MEDICAL REASONS FOR PROHIBITION:
Cardiac Consequences of Alcoholism

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INTRODUCTION

The Divine Commandment concerning the prohibition in Islam is categorical, undeniable and unquestionable.[1] The attitude of Islam toward the type and quantity of alcoholic beverages is, from the saying of Prophet clear and unambiguous.[2] The non-believers and non-conformists alike have questioned the ethical and medical consequences of consuming small amounts of alcohol. It is argued that small amounts that do not intoxicate are neither prohibited nor injurious. The fact that alcohol at least in moderate amounts has been used for medicinal purposes lends credence to this notion.

It behooves the faith that logic and "scientific evidence" has to be presented to the non-conformist to convince him the value of practicing divine laws. Prohibition appears no exception. This study was undertaken to assess the cardiotoxicity of alcohol in non-intoxicating doses in normal man and of chronic use in moderate amounts in both man and experimental animal.

MATERIAL AND METHODS

The effects of acute administration of alcohol were studied in nine normal volunteers, 23-30 years of age, who had a history of infrequent ingestion of alcohol. Six ounces of 43% alcohol in the form of diluted scotch whiskey was administered to six subjects over a two hour period (Group I). To evaluate the effects of rate of administration, five subjects were fed the alcohol over a one hour period (Group II). Two ounces were ingested during the first 15 minutes in both groups and the remaining four ounces during the next 105 minutes in Group I and during the next 45 minutes in Group II. To study the non-specific effects of elementation, five subjects (Group III) received an isothermic, isocaloric, and isovolumic solution of sucrose administered over one hour. All subjects were fasting and supine. All studies were done between 8 and 11 a.m.

To preclude the necessity of left ventricular catheterization in this group of normal volunteers, the systolic time intervals were used to provide information concerning the contractile state of the left ventricle. The technique of measuring the contractile state non-invasively has provided a valid index in patients in whose left ventricular function is not compromised by extra-myocardial hemodynamic abnormalities.[3] The systolic time intervals were measured using the method and instrumentations described by Weissler and his associates,[4] from simultaneous electrocardiograms, phonocardiograms and carotid pulse tracings on an Electronics for Medicine osciloscopic recorder at a paper speed of 200 mm/sec with time markers at 0.02 sec. (Fig. 1). The intervals were derived as reported earlier.[3]

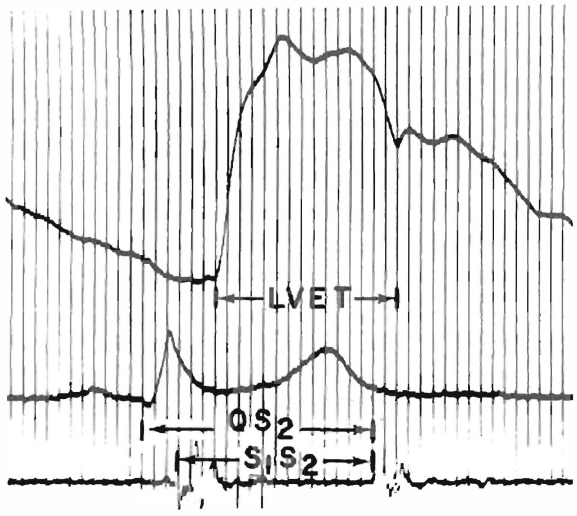

FIGURE 1:
Simultaneous recording of electrocardiogram (lead II), phonocardiogram and carotid pulse tracing at paper speed of 200 mm. sec. with time markers at 0.02 sec. The variables measured directly are Q-S2, S1 S2, and LVET (abbreviations defined under Methods) as shown. From these, PEP, and IVT are obtained by calculation. Reproduced by permission of American Heart Association.[15]

To assess the cumulative effects of long-term ingestion of ethanol, 41 patients with a history of heavy ethanol consumption and 23 normal subjects were studied by right and left heart catheterization in the basal, post-absorptive state under mild barbiturate sedation and local procaine analgesia. The 23 control subjects were studied because of heart murmur and/or cardiac symptoms. All were hemodynamically normal, none of them had an abnormal electrocardiogram or chest x-ray.[5]

The 41 patients were hospitalized with a history of ethanolism and cardiovascular symptoms, and signs,

dysrrhythmias and findings of decompensation. Informed consent was obtained in each case prior to the study.

Catheters were placed in the main pulmonary artery, left ventricular apex and aortic root. Pressures were recorded simultaneously from the left ventricle and aorta using Statham P23 Gb and Db gauges respectively and Electronics for Medicine osciloscopic recorder. The maximum rate of left ventricular pressure rise (dP/dt max) was obtained using the resistance-capicitance differentiating circuit.

Cardiac output was measured from Indocyanine green dilution curves sampled from the aortic root following pulmonary artery injection.[6] The left ventricular ejection fraction was measured by indicator dilution using Indocyanine green dye introduced into the left ventricle by rapid injection and sampling the blood in the aortic root at 2 cc/sec through a Gilford densitometer by means of a Harvard pump.[7] Validation of measuring pressures, ejection fraction and end-diastolic volume by this technique has been reported previously.[7]

Left ventricular function and contractility were estimated in several ways. Contractility was assessed by an index expressing end-isometric force-velocity relationship normalized for initial fiber length.[8] A simple ratio of dP/dt max to simultaneous left ventricular pressure was also used in accord with Levine et al.[9] The isovolumic relaxation phase of the left ventricular myocardium was assessed by measuring negative dP/dt with or without correction for simultaneous pressure and/or volume.[10]

To eliminate some of the variables, which may be operative in the production of cardiomyopathy in humans, a group of young adult male beagle dogs was maintained in a relatively normal nutritional state while receiving up to 20% of calories as ethanol, approximating the quantity reported in a population of human alcoholics.[11] Body weight, hematocrit, serum protein and electrolytes were monitored throughout. At the end of the study which lasted 18 months, these animals were anesthetized with morphine sulphate (3 mg/kg) and sodium pentobarbital (15-20 mg/kg) 18 hours after eating and placed in the right lateral position. After insertion of a cuffed endotracheal tube, respiration was regulated with a Harvard respiratory pump, to facilitate the maintenance of arterial pH, P02 and PC02 in the normal range.[12]

The hemodynamic data including pressures, outputs and volumes were obtained with the chest intact as in humans. Information regarding the myocardial function both in terms of contractile and relaxation properties was obtained as in the humans.

At the conclusion of these studies, the heart was rapidly arrested with iced Ringer's solution. Samples of the left ventricle, approximately 15 grams were taken from the peri-apical region for analysis of cation and myocardial lipids as reported earlier.[13]

Statistical analyses in each of the three experimental settings were performed using conventional methods for small samples and variations reported as standard error. The differences between the groups were evaluated by student's unpaired t test. The t test for paired samples was used to evaluate the response to the ingestion of alcohol or sucrose within the group.

RESULTS

Figure 2 shows typical results in one experiment of acute alcohol ingestion in small amounts in normal volunteers. It will be seen that over the two hours during which the subject's blood alcohol rose to 115 mg%, there was a progressive increase in pre-ejection period (PEP) and isovolumic contraction time (IVT). Left ventricular ejection time (LVET) did not change in these patients. But, because of the prolongation of PEP, the PEP/LVET ratio also increased. In Group I of normal volunteers, at the mid-point of the study (one hour), when four ounces of alcohol had been consumed and mean blood alcohol was 74 mg%, IVT was prolonged in all subjects and PEP in all but one, mean IVT and PEP/LVET had risen significantly. At the end of this study (two hours), when six ounces of alcohol had been consumed and mean blood alcohol had increased to 111 mg%, there was a further rise in mean IVT, PEP/LVET, and PEP, all of which differed significantly from pre-alcohol values. There were no significant changes in heart rate, blood pressure, QS2, and LVET (Table I, Figure 3).

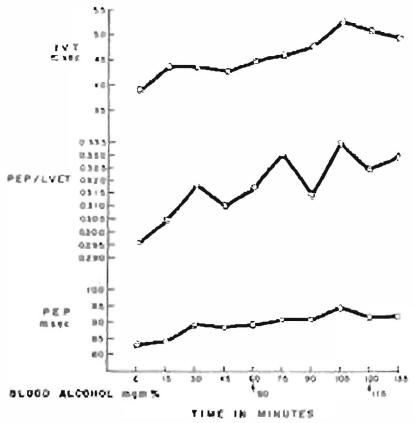

FIGURE 2:
Response of systolic time intervals to Scotch whiskey (six ounces in two hours) in a young normal adult. Reproduced by permission of American Heart Association.[15]

In the normal volunteers of Group II in whom the ingestion rate was doubled, at both the mid-point when four ounces of alcohol had been consumed in 1/2 hour (mean blood alcohol 50 mg%), and the end

TABLE I

RESULTS OF ALCOHOL OR SUCROSE INGESTION IN NORMAL SUBJECTS

Group	State*	Blood Alcohol mg%	Heart Rate	Blood Pressure S	D	$Q\text{-}S_2$	LVET	PEP	PEP/LVET	S1-S2	IVT
I											
Mean	C		63.5	121	78	389	314	90	.299	343	44
SE			3	3.1	3.1	6.7	13.5	2.2	.009	8.5	3.5
Mean	M	74.4	66.1	116	78	392	296	96	.323	348	52
SE		3.0	4	3.1	3.1	7.2	4.8	3.1	.01	7.4	4
P value, M vs C		<0.001	NS	NS	NS	NS	NS	NS	<0.05	NS	<0.01
Mean	E	110 5	66	120	83	395	298	98	.328	352	55
SE		6	3.5	4	3	6.8	5.6	2.5	.009	7.5	4.3
P value, E vs C		<0.001	NS	NS	NS	NS	NS	<0.05	<0.05	NS	<0.01
II											
Mean	C		76.2	111	71	373	289	85	.296	319	30
SE			3.5	5.9	3.5	8.8	10.6	3.9	.022	9	3.6
Mean	M	50	78.8	116	77	375	285	90	.320	323	39
SE		2.5	3.9	8.6	4.8	9.8	11.1	3.3	.048	10.5	2.5
P value, M vs C		<0.001	NS	NS	<0.05	NS	NS	<0.05	<0.05	NS	<0.02
Mean	E	107	78.7	114	76	384	289	95	.331	330	41
SE		6.1	4.8	6.9	5.2	9.2	9.7	3.7	.019	9.7	2.7
P value, E vs C		<0.001	NS	NS	NS	NS	NS	<0.05	<0.05	NS	<0.02
III											
Mean	C	84*	73.4	108	68	381	294	87	.300	332	38
SE		3.8	5.8	7.0	4.5	13.6	14.8	2.8	.023	11.4	4.3
Mean	M		73.1	108	67	385	302	83	.278	334	32
SE			5.5	5.8	5.1	12.6	13.9	2.7	.02	10.7	4.6
P value, M vs C			NS	NS	NS	NS	NS	<0.01	<0.001	NS	<0.01
Mean	E	98	78.1	109	66	368	288	78	.275	318	29
SE		5.7	6.4	6.8	5.6	14.3	16.2	3.6	.028	13.2	3.4
P value, E vs C		<0.05	NS	NS	NS	NS	NS	<0.01	<0.05	NS	<0.05

*C = control, M = midpoint of study, E = end of study, † blood sugar. Units for the systolic time intervals are msec.

point (6 ounces, one hour), the IVT, PEP/LVET were all significantly elevated above the control values. Again, there was no significant change in other systolic intervals or in heart rate or systolic pressure (Table I. Figure 3).

In contrast the drinking of isovolumic, isocaloric, and isothermic sucrose solution in group III did not affect the heart rate, blood pressure, or other systolic time intervals; a significant decrease was observed in mean IVT, PEP, and PEP/LVET. The abbreviation in systolic times and fall in ratio was observed in all subjects (Table I, Figure 3).

The average age among 41 patients with history of heavy alcohol consumption was 43 years, with range of 21-65 years. 28 black man, 6 black women and 7 white men comprised the patient population.

Symptoms in Groups I and II were limited to palpitations and angina and heart size was normal on

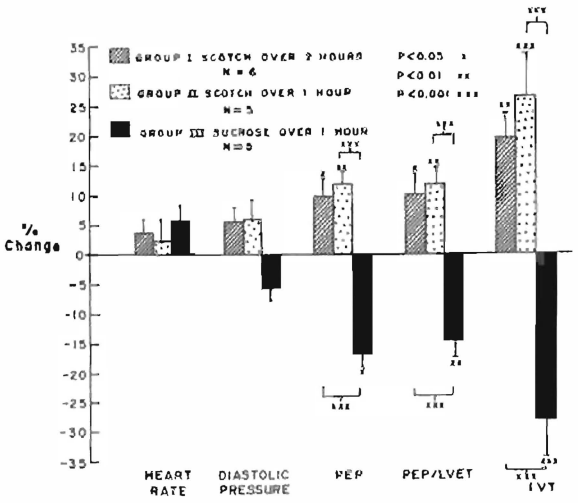

FIGURE 3:
Comparison of the peak systolic-time responses to the control solution and to alcohol at the two dose rates. Values shown are the mean percent changes from control values at the conclusion of the one or two hour study. Reproduced by permission of American Heart Association.[15]

chest x-ray. However, Group II had an enhanced left ventricular end-diastolic volume in contrast to Group I. Eighteen patients with a history of dyspnea had cardiomegaly on x-ray without evidence of mitral regurgitation (Group III). The 23 control subjects included in this study were found to be hemodynamically normal on cardiac catheterization and were similar in age. None had a history of congestive heart failure and had imbibed ethanol only on social occasions.

The significant clinical, x-ray and electrocardiographic findings are shown in Table II. The auscultatory findings of S3, S4 or ejection murmur were variable in the three groups. None amongst the Groups I and II had an abnormal heart size on x-ray. All 18 patients of Group III had an evident cardiomegaly. Electrocardiographic abnormalities included left axis deviation in three, and absence of normal septal Q in only one patient of Group I. In Group II one patient had right bundle branch block, another had left axis deviation. Septal Q waves were absent in six. All 18 patients of Group III had abnormal electrocardiograms ranging from ST-T changes or left axis deviation to conduction abnormalities. A septal Q was present in only 4/18 patients.

The hemodynamic data in these alcoholic subjects are presented in Table III and Figures 4 and 5. There was a small difference of heart rate compared to the normal controls, Group I however exhibited a small but significant difference of aortic mean pressure versus controls (Table III). The end-diastolic pressure was significantly higher than normal in Groups I and II, and was even higher in patients of Group III. The end-diastolic volume was significantly lower in Group I. By contrast, both Groups II and III had a higher volume than controls as well as Group I. Calculated end-diastolic tension was significantly higher in Group II, and more substantially elevated in patients of Group III (Figure 4). All patients exhibited a reduction in stroke volume without a significant difference between the patient groups. The index of contractility was substantially reduced in all three groups, the depression being significantly greater in Group III than in Group I. The calculated index of myocardial relaxation paralleled the findings of dP/dt max. Ohter systolic parameters exhibited progressive abnormality from Group I to Group III compared to the normal controls in terms of stroke work, mean rate

TABLE II

CLINICAL FEATURES IN ALCOHOLIC PATIENTS

Group	Age*	M/F	S_3	S_4	Apical Murmer	Abn Axis	NSR	Absent Septal Q	LAH	LVH	Increased CT Ratio
I (N = 12)	40.4	10/2	2	1	3	3	12	1	2	3	0
	± 2.4		(16)	(8)	(25)	(25)	(100)	(8)	(6)	(25)	(0)
II (N = 11)	44.2	9/2	0	3	2	2	11	6	2	2	0
	± 3.1		(0)	(27)	(18)	(18)	(100)	(55)	(18)	(18)	(0)
III (N = 18)	39.9	16/2	7	7	7	6	15	14	(13)	(14)	18
	± 2.01		(39)	(39)	(39)	(33)	(83)	(78)	(72)	(78)	(100)

*Age in years; ± = SEM; M/F = ratio of males to females; S_3, S4 = third and fourth heart sounds; Abn Axis = abnormal axis, NSR = normal sinus rhythm; LAH, LVH = left atrial and left ventricular hypertrophy by ECG; CT = cardiothoracic ratio on chest x-ray; figures in parenthesis indicate percent of total numbers of each group.

TABLE III

HEMODYNAMICS IN ALCOHOLIC SUBJECTS

Group		HR	AOM	MST	SW	MRFS	dP/dt	Vce
Normals		85	96	3.94	56.5	16.0	2111	27.2
(N = 23)	±	4	2	0.23	3.3	0.7	87	0.8
I		80	107	4.23	45.6	13.0	1501	16.8
(N = 12)		4	4	0.33	3.1	0.8	106	3.8
P vs N	<	NS	0.009	NS	0.04	0.01	0.0001	0.001
II		72	99	6.36	54.3	10.8	1406	16.8
(N = 11)		3	6	0.53	4.3	1.0	91	1.0
P vs N	<	0.02	NS	0.0001	NS	0.001	0.001	0.001
I	<	NS	NS	0.002	NS	NS	NS	NS
III		88	95	6.06	36.9	6.1	1142	15.0
(N = 18)		3	4	0.35	3.6	2.0	83	1.1
P vs N	<	NS	NS	0.0001	0.0001	0.007	0.001	0.001
I	<	NS	0.04	0.001	NS	NS	0.01	NS
II	<	0.001	NS	0.002	0.005	NS	0.05	NS

HR = heart rate in beats/min; AMO = mean aortic pressure in mmHg; MST = mean systolic tension in megadynes. SW = stroke work g-M/m²; MRFS = mean rate of fiber shortening in cm/sec; dP/dt = first derivative of LV pressure rise in mmHg/sec; Vce = velocity of contractile element at peak isometric stress in sec-1; ± = standard error of mean; P = probability using unpaired t test.

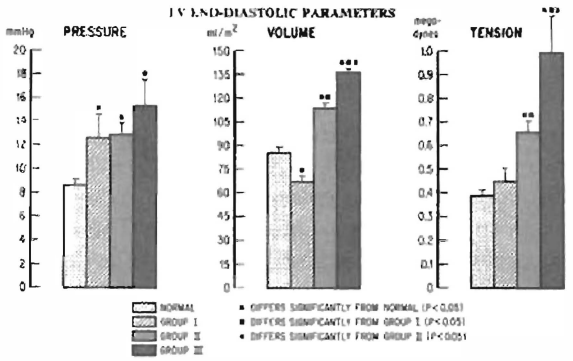

FIGURE 4:
Left ventricular end-diastolic pressure, volume, and tension in normals and alcoholic patients. Reproduced from Clinical Cardiology[5] with permission from the publishers.

of fiber shortening, ejection fraction, dP/dt and VCE (Table III and Figure 5).

The hemodynamic data in the alcoholic dogs is shown in Table IV. Whereas the body weight and heart weight were essentially similar to those of the control dogs, the aortic pressure was significantly higher in dogs consuming alcohol. In terms of end-diastolic parameter both the pressures and volumes were essentially unchanged. The left ventricular ejection fraction as in the alcoholic subjects was significantly depressed. The contractile deficit in the left ventricular myocardium was again apparent in dogs consuming alcohol; both the VCE and the Cy Ix were significantly reduced in contrast to control dogs (Table IV). Ventricular hypertrophy, inflammation and coronary vascular changes were not present on autopsy.

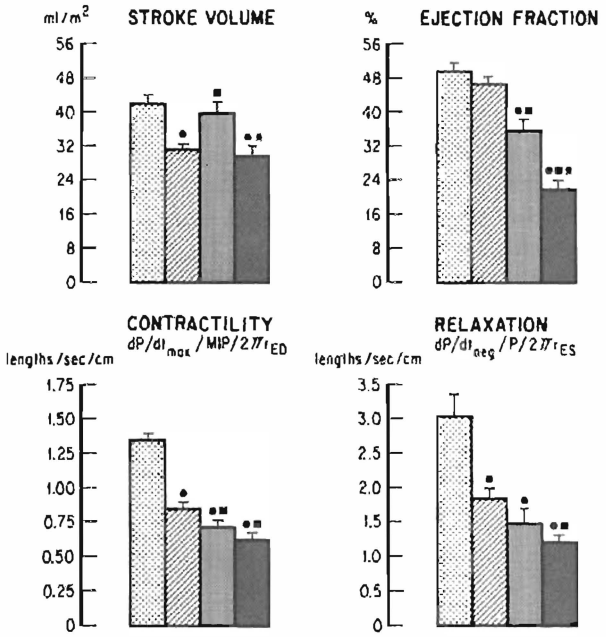

FIGURE 5:
Left ventricular systolic parameters, stroke volume, ejection fraction, contractility, and relaxation in alcoholics and normal subjects. A progressive decline is noted in the "indices" of left ventricular contraction. The ejection fraction is unchanged from the normal in Group I only. An increase in the end-diastolic volume in Group II normalizes the stroke output but the ejection fraction declines. Further increase in end-diastolic volume in Group III fails to increase the stroke volume, and the ejection fraction is further reduced. The key is in Fig. 4. Reproduced from Clinical Cardiology[5] with permission from the publishers.

TABLE IV

LEFT VENTRICULAR FUNCTION IN THE NORMAL AND ALCOHOLIC DOGS

	Body Wt. Kg	HR	AoS	AoD	EDP	EDV	SV	EF	dP/dt	Vce	Cy Ix
					Control dogs (n = 7)						
Mean	11.6	133	121	83	6.4	4.06	1.30	37	2355	30.0	2.18
SEM	1.4	13	4	5	0.8	0.61	0.20	2.8	88	2.5	0.30
					Dogs Consuming Alcohol (n = 7)						
Mean	12.4	146	143	109	7.3	3.47	1.23	27	1991	17.6	1.21
SEM	0.7	7	13	10	0.9	0.70	0.22	1.6	309	1.2	0.13
P (2 vs 1)	NS	NS	NS	<.005	NS	NS	NS	<.01	NS	<.005	<.003

AoD, AoS = aortic diastolic and systolic pressures (mmHg); Cy Ix = Frank-Levinson index of contractility (ML/sec/cm); dP/dt = first derivative of left ventricular pressure (mmHg/sec); EDP = left ventricular end-diastolic pressure (mmHg); EDV = left ventricular end-diastolic volume (ml/kg); EF = ejection fraction (percent); HR = heart rate (beats/min); NS = not significant; P = probability; SEM = standard error of the mean; SV = left ventricular stroke volume (ml/kg); Vce = velocity of contractile element at peak dP/dt (ML/sec).

Analysis of the myocardial lipid and cation analysis revealed significantly reduced potassium in animals consuming alcohol (Table V). There were no significant differences in the myocardial contents of sodium and lipid amongst the two animal groups.

DISCUSSION

The toxic effects of chronic ethanol abuse in terms of cerebral and hepatic function have long been recognized. A role as an etiologic factor in heart disease has however been disputed over the years and attributed when present to co-existent malnutrition. The latter factor, however, has been disassociated from ethanol use in many patients with congestive cardiomyopathy.[14]

As for the demonstration of acute hemodynamic responses to ingestion of ethanol it is apparent that it depends upon dose, duration of administration, variables measured, and time of measurement as well as upon the prior alcohol usage and current hemodynamic state of the subject.[15] In the present study the increases in PEP, IVT and PEP/LVET, in the absence of systematic and significant changes in heart rate and afterload indicated reduction of contractile state of left ventricle. We conclude, therefore, that the changes shown in the present study indicate that non-intoxicating blood levels of ethanol, produced by the ingestion of six ounces of scotch over the two hour period, elicit definite myocardial depression in normal subjects not habituated to ethanol. This depression is not attributable to the effects of elementation since responses to the feeding of sucrose were opposite in direction to those observed with ethanol.

In the alcoholic subjects despite the substantial difference in physical findings, all three groups exhibited a significant increase in end-diastolic pressure. Major change in the contractile function of the left ventricular myocardium as well as in the rate of relaxation, occurred in Group I. In those with an enhanced diastolic volume, further moderate depression of these indices was observed.

The changes in the systolic parameters and muscle functions of the canine heart are similar to those observed in alcoholic subjects. The decrease in systolic function is presumably due to a different process than

TABLE V

MYOCARDIAL LIPIDS AND CATIONS IN DOGS

(mean ± standard error)

Group	LV Wt	Trig	Chol	Na	K	H_2O
Control	4.4	2.3	5.41	45	72	79
	± 0.4	0.8	0.31	4	2	1
Alcoholics	4.7	3.3	5.34	40	64	79
	± 0.4	0.7	0.15	3	2	1
P vs 1	NS	NS	NS	NS	<.003	NS

Chol = cholesterol (umol/g wet weight); LV Wt = weight of left ventricle and septum (g/kg); K = potassium (uEq/g wet weight); Na = sodium (uEq/g wet weitht); trig = triglycerides (umol/g); H20 = water (percent).

that leading to the change in compliance in earlier stages of the disease. Progression to a stage of cardiac decompensation depends upon the intensification of these processes that are present in the early stages. The pathogenesis of altered contractility in both the human and the animal study is not clear. The alteration of cation composition as a basis for decreased contractility remain speculative. Inhibition of sodium-potassium ATPase has been described in several organs as the result of chronic ethanol feeding.[16] An impairment of inward transport of calcium in association with an outward movement of sodium may limit the amount of calcium available to the contractile protein. Alternatively, if the orientation of the latter is distorted by interfibrillar water accumulation, a potential effect on contractility may be postulated.

CONCLUSION

From the data obtained from these studies we conclude that alcohol when used even in non-intoxicating doses elicits a depression of cardiovascular function in normals and unhabituated subjects. The chronic alcohol usage results in the deterioration progressing from isolated impairment of muscle function to stages characterized successively by impaired pump performance, cardiomegaly, symptomatology and eventually decompensation. As observed in the canine study, the changes in myocardial cations, collagen accumulation and/or excess of calcium in the myofibrils may be the main pathogenetic mechanism responsible for cardiac dysfunction. Thus, alcohol use when consumed in any amount over any time period not only ails the faith but the heart in severely injurious ways.

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