	27.8(±7.0)	39.9(±8.7)	43.7(±6.0)	47.1(±7.0)	46.3(±9.1)
Mean O_2 Uptake/ 100 gms left ventricle	11.9(±1.1)	14.2(±1.3)	15.7(±1.5)	14.9(±1.0)	14.1(±3.2)
PO_2 (A)	73(±6)	76(±8)	74(±7)	74(±4)	76(±7)
PO_2 (V)	26(±3)	34(±5)	42(±2)	43(±4)	40(±5)
PCO_2 (A)	26(±2)	29(±1)	32(±3)	28(±3)	25(±3)
PCO_2 (V)	33(±2)	34(±2)	37(±2)	34(±3)	29(±4)
Mean CO_2 Content (A)	33.0(±2.9)	29.5(±3.4)	28.3(±3.1)	22.4(±2.4)	19.6(±2.9)
Mean CO_2 Content (V)	40.3(±3.6)	35.7(±4.2)	33.5(±3.8)	26.9(±3.5)	24.7(±3.9)
Mean CO_2 Production/ 100 gms left ventricle	10.1(±0.9)	12.1(±1.2)	13.5(±1.3)	11.3(±0.5)	13.1(±1.1)
RQ	.85(±.02)	.85(±.02)	.86(±0.02)	.85(±0.07)	.81(±0.08)
pH (A)	7.37(±0.03)	7.32(±0.04)	7.24(±0.06)	7.19(±0.04)	7.22(±0.03)
pH (V)	7.34(±0.03)	7.29(±0.04)	7.22(±0.06)	7.17(±0.04)	7.21(±0.02)

*Other parameters maintained constant: cardiac output, 76 cc/min/kg; blood temperature, 37-39°C

TABLE III. Effect of Splanchnic Arterial Occlusion on Myocardial Performance and Hemodynamics (Mean ± SE; 150 mm Hg Afterload)

	Pre-Occlusion	During Occlusion		Post-Occlusion	
	(N = 7)	(N = 7)	(N = 7)	(N = 7)	(N = 5)
		60 min	120 min	0–20 min	20–90 min
LVEDP (mm Hg)	+5.1(±1.3)	−0.8(±0.3)	+5.4(±2.5)	+2.3(±0.7)	+2.1(±1.4)
dP/dt (mm Hg/sec)	4810(±670)	7909(±563)	3854(±604)	5513(±587)	5994(±573)
Power/kg dog wt (work/sec)	2.6(±0.1)	2.6(±0.1)	2.5(±0.1)	2.5(±0.1)	2.6(±0.1)
Coronary Flow (cc/min/ 100 gms left ventricle)	287(±54)	652(±105)	354(±114)	614(±99)	365(±73)
Heart Rate (beats/min)	130 (±15)	172 (±7)	143(±5)	128(±7)	143(±12)

TABLE IVa. Effect of Endotoxin Following Acute Pancreatectomy on Myocardial O_2 Uptake and CO_2 Production (Mean ± SE)*

	100 mm Hg (Afterload)				150 mm Hg (Afterload)			
	N	Control	N	Endotoxin	N	Control	N	Endotoxin
Mean O_2 Content (A)	6	17.0(±1.4)	4	16.7(±1.6)	6	17.1(±1.7)	3	16.1(±1.9)
Mean O_2 Content (V)	6	8.4(±1.3)	4	11.7(±1.7)	6	11.0(±1.4)	3	9.3(±2.8)
Mean O_2 Uptake/ 100 gms left ventricle	6	14.6(±1.2)	4	13.0(±1.8)	6	20.9(±1.8)	3	23.0(±6.2)
Mean CO_2 Content (A)	6	32.2(±4.2)	4	38.6(±1.5)	6	28.6(±4.1)	3	38.6(±1.1)
Mean CO_2 Content (V)	6	39.9(±3.7)	4	42.7(±1.6)	6	34.6(±4.7)	3	45.2(±0.5)
Mean CO_2 Production/ 100 gms left ventricle	6	12.0(±1.3)	4	11.0(±2.2)	6	20.5(±2.0)	3	22.1(±4.9)
RQ	6	.83(±.06)	4	.83(±.06)	6	1.1(±.26)	3	.99(±.06)

*Due to intervention of heart failure, not all hears could sustain the indicated afterloads. In addition, only 6 of 7 controls were evaluated.

TABLE IVb. Effect of Endotoxin Following Acute Pancreatectomy on Myocardial Arterial and Venous PO_2, PCO_2 and pH (Mean ± SE)*

	100 mm Hg (Afterload)				150 mm Hg (Afterload)			
	N	Control	N	Endotoxin	N	Control	N	Endotoxin
PO_2 (A)	7	66 (±4)	4	71 (±3)	7	69 (±4)	3	63 (±6)
PO_2 (V)	7	28 (±2)	4	36 (±3)	7	36 (±4)	3	30 (± 4)
PCO_2 (A)	7	30 (±3)	4	29 (±2)	7	27 (±2)	3	30 (±1)
PCO_2 (V)	7	37 (±2)	4	33 (±3)	7	33 (±2)	3	37 (±1)
pH (A)	7	7.38 (±.03)	4	7.47 (±.04)	7	7.37 (±.06)	3	7.44 (±.01)
pH (V)	7	7.35 (±.02)	4	7.44 (±.04)	7	7.35 (±.06)	3	7.41 (±.00)

*Due to intervention of heart failure, not all hearts could sustain the indicated afterloads.

TABLE V. Effect of Endotoxin Following Acute Pancreatectomy on Coronary Blood Flow, Myocardial Oxygen Delivery and Oxygen Uptake (Mean ± SE)*

	100 mm Hg (Afterload)				150 mm Hg (Afterload)			
	N	Control	N	Endotoxin	N	Control	N	Endotoxin
Coronary Flow (cc/min/100 gms left ventricle)	7	180 (±23)	4	266 (±33)	7	404 (±73)	3	349 (±65)
O_2 Delivery to Myocardium (cc/min/100 gms left ventricle)	6	29.1 (±3.4)	4	42.8 (±2.8)	6	67.3 (±11.7)	3	52.2 (±1.7)
O_2 Uptake (cc/min/100 gms left ventricle)	6	14.6 (±1.2)	4	13.0 (±1.8)	6	20.9 (±1.8)	3	23.0 (±6.2)

*Due to intervention of heart failure, not all hearts could sustain the indicated afterloads.