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Research Article

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Cardiac Hemodynamics in Alcoholic Patients with Chronic Liver Disease and a Presystolic Gallop

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ABSTRACT 10 male subjects with chronic liver disease and with normal cardiovascular findings, except for the presence of a presystolic gallop, underwent right and left heart catheterization. In general, all of the patients had a high resting cardiac output, narrow arteriovenous oxygen difference, a low peripheral vascular resistance, and normal left ventricular end-diastolic pressures and volumes. The plasma volume was increased in the seven patients in which it was determined.

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INTRODUCTION

A hyperkinetic circulatory state has been described in chronic liver disease (1–3). However, despite the number of published studies, there is considerable uncertainty concerning the character of the hemodynamic changes in this entity. This uncertainty can be attributed to a number of factors: (*a*) these studies have been limited to right heart catheterizations so that left ventricular function could not be precisely analyzed; (*b*) the cardiac status of the patients was not clearly defined; and (*c*) more importantly, most of the data available on the effects of alcohol on the cardiovascular system has been derived from acute infusion studies on human beings or animals (4–6).

The following report describes the circulatory changes at rest and during exercise, in 10 patients with chronic liver disease, all of whom had an elevated resting cardiac output.

METHODS

Selection of patients. 10 hospitalized male patients, ages 41–58, with clinical and laboratory evidence of chronic parenchymal disease of the liver were studied. Results of laboratory studies in these patients are shown in Table I. All gave a long history of excesive intake of alcoholic beverages, and none of the patients had either ascites or peripheral edema. In addition, a liver biopsy established the diagnosis of Laënnec's cirrhosis in seven patients and fatty infiltration of the liver in one patient (case No. 6). Patient Nos. 2 and 10, who had the laboratory and clinical evidence of advanced Laënnec's cirrhosis, did not have a liver biopsy because of a very low prothrombin time. All of the patients had been hospitalized for several weeks and were receiving nutritious diets.

An electrocardiogram, vectorcardiogram, double master's 2 step test, and chest X-ray were obtained in every subject, and revealed no abnormalities. During the selection phase of the study, it was observed that some patients with Laënnec's cirrhosis had a presystolic gallop while other patients did not show this finding. To maintain uniformity, only patients with a definite presystolic gallop, confirmed by a phonocardiagram, were selected for inclusion in the study. (Fig. 1). The procedure was explained in detail to the subjects and the investigative nature of the study was stressed. An informed consent was then obtained from all of the patients.

Procedures. Catheterization of the left ventricle was performed by retrograde arterial catheterization through a brachial arteriotomy. A Cournand needle was placed into the opposite brachial artery. To insure high fidelity tracings,

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TABLE I
Clinical Data

Patient No.	Age	BUN	Serum Na	Serum K	Albumin globulin	Hct	Serum bilirubin	Ceph. Floc.	Alkaline phosphatase
	yr	*mg/100 ml*	*mEq/liter*	*mEq/liter*	*gm/100 ml*	*%*	*mg/100 ml*	*48 hrs*	*shinowara units*
1	58	10	136	4.5	3.0/5.4	30	2.3	Neg	16.7
2	50	4	136	4.7	2.6/6.3	38	1.2	Neg	10
3	49	5	135	3.5	3.7/3.7	39	2.1	Neg	7.3
4	44	4	145	5.5	3.2/3.8	43	1.2	Neg	8.9
5	56	15	133	4.2	3.1/3.2	38	1.1	Neg	7.7
6	44	9	140	4.7	4.2/3.9	40	0.3	Neg	3.4
7	41	11	134	4.1	3.4/3.7	39	2.7	Neg	15.3
8	46	11	135	4.3	3.6/3.9	39	0.4	Neg	7.6
9	41	7	138	4.8	3.7/5.4	42	0.8	Neg	6.6
10	44	12	142	4.6	2.5/4.0	38	2.8	4+	12.6

the needle was directly connected to a Statham pressure transducer, model P23Db. The first derivative of the brachial artery pressure could then be computed by a R-C differentiating circuit. This system provides a uniform response to frequencies of 40 cycle/sec. A No. 7 Goodale-Lubin catheter was placed in the pulmonary artery. Cardiac output was determined in duplicate by the Fick technique, and the results did not differ by more than 7%. Oxygen consumption was determined by measuring ventilation with a Tissot spirometer, and analyzing the expired gas with a Micro-Scholander apparatus. Two tonometers were used for the gas collections, and the results of the analysis of the two gas samples had to agree by 0.04%. Mixed venous blood was obtained from the pulmonary artery and arterial blood from the brachial artery. Arterial and mixed venous oxygen contents were determined by the method of Van Slyke and Neill. The blood samples were analyzed in two different machines, and the results did not differ by more than 0.2 vol/100 ml.

Left ventricular, pulmonary arterial and systemic arterial pressures, and cardiac output were measured in the resting state. All pressures were obtained using the mid-thoracic level as the reference point. The brachial artery dp/dt and the left ventricular dp/dt were also obtained. The latter was recorded through a catheter manometer system using a R-C differentiating circuit and a 15 cycle/sec filter. Measurements were made only when the pressure curves showed an undistorted wave form. The frequency response of this system is uniform to 15 cycle/sec. Calibration of the derivative was carried out by electrical introduction of a straight line pressure trace at maximum paper speed. A calibration factor K was derived from deflection of the first derivative as it related to height and slope of the pressure trace.

The left ventricular end-diastolic volume was calculated cineangiographically, in eight patients in the resting state, using a method based on the uniplanar modification of the methods of Dodge et al. (7) and Klein et al. (8). Ventriculograms were taken in the 30° right anterior oblique projection with a fixed distance from X-ray tube to table top. Cine films of a grid were made at the approximate level of the cardiac apex. The projected distance of this grid image was adjusted until actual and projected measurements were matched to provide left ventricular silhouettes free from the error of distortion and magnification. The end diastolic area (A) of the image was obtained by planimetry. The long axis (L) was measured directly. The width (W) was calculated from the equation $W = 4A/\pi L$. The left ventricular end-diastolic volume (LVEDV) was then obtained from the equation $LVEDV = 4/3\ \pi \times (W/2)^2 \times L/2$.

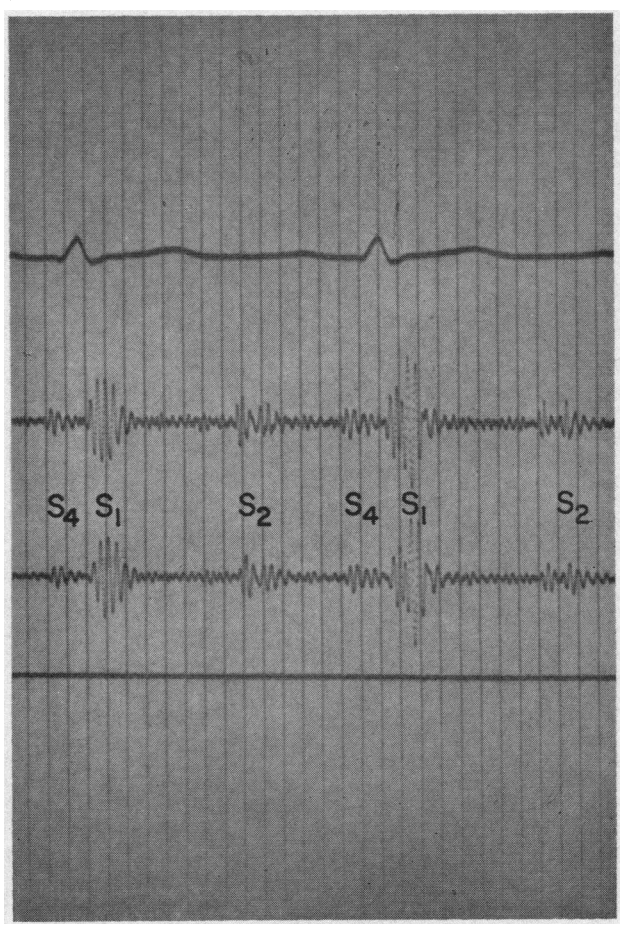

FIGURE 1 Phonocardiogram from patient No. 4 with high cardiac output and Laënnec's cirrhosis. Note the prominent presystolic gallop.

Approximately 15 min after the left ventricular angiogram the patient's feet were elevated 5 cm off the table and attached to a bicycle ergometer. The pressure in the pulmonary artery as well as the pressures and first derivative in the left ventricle and brachial artery were found to be unchanged from the control values. Thus, the dye injection and the minimal elevation of the legs and no effect on cardiac pressures. The patients then pedalled the bicycle ergometer for 6–7 min in the supine position. Pressures and cardiac output were measured 5 min after the onset of exercise. An aortic root angiogram was also performed to evaluate the patency of the coronary arteries.

TABLE II
Complete Hemodynamic

Patient No.	Experimental state	RA mean	RV S/D	PA S/D	M	LV S/End-D	LV A wave	LV dp/dt	BA S/D	M	BA dp/dt	Rate	SET	SET Rate correction
		mm Hg	*mm Hg*	*mm Hg*		*mm Hg*	*mm Hg*	*mm Hg/ sec*	*mm Hg*		*mm Hg/ sec*	*beats/ min*	*sec/beat*	
1	Rest	0	16/0	16/7	10	95/0		1380	128/75	93	386	115	0.32	0.51
	Exercise			50/17	28	125/16	20	1670	130/70	90	600	125	0.32	0.52
	Rest	0	20/0	20/7	12	120/3	5	1400	120/70	87	415	88	0.34	0.48
	Exercise			34/12	19	140/10	17	2270	140/75	97	710	125	0.34	0.54
3	Rest	3	25/3	25/12	16	128/6		1350	128/70	90	480	65	0.34	0.44
	Exercise			46/20	28	135/22	27	2300	155/80	105	910	84	0.36	0.49
4	Rest	1	22/1	22/10	14	96/10	13	1390	92/58	70	378	88	0.32	0.46
	Exercise			50/26	34	145/28	32	1920	145/85	107	575	150	0.32	0.56
5	Rest	1	25/1	25/8	13	137/5		1600	135/70	92	610	88	0.28	0.42
	Exercise			50/20	30	170/20		1820	178/88	118	1380	115	0.30	0.48
6	Rest	0	23/0	23/10	15	150/11	14	1320	150/85	107	630	75	0.32	0.44
	Exercise			47/20	30	160/18	22	2030	170/100	124	700	84	0.36	0.49
7	Rest	0	20/0	20/8	12	140/5	8	1550	140/70	94	540	75	0.28	0.40
	Exercise			45/17	26	155/18	21	2000	170/90	117	685	115	0.30	0.48
8	Rest	3	32/3	32/13	20	150/8		1000	152/88	110	560	84	0.32	0.45
	Exercise			50/25	34	175/25	28	3000	185/100	129	960	100	0.34	0.50
9	Rest	3	37/3	37/12	20	145/7		1085	145/87	106	575	84	0.27	0.40
	Exercise			55/22	33	162/18	23	1400	165/87	113	950	107	0.28	0.45
10	Rest	0	23/0	23/10	15	125/7		1980	130/75	93	505	79	0.34	0.47
	Exercise			43/20	27	162/18		2370	175/90	118	785	107	0.34	0.51

SET = systolic ejection time; M = mean; PA = pulmonary artery.

Left ventricular function was assessed according to the following parameters:

1) $LVSW = LV_S - (LV_D)/100 \times SI \times 1.36 \times 1.050$.
2) $LVSP = LVSW/SEP$.
3) $MSER = SI/SEP$.
4) $TTI_B = LV_s \times SEP$.
5) $TTI_m = LV_s \times SEP \times HR$.
6) $LVW = CI \times (1.36 \times 1.050)/100 \times BA_m$.
7) $PR = (BA_m \times 1332)/(CO)$.

Where BSA = body surface area in square meters; LVSW = left ventricular stroke work (g-M/beat/m² BSA); SI = stroke index (ml/beat/m² BSA); LV_s = mean left ventricu-

Data on the 10 Patients

Arterial saturation	A-V O_2 difference	O_2 consumption	CI	SI	LVSW	LVSP	MSER	TTI_B	TTI_M	LV work	Peripheral resistance
%	*vol/100 ml*	*ml/min/m²*	*liters/ min/m²*	*ml/beat/ m²*	*g-m/beat/ m²*	*g-m/beat/m²/ systol sec*	*ml/beat/m²/ systol sec*	*mm Hg/ sec/beat*	*mm Hg/ sec/min*	*kg-m/ min/m²*	*dyne-sec-cm^{-5}*
95	3.1	130	4.2	37	50	156	109	30	3495	5.6	1075
91	4.7	214	4.54	37	58	181	116	40	5000	5.8	970
98	3.8	180	4.75	54	90	264	159	41	3590	5.9	768
91	6.0	475	7.9	63	117	344	185	48	5940	11.0	516
94	2.6	132	5.1	78	136	400	230	44	2830	6.6	748
94	6.7	369	5.52	55	89	248	153	49	4100	8.3	810
97	2.7	122	4.51	52	64	200	163	31	2700	4.5	675
88	6.9	382	5.54	37	62	193	116	46	6850	8.5	840
97	3.3	164	4.96	57	108	386	203	38	3380	6.5	857
97	6.2	244	3.93	34	73	243	113	51	5860	6.6	1390
98	3.5	144	4.11	55	110	344	172	48	3600	6.3	965
99	6.1	308	5.0	60	122	340	167	58	4840	8.9	908
98	4.0	176	4.41	59	114	402	211	39	2940	5.9	910
97	7.7	290	3.77	33	65	217	110	46	5340	6.3	1320
94	3.5	132	3.76	50	101	316	156	48	4040	5.9	1220
95	6.0	360	6.03	60	129	380	176	60	5950	11.0	890
99	3.4	195	5.74	68	134	496	252	39	3290	8.7	734
100	6.9	305	4.44	42	86	307	150	45	4850	7.2	1020
95	3.1	134	4.33	55	93	274	150	44	3360	5.8	930
97	6.0	350	5.84	54	111	326	159	55	5900	9.8	885

lar systolic pressure (mm Hg); LV_D = left ventricular end-diastolic pressure (mm Hg); LVSP = mean left ventricular stroke power (g-m/beat/m^2 BSA/systolic sec); SEP = mean systolic ejection period (sec); MSER = mean systolic ejection rate (ml/beat/m^2 systolic sec); TTI_B = tension time index per beat (mm Hg sec/beat); TTI_m = tension-time index per minute (mm Hg sec/min); HR = heart rate (beats/min); LVW = left ventricular work (k-m/min/m^2 BSA); BA_m = mean brachial artery pressure (mm Hg); PR = systemic peripheral resistance (dyne-sec-cm^{-5}); CO = cardiac output (ml/sec); 1.36 = conversion factor from mm Hg to cm H_2O; 1.050 = whole blood specific gravity; and CI = cardiac index (liters/min/m^2).

Shortly after the cardiac catheterization, blood volume determinations were performed on seven subjects, utilizing the ^{131}I-labeled serum albumin method.

RESULTS

Complete hemodynamic data on all 10 patients are presented in Table II. In addition, average values and the per cent change from the control values after exercise are listed in Table III.

Observations at rest. In general, all patients had normal cardiac pressures. The first derivative of the brachial artery pressure was subnormal in these subjects, ranging from 378 to 630 mm Hg/sec with an average of 508. The normal brachial artery dp/dt determined in 12 patients in our laboratory ranged from 607 to 980 mm Hg/sec with an average of 717. This is similar to the results obtained by Mason and his associates (9) who found in 23 normal patients that the average brachial artery dp/dt was 811 ±185 mm Hg/sec. The left ventricular first derivative averaged 1406 mm Hg/sec with a range of 1000–1980 mm Hg/sec.

The cardiac index was increased in all patients, averaging 4.59 liters/min per m^2, and was associated with a relatively low peripheral resistance. The resting heart rate tended to be normal, and the elevated cardiac output was due primarily to the increased stroke index. The arterio-venous oxygen difference was decreased in all subjects, with an average of 3.3 vol/100 ml.

As shown in Table IV, the left ventricular end diastolic volumes varied from 63 to 95 cc/m^2, normal 70 ±20 (10). The aortic root angiograms visualized the coronary arteries in all of the patients, and within the limitations of this technique, no abnormalities were observed.

Effects of exercise. The oxygen consumption increased by 119% and the arterio-venous oxygen difference widened by 91%. The cardiac index rose by 14%; this was associated with an 8% rise in the peripheral resistance. The rise in the cardiac index was due to the 32% increase in the heart rate; the stroke index fell by 16%. In cases 5, 7, and 9 the cardiac index and stroke index actually declined during exercise. The

TABLE III

Average Changes of Hemodynamic Parameters before and after Exercise

	Rest	Exercise	Per cent change	*t* value	Significance level
Oxygen consumption, *ml/min/m^2*	151	330	+119%	−7.22	0.1%
Stroke index, *ml/beat/m^2*	57	48	−16%	1.89	
Systemic peripheral resistance, *dyne-sec-cm^{-5}*	888	955	+8%	−0.75	
Brachial artery systolic pressure, *mm Hg*	132	161	+22%	−6.18	0.1%
Pulmonary artery systolic pressure, *mm Hg*	24	47	+96%	−12.47	0.1%
Arteriovenous oxygen difference, *vol/100 ml*	3.3	6.3	+91%	−11.32	0.1%
Cardiac index, *liters/min/m^2*	4.59	5.25	+14%	−1.47	
Pulse rate, *beats/min*	84	111	+32%	−5.35	0.1%
Left ventricular stroke work, *g-m/beat/m^2*	100	91	−9%	0.86	
Left ventricular stroke power, *g-m/beat/m^2/systol. sec*	324	278	−14%	1.34	
Mean systolic ejection rate, *ml/beat/m^2/systol. sec*	181	145	−20%	−2.16	
Left ventricular work, *kg-m/min/m^2*	6.2	8.3	+34%	−2.94	5%
Tension time index per minute, *mm Hg/sec/min*	3323	5463	+65%	−7.79	0.1%
Tension time index per beat, *mm Hg/sec/beat*	40	50	+25%	−9.28	0.1%
Left ventricular end diastolic pressure, *mm Hg*	6.0	19	+216%	−10.40	0.1%
Brachial artery dp/dt, *mm Hg/sec*	508	826	+63%	−5.12	0.1%
Left ventricular dp/dt, *mm Hg/sec*	1406	2078	+50%	−4.03	0.5%
Systolic ejection period, *sec/beat*	0.31	0.33	+6%	−4.19	0.5%
Systolic ejection period, *rate corrected*	0.45	0.50	+11%	−7.86	0.1%

TABLE IV
Ventricular Volumes

Patient No.	End-diastolic volume	End-diastolic volume
	cc	*cc/m²*
2	120	68
4	115	63
5	121	70
6	181	84
7	180	95
8	117	61
9	171	85
10	131	71

mean systolic ejection rate, left ventricular stroke work, and left ventricular stroke power fell, mainly due to the decrease in the stroke index. The brachial artery systolic pressure rise of 22% and the 32% increase in heart rate explain the 65% increase in the tension time index per minute. The left ventricular and brachial arterial dp/dt rose 50 and 63%, respectively, due presumably to an increase in the left ventricular contractility. The left ventricular end diastolic pressure rose 216% with exercise and prominent left atrial A waves were observed in the left ventricular pressure recordings.

Blood volume. The total blood volume was elevated in the seven subjects. Most of the increase was in the plasma volume fraction with only a slight change in the red cell mass (Table V).

DISCUSSION

All of the patients selected for this study had chronic liver disease, with normal cardiovascular findings, except for the presence of a presystolic gallop. It has recently been demonstrated that a presystolic gallop is a characteristic finding in patients with nonobstructive primary myocardial disease (11), and the presence of the presystolic gallop in the present group of patients suggested that they, too, might have a hemodynamic abnormality. All of the patients with the presystolic gallop had, at cardiac catheterization, a high resting cardiac output, narrow arterio-venous oxygen difference, and a low peripheral vascular resistance. Murray, Dawson and Sherlock (3) also observed that, in general, patients with portal cirrhosis and a high cardiac output have an associated presystolic gallop. We recently studied three additional alcoholic patients without a presystolic gallop who had a high resting cardiac output. Therefore, we can conclude that the presence of a presystolic gallop is not an invariable finding in the high output state.

The warm skin and bounding pulse previously described (3) in patients with a high blood flow and low peripheral resistance were not present in our patients. Tristani and Cohn (12) had also observed that the presence of a bounding pulse and warm skin were not invariably accurate in predicting the hemodynamic status of an individual patient. Since these physical signs are so subjective, errors in over, and underestimating their importance can be easily made.

The genesis of the gallop in this group of patients is open to question. The usual explanation of an altered left ventricular compliance cannot be applied since this group had normal resting left ventricular end-diastolic volumes and pressures. A prominent left atrial A wave was not seen in the normal pulmonary artery wedge recordings or in the left ventricular pressure pulse recordings. There are, however, two additional possible explanations: (*a*) the high cardiac output produced the fourth heart sound, and/or (*b*) a decrease in left ventricular contractility is the initiating event. It is difficult to separate and evaluate these two factors. However, there is considerable evidence which supports alcohol's depressant action on cardiac contractility. Wendt and his coworkers (13) have recently demonstrated in chronic alcoholics a consistently negative

TABLE V
Blood Volumes

Patient No.	Plasma volume			RBC volume			Total blood volume		
	ml	*ml/kg*	*ml/cm ht.*	*ml*	*ml/kg*	*ml/cm ht.*	*ml*	*ml/kg*	*ml/cm ht.*
2	4320	59.2	23.8	2300	31.5	12.7	6620	90.7	36.5
4	3980	63.2	22.5	2900	46.1	16.4	6880	109.3	38.9
5	3840	60.9	23.0	2140	33.9	12.8	5980	94.8	35.8
6	4000	44.5	20.8	2300	25.8	12.1	6230	70.3	32.9
7	3650	51.5	20.5	2280	32.2	12.8	5930	83.7	33.3
8	3810	49.4	21.1	2140	27.7	11.9	5950	77.1	33.0
9	3740	41.5	21.4	2660	29.5	15.2	6300	70.0	36.0
Normal values		40	16		30	12		70	28

myocardial balance of isocitric dehydrogenase and malic dehydrogenase. These findings suggested to these authors that intramitochondrial enzymes are affected by clinical alcoholism even in patients without clinical, hemodynamic, or other biochemical evidence of heart disease. Gimeno, Gimeno, and Webb (14) have studied the effects of alcohol on the isolated rat atrium and have found that an almost linear relation exists between the concentration of alcohol and the decline in myocardial contractility.

We have recently catheterized five normal patients with functional murmurs and determined their left ventricular maximum dp/dt utilizing a catheter manometer system. The left ventricular first derivative averaged 1756 mm Hg/sec with a range of 1562–2146 mm Hg/sec. In comparing the left ventricular dp/dt in our present group of patients to these normal controls, we found that 8 out of 10 patients had a low left ventricular derivative. Since the catheter manometer system has a low frequency response and may be subject to error (15), these data only suggest that these patients have a depressed resting left ventricular contractility. However, other workers (16, 17) have shown that the conventional catheter system using R-C differentiating circuits provide a satisfactory method for recording dp/dt in human subjects up to a peak dp/dt of 2000 mm Hg/sec. Further, 95% of the energy components of significance occurred at 15 cycle/sec or less, even for high heart rates.

The brachial artery dp/dt was markedly decreased in all of the subjects. In fact, such low derivatives have only been recorded in patients with severe aortic stenosis (9, 18). An increase in the heart rate, stroke volume, mean aortic pressure, contractility, or peripheral vascular resistance will produce an increase in the maximal brachial artery dp/dt, while a decrease in these parameters will lead to a decline in the brachial artery dp/dt (18). The low brachial artery first derivative in our patients can best be explained by the low peripheral resistance. From the clinical standpoint, the tactile sensation of a rapidly rising pulse seen in aortic insufficiency correlates directly with an elevated brachial artery dp/dt, while a slow rising pulse seen in aortic stenosis correlates with a diminished first derivative (18). A decreased first derivative thus supports the clinical finding in our patients of a weak rather than a bounding pulse.

Many factors have been invoked to explain the high resting cardiac output. The plasma volume, as measured by the Evans blue dye method, has been characteristically increased in these high output patients (2, 3). In our present study, we were able to verify these observations. Murray and his associates (3) demonstrated that an increased portal venous network did not account for the increased blood volume in portal cirrhosis, as patients with extra hepatic portal vein obstruction had virtually normal blood volumes. These workers also demonstrated a high cardiac output in a patient with subacute hepatitis and liver failure who showed no portal collateral circulation at autopsy. They concluded that (*a*) some degree of liver failure is the essential factor in producing the high cardiac output, but extra hepatic portal systemic shunting can be contributory, and (*b*) the association of increased cardiac output and a portal systemic collateral circulation may represent merely two independent aspects of a progressive chronic disease, or they may be more casually related, due to shunting away from the liver of some vasodilator substance normally metabolized by the parenchymal cells.

An increased plasma volume has been correlated with arterial desaturation due to shunting of systemic venous blood through pulmonary arteriovenous anastomoses (19). None of the patients in the present series were unsaturated at rest, and if such shunts were present they were probably of little significance. However, during exercise patients No. 1, 2, and 4 did become unsaturated.

Anemia is associated with an elevation of the cardiac output when the hematocrit is about 20% (20). Anemia of such a degree was not seen in our patients, and this does not adequately explain the elevated output. However, a mild anemia may lead to a minimal increase in the cardiac output.

Beriberi heart disease is not a likely diagnosis. All of the patients were well nourished, and clinical evidence of thiamine deficiency was not present, i.e., heart failure, cardiac enlargement, or neuritis.

Anxiety which may elevate the cardiac output was not present in our subjects. They were hospitalized for several weeks, and revealed no overt resentment to the absence of liquor. Furthermore, the high cardiac output was not caused by an increase in the oxygen consumption, but was due to a narrow arteriovenous oxygen difference.

The increase in the cardiac output, as first proposed by Kowalski and Abelmann (1), is probably due to generalized peripheral arteriolar dilatation, acting in effect like multiple arterio-venous shunts in parallel.

Do these patients with an increased resting cardiac output tolerate the added circulatory burden without decompensation? Abelmann, Kowalski, and McNeely (21) determined that with mild exercise the cardiac output rose above normal values in 9 out of 11 patients with high resting cardiac outputs, and with no evidence of cardiovascular abnormalities on clinical examination. They concluded that there was no evidence of a decrease in the cardiac reserve, but added that the hemodynamic response of such patients to maximal exercise

and the end-diastolic ventricular response during exercise remains unknown.

Ross and his associates (22) have determined that the normal response of the left ventricle to exercise is characterized by a fall or no change or a minimal increase ($\leqq 2$ mm Hg) in the left ventricular end diastolic pressure. Gorlin et al. (23) also noted only minimal changes in the left ventricular end-diastolic pressure during exercise in 20 patients without heart disease or with mild valvular lesions.

None of our patients had a normal exercise response. They demonstrated a significant increase in the left ventricular end diastolic pressure and mean pulmonary artery pressure, and prominent atrial A waves were observed in the left ventricular recordings. In spite of this very forceful left atrial contraction, in seven patients the stroke index remained the same or fell. It appears reasonable to consider that such an increase in the left ventricular end-diastolic pressure should be associated with an increase in the left ventricular end diastolic volume. Since volume was not measured during exercise in this study, this must remain an inference.

Recently, Regan and his associates (24) studied a group of alcoholic patients, who had normal cardiovascular findings and mild to moderate amounts of fat, without cirrhosis on liver biopsy. They progressively elevated the aortic pressure with infusions of angiotensin and observed the relationship of ventricular filling pressure to stroke output and work of the left ventricle. During the infusion of angiotensin in control subjects, there was a progressive rise in stroke output as end-diastolic pressure increments were produced. In the alcoholic subjects, a greater rise in ventricular end diastolic pressure occurred while stroke output failed to increase. They observed that this hemodynamic relationship resembled the findings in patients with known cardiac disease. Their observations, taken in conjunction with our findings, demonstrate that the alcoholic patients without clinical evidence of cardiac disease can exhibit an abnormal ventricular response to exercise or an after load test. It would appear reasonable to assume that the excessive intake of alcohol is associated with an impairment in the metabolic and contractile properties of the left ventricle, and the resultant hemodynamic effects may not be readily discerned in the resting state. Our study also demonstrates that patients with an increased plasma volume or a congested circulation as described by Eichna (25) can, under stress, show abnormal cardiac dynamics.

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