HEART MUSCLE DISEASES — THE CARDIOMYOPATHIES. PART III. CARDIOTOXICITY OF ALCOHOLISM

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Whereas the toxic effects of acute or chronic ethanol use on cerebral and hepatic function have long been recognized, its role as an etiologic factor in the heart disease has however been disputed. In fact, alcohol, at least in modest amounts has commonly been used as a medicinal agent. Appearance of heart disease in an alcoholic individual usually was attributed to underlying heart disease of rheumatic, hypertensive, or coronary etiology often without good supporting evidence. As the administration of thiamine provided frequent success in the treatment of beri-beri heart disease, malnutrition was considered the causative factor (1). The latter, however has been disassociated from ethanol use in many patients with congestive cardiomyopathy(2).

A number of recent observations have indicated that ethyl alcohol may indeed have chronic toxic effects on the cardiovascular system (3-4). Results of an epidemiologic study revealed a significantly higher mortality rate from cardiovascular diseases and sudden death than in non-addicted individuals. This difference was not attributable to the traditional cardiac risk factors (5).

Experimental Evidence of Myocardial Toxicity:

Problems such as the uncertainty as to the quantity of ethanol intake, the nutritional status of the patient, and possibility of heart disease from other causes have obscrued an understanding of the pathogenesis of this form of myocardial disease. To eliminate some of the variable as mentioned above which exist in a clinical setting, a group of young adult, male beagle dogs were maintained in a relatively normal nutritional state while receiving upto 30% calories as ethanol, approximating the quantity reported in a population of human alcoholics (6). After an average of 18 months, whereas the body weight, hematocrit, serum protein, vitamins and electrolytes and heart weight were found to be essentially similar to those of the control dogs, there was a distinct

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abnormality in the cardiac function, and of cell structure on microscopic examination. The aortic pressure was also 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 however was significantly depressed. The contractile deficity in the left ventricular myocardium was again apparent in dogs consuming alcohol. Vevntricular hypertrophy, inflammation and coronary vascular changes were not present on autopsy. Results of the myocardial lipid and cation analysis revealed significantly reduced potassium in animals consuming alcohol. There were no significant changes in the myocarial content of sodium and lipid in the alcoholic dogs. Results of similar studies conducted on mongrel dogs appear to be identical and supportive (7,8).

Acute Hemodynamic Effects :

Conflicting results have been reported following the administration of small to moderate amounts in normal man. Whereas some studies reported no change in stroke volume (9) or brachial artery dP/dt maximum either at rest or after exercise (10), others indicated depression of cardiovascular function even with non-intoxicatlg doses in normal unhabituated subjects (11). It is thus obvious that demonstration of acute hemodynamic responses to ingestion of ethanol depends upon dose, duration of administration, variables and time of measurement as well as upon the prior alcohol usage and current hemodynamic status of the subject.

Preclinical Malfunction in Man :

Presence of an equivalent functional abnormality was demonstrated by studies undertaken of alcoholic subjects with no symptoms or clinical evidence of heart disease or malnutrition (12). These non-cardiac alcoholics had consumed on the average 0.5 to 2 pints per day of alcohol mainly in the form of whiskey over ten to fifteen years. Whereas absence of fibrosis excluded Laennec's cirrhosis, changes of fatty liver on liver biopsy provided proof of chronic alcoholism. Following the stress of increased afterload with angiotension infusion, a significantly greater rise of ventricular end-diastolic pressure with a minimal increment of stroke volume was observed in the alcoholics compared to non-alcoholic controls. Similar observations have subsequently been made during exercise in cirrhotic patients without clear evidence of cardiac diseae (13). The significantly reduced contractility index in the non-cardiac alcoholic provided a firmser basis for concluding that a preclinical state of cardiac abnormality can exist in the chronic alcoholic (12).

Non-invasive measurements of the systolic time intevals have also confirmed that many asymptomatic individuals have modest depression of left ventricular function (14,15). Non-cardiac alcoholics have been shown to accumulate PAS-positive material in the myocardial interstitium which may be a basis for the functional abnormality (16), as positulated in the canine studies (7). Some degree of interstitial fibrosis may be present at this stage as suggested by post-mortem studies of alcoholics who died without clinical evidence of cardiac disease (17).

Progression to Heart Failure :

The proof of the thesis that cumulative effects of ethanol result in cardiac abnormality despite adequate nutrition was provided by a utsdy of reversible effects of feeding alconol

over 5-1/2 months in a well nourished patient (12). A recent study examined the diastolic and systolic performance characteristics of left ventricle in alcoholism (18). Three patient groups with a history of heavy alcohol consumptin were compared with normal subjects. In those with symptoms related to chest pains or palpitation, heart size was normal on x-ray. In groups 3 and 4 dyspnea was associated with varying degrees of cardiomegaly and high prevalence of absent seqptal q waves on the electrocardiogram.

Despite substantial differences in physical findings, all three grups exhibited a significant increase in end-diastolic pressur. Group I was distinguished by the fact the end-diastolic volume was not increased but actually somewhat diminished. Gruops 2 and 3 were characterized by a significant increase in end-diastolic volume and tension. The latter was enchance to a significantly greater extent in group 3 and was the most prominent hemodyanimic abnormality in this group. A major change in the index of contractility, as well as in the rate of relaxation occurred in Group 1. Furthermore, this depression of these indices was observed in the group with enhanced diastolic volume. In patients who had mitral regurgitation a more severe depression of left ventricular function was present in the alcohlic group than than in non-alcoholic control group, and was presumably due to the toxic effects of ethanol on the left ventricle.

Thus in those alcohlic patients who developed cardiac alterations, the earliest abnormality was characterized by diminsihed left ventricular compliance and a moderate contractility deficit without heart failure. In those who progressed, end-diastolic tension was substantially enhanced and further reduction in contractility indices was observed.

No clear precipitating factors were readily identified as inducing the episode of heart failure. There was no evidence of hypokalemia (19), hypophosphatemia (20) and no suggestion of cobalt (21) or lead ingestion (22) was present.

Arrhythmias and Conduction :

An association between alcohol and cardiac arrhythmias, particularly atrial fibrillation has long been suspected (23). Both atrial and ventricular arrhythmias have been observed after the onset of heart failure in the alcoholic (24). Cardiac arrhythmias have also been shown to occur during alcohol withdrawal and during the preclinical state of alcoholic cardiomyopathy (25). Among 36 acutely intoxicated, chronic alcoholics who were monitored for arrhythmias over a 12 hour period, only three were completely normal, ventricular premature contractions were demonstrated in 39%. Ettinger et al (25) demonstrated 32 separate symptomatic dysrrhythmic episodes in 24 patients who drank heavily and who were hospitalized for control of arrhythmias. Though over alcoholic cardiomyopathy was not present and plasma electrolytes were usually normal, invasive studies performed in some of them few weeks later did demonstrate cardiac dysfunction. Moderate conduction delays were also found on high speed electrocardiogram recorded approximately one week after restoration of normal sinus rhythm. These were considered the background for the induction of acute arrhythmias. Experimental studies of chronic alconolism in dogs, by demonstrating intraventricular conduction abnormalities and morphological alterations provide a proof for this hypothesis (26,27).

Atypical Myocardial Infarction:

Although the absence of septal Q waves in the alcoholic has been suggested as grounds for considering the diagnosis of cardiomyopathy, and the localized absence or reduced amplitude of R wave may simulate the changes of myocardial infarction, transmural myocardial scars have been found at post-mortem examinations in alcohlolic patients who had no significant coronary atherosclerosis (16,28). Ten of twelve patients without traditional coronary risk factors admitted to coronary care unit with histories of classical ischemic pains were found to have high levels of progressive cardiac enzymes. Examination of the coronary arteries at post-mortem or by angiography revealed no significant occlusive lesions.

Morphological examination of the myocardium revealed concentric peri-arterial fibrosis, which was postulated to restrict cornary flow increments during periods of high blood flow requirements. This phenomenon was considered analogous to cardiac muscle necrosis associated with periarterial lesions of constrictive pericarditis, perhaps conditioned by the abnormal metabolism of cardiac cells in chronic alcoholism. The absence of the change in platelet count and evidence of embolization to any organ was exlcuded as the possible etiologic factor in the myocardial necrosis.

Conclusions:

Thus it is obvious 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 deterioration progressing from isolated impariment of muscle function to stages characterized successively by impaired pump performance, cardiomegaly, symptomatology and eventually decompensation. Various conduction abnormalities and arrhythmias are also common and myocardial infarctions may appear on non-coronary basis but related to chronic ethanolism. As observed in the canine study, the changes in myocardial cation, collagen accumulation and/or excess of calcium in the myofibrils may be the main pathogentic mechanism responsible for cardiac dysfunction.'

The management of alcoholic cardiomyopathy (29) would depend upon the stage of the disease when the addicted individuals are first seen. Even in the absence of cardiac failure or enlargement, unexplained arrhythmias or absent septal q wave should raise a high index of supicion requiring positive proof of a negative history for alcoholism (obtained not from the patient but from the close relatives and/or friends).

The key to treatment at all stages involves complete abstinence. Although partial abstinence may be theoretically possible, an effective program would involve an individual physician-patient basis of group therapy.

After the onset of clinical manifestations, traditional antiarrhythmic agents, DC electric shock treatments, digitalis and diuretics may be used as needed. Electrolyte abnormalities which may exist during the acute stage or develop readliy in patients with low salt intake during diuresis must be corrected. Since thromboembloism from endocardial thrombi is a prominent feature occurring in as many as 80% of individuals, anticoaguation should be an important therapeutic modality. Finally, where facilities are available, prolonged bedrest may reduce the

size of an excessively dilated heart and more importantly may contribute to control of alcohol intake.

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