Papers and Originals

Alcoholic Heart Disease

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An association between excessive alcohol consumption and heart disease has been known for a long time. Aalsmeer and Wenckebach (1929) described the cardiac manifestations of Oriental beriberi, and thereafter this condition was recognized in the Occident as being mainly the result of alcoholism. Furthermore, it was thought that this was the only way in which alcohol affected the heart, and many physicians still adhere to this view. Keefer (1930) had found that only one-third of the cases of Oriental beriberi seen in China had a hyperkinetic circulatory state, and while Weiss and Wilkins (1936) recognized the close resemblance of some of their cases to Oriental beriberi they found that many patients presented with chronic myocardial disease. Blankenhorn *et al.* (1946) also drew attention to hypokinetic heart failure as a manifestation of alcoholic beriberi, and Benchimol and Schlesinger (1953) include such cases in their account of beriberi heart disease. Some confusion arises from the use of the term "beriberi"; it should be restricted to patients with a hyperkinetic circulatory syndrome and a response to aneurin.

Perusal of case histories presented in the many papers on non-coronary myocardial disease (appearing under a diversity of titles which testify to the deficiencies in our knowledge of this subject) reveals a remarkably frequent mention of alcohol, which is often ignored by the authors. A causal relation is, however, recognized with varying degrees of conviction by others, including Brigden (1957), Evans (1959), Hickie and Hall (1960), and Wendt *et al.* (1962). In spite of their earlier account of alcoholic heart disease Burch *et al.* (1963), when reporting the value of prolonged bed rest in "the treatment of the large heart associated with myocardial disease of unknown cause," state that "approximately one-half of the males were considered to be chronic alcoholics."

Isolated non-coronary myocardial disease (cardiomyopathy) is being recognized with increasing frequency. It is known that many different pathological processes, including congenital, inflammatory, nutritional, metabolic, and allergic disorders, may be causative, but the exact aetiological diagnosis is often obscure at the time of presentation with heart failure. We believe that an excessive consumption of alcohol is a causal factor in many patients with cardiomyopathy, but we are unable to make an overall assessment of the frequency of the condition. A study of 50 patients who have heart disease associated with a huge consumption of alcohol over a long period of time is presented.

The Patients

This report is based on 50 patients seen at the London Hospital and the National Heart Hospital between 1952 and

1963; the criteria for their inclusion in this series were a long history of a very high consumption of alcohol and evidence of heart disease which was not due to hypertension, coronary artery disease, valvular disease, or any other disorder known to cause heart disease.

With one exception all were men; their ages ranged from 33 to 72 and most were between 45 and 65. All had drunk heavily and continuously for more than 10 years. One-third drank beer only, an average consumption being 15 pints (8.5 litres) a day; one-quarter consumed only spirits at a rate of one bottle a day or more; and the remainder drank beer and spirits in large quantities. Their occupations were of interest, for 17 worked in the liquor trade or in some close association with it (barmen, hoteliers, waiters, brewery workers).

All have been examined on several occasions, and have had chest x-ray examinations, electrocardiograms (E.C.G.s), urinalyses, E.S.R.s, haemoglobin estimations, leucocyte counts, and many had other investigations, including liver-function tests and serum protein analyses. Twenty-five of these 50 patients have died. Nine were examined at necropsy and none showed significant coronary disease. The majority (19) died of heart failure, two died of pulmonary embolism, and one of cancer; the cause of death was uncertain in three. Thirteen of the series were included in a previous study on non-coronary myocardial disease (Brigden, 1957).

Case Reports

The following abbreviated case reports have been selected to illustrate some of the main features and the range of syndromes from beriberi, arrhythmias, and chronic myocardial failure encountered in alcoholic heart disease.

Case 15.—A man aged 46 started regular beer-drinking at the age of 15, and from the age of 30 he consumed from 15 to 20 pints (8.5 to 11.4 litres) a day. During the 24 hours prior to admission to hospital he drank no less than 36 pints (20.5 litres) of beer. He had been short of breath on effort for the previous year and had had intermittent oedema of the ankles. He was in severe congestive cardiac failure with massive oedema. The jugular venous pressure was raised 10–15 cm. above the sternal angle at 45 degrees. He had a tachycardia and the peripheral pulse volume was full. There was a summation gallop rhythm with a soft pansystolic murmur. The liver was moderately enlarged and tender. His E.C.G. showed rather flat T waves and his chest x-ray film showed moderate cardiomegaly and pulmonary venous congestion (Fig. 1). Digitalis and diuretics produced little response during the first four days. On the fifth day 100 mg. of aneurin produced a great diuresis. Aneurin was continued in the same dosage for the next week. Recovery was rapid and apparently complete in three weeks. He has been free of symptoms during a long period of total abstinence.

Case 35.—A 38-year-old man was a heavy beer-drinker for many years (10–12 pints (5.7–6.8 litres) a day). One year after partial

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gastrectomy* for chronic duodenal ulcer he complained of fatigue, dyspnoea, swelling of the ankles, and excessive sweating. Three months later nocturnal dyspnoea occurred. He was admitted to hospital in congestive cardiac failure; his blood-pressure was 115/55. X-ray examination showed moderate cardiac enlargement and pulmonary venous congestion. He complained of aching legs and was found to have very tender calves and depressed ankle-jerks. His E.C.G. showed a prolonged P-R interval and pathological Q waves in leads II and III. He was treated with bed rest, restricted salt, digitalis, and diuretics; following a diuresis he improved. He was well for several months (continuing digitalis and diuretics), but congestive cardiac failure reappeared abruptly and gradually increased in severity, necessitating readmission. He had gross congestive heart failure, and x-ray examination showed an increase in heart size (Fig. 2). There was little response to therapy with bed rest, salt restriction, and diuretics, but when aneurin was added to the regime diuresis followed, his haemoglobin concentration increased, and heart size rapidly decreased to normal (Fig. 2). He became symptom-free again. He has stopped drinking alcohol and has remained in good health until the present time (six years); however, the E.C.G. remains slightly abnormal.

Case 14.—This patient was 40 years old when he was first seen with a paroxysm of atrial fibrillation. He was obese and had consumed beer, wine, and spirits in large quantities for some 15 years. One year later atrial fibrillation recurred and conversion to sinus rhythm was achieved with quinidine (Fig. 3). However, during the next two years atrial fibrillation recurred for variable

periods and became permanent five years after the initial attack. By this time there was some cardiac enlargement and the E.C.G. showed some prolongation of QRS time. Thereafter congestive heart failure recurred episodically with diminishing response to treatment. Subsequent E.C.G.s showed left bundle-branch block (Fig. 3). He died of heart failure.

Case 16.—A man aged 51 had been a very heavy beer-drinker for 25 years (10 pints (5.7 litres) a day average) and during the past 10 years had consumed a bottle of whisky a day whenever possible. He had done no regular work since discharge from the Army 15 years before and had a small private income. He presented with severe congestive cardiac failure, having first noticed undue breathlessness and occasional ankle-swelling five years previously. There was a history of oedema and breathlessness 15 years previously, which had been treated with vitamin B₁ and which strongly suggested beriberi. There was no history of cardiac pain and no evidence of valve disease or hypertension. His E.C.G. showed nodal rhythm, which progressed over five years to complete heart-block (Fig. 4). X-ray examination showed moderate cardiac enlargement. His haemoglobin was 16.5 g./100 ml., and serum cholesterol was 200 mg./100 ml. He died in congestive heart failure. At necropsy the left ventricle was moderately hypertrophied and the other chambers were dilated (Fig. 5). There was patchy microscopic fibrosis, chiefly in the left ventricle (Fig. 6). The coronary arteries were patent.

Case 7.—A West Indian man aged 40 first attended hospital because of breathlessness and palpitation on effort, which had increased over the previous 18 months.

He had never suffered from chest pain, ankle-swelling, or nocturnal dyspnoea. For 10 years he had consumed regularly one bottle of spirits (whisky or rum) a day, and during this period he had had two attacks of delirium tremens. He was obese, the arterial pulse was irregular from frequent extrasystoles, and the jugular venous pressure and pulse were normal at this time. The cardiac impulse indicated moderate left ventricular hypertrophy and there was a late systolic murmur at the apex, wide splitting of the second sound, and a loud left

FIG. 1.—Case 15. Beriberi due to alcoholism. Pulmonary congestion and cardiomegaly returned to normal two weeks after treatment with aneurin. E.C.G.s (V₁, V₄, V₆) show flat T waves becoming normal during same period.

FIG. 2.—Case 35. Radiographs showing return to normal heart size after four weeks' treatment with aneurin, digitalis, and diuretics.

FIG. 3.—Case 14. E.C.G.s (lead I) recorded at intervals over six years. (a) In first attack of atrial fibrillation which was converted to sinus rhythm with quinidine. (b) Two years later. (c) QRS slightly prolonged, T waves lower, and atrial fibrillation. (d) Two years later showing congestive heart failure; atrial fibrillation and tachycardia with left bundle-branch block. (e) Persistent atrial fibrillation and left bundle-branch block on maintenance digitalis.

ventricular third sound. His blood-pressure was 130/75. His E.C.G. showed sinus rhythm with frequent ventricular extrasystoles and left bundle-branch block (Fig. 7). X-ray examination showed gross enlargement of the left ventricle with pulmonary

FIG. 4.—Case 16. E.C.G.s showing (a) normal QRS with P waves superimposed on T waves—probably greatly delayed retroconduction from nodal rhythm; patient had minor syncopal episodes at this time; and (b) five years later, complete heart-block, loss of R waves in mid-chest leads, and steeply inverted T waves—a few weeks before death.

FIG. 5.—Case 16. Transverse section through ventricle showing hypertrophy of left and some dilatation of right. Minimal macroscopic fibrosis.

FIG. 6.—Case 16. Microscopic fibrosis in left ventricle.

venous congestion (Fig. 7). There was no evidence of peripheral neuritis or of cirrhosis of the liver. During the next 18 months he had episodes of heart failure, and finally died after an abdominal operation (for mesenteric embolus). Necropsy showed hypertrophy of the ventricle with small macroscopic areas of fibrosis and organized mural thrombi (Fig. 8). The coronary arteries were widely patent with no significant atheroma.

FIG. 7.—Case 7. Radiograph showing great cardiomegaly and pulmonary venous congestion, and E.C.G. showing extreme left bundle-branch block (QRS 0.36 sec.) with Q waves in V_6 .

FIG. 8.—Case 7. Open left ventricle with small patches of endocardial fibrosis overlying local areas of muscle necrosis.

Clinical Features

Cardiovascular symptoms appeared slowly over one or two years owing to the gradual development of heart failure in the majority of patients; however, in some the onset was abrupt because of the development of an irregular rhythm or an attack of paroxysmal nocturnal dyspnoea. All had dyspnoea on effort, which was thus the commonest symptom. In some patients this had been erroneously attributed entirely to associated features such as obesity or bronchitis. Nearly half had had one or more attacks of paroxysmal dyspnoea.

Heart Failure

Unlike the progress of heart failure in coronary disease, hypertension, and valvular disease, there were phases of spontaneous remission in some patients. When first seen the jugular venous pressure was elevated to varying degrees in almost all of those who were untreated and in 75% of the whole series. Oedema was present in many, though not in all of those with a raised jugular venous pressure. (In some patients diuretics had been previously administered.) As in all forms of myocardial failure, triple rhythm due to addition of the third heart sound was common. The liver was enlarged

in 70% and in many the enlargement and firmness seemed greater than might have been expected from the duration and degree of heart failure. However, with few exceptions liver-function tests showed only mild abnormality. None showed clear evidence of cirrhosis and none showed as much hepatic dysfunction as may be found in some other forms of chronic heart disease such as constrictive pericarditis.

A few patients presented with features of beriberi heart failure. The venous pressure was high and there was gross oedema without evidence of severe myocardial disease as judged by the presence of signs indicating a normal or raised cardiac output, a near normal E.C.G., and a rapid and good response to treatment, especially when aneurin was included in the regime—for example, Case 15. Three who had this disorder had previously had a partial gastrectomy and all were heavy beer-drinkers. Alcohol might have been tolerated by the cardiovascular system in these patients without the additional nutritional disadvantage of a gastrectomy.

In contrast, a small group presented in the late stages of myocardial disease with severe heart failure and evidence of a very low cardiac output. The pulse pressure was small and there was intense peripheral vasoconstriction. In these the venous pressure remained high, triple rhythm persisted, oedema remained in spite of treatment, and the ventricular complex of the E.C.G. was always grossly abnormal.

Between these two groups of patients with different types of heart failure there were a majority of patients who were not in a state of intractable heart failure, but their lack of evidence of raised cardiac output and their slow response to treatment (although in some spontaneous remissions had occurred) distinguish them from the beriberi group. Some of these patients appeared to develop heart failure because of the onset of atrial fibrillation. Full compensation was restored for a time after conversion to sinus rhythm in some cases. Other patients in this intermediate group have progressed to intractable low output failure (Case 14), but we have not personally observed this sequence in the beriberi group. However, one patient who had recurrent heart failure and died in a gross low-output state had given a clear history of aneurin-responsive disease some 15 years previously (Case 16).

The arterial pressure was never permanently elevated, but during heart failure there was often a rise of diastolic pressure. When response to treatment was satisfactory the pulse pressure became normal.

Palpitations

Tachycardia was present whether there was sinus rhythm or not. Ectopic beats were common and were often multifocal in origin as described by Evans (1959). Twenty-five patients had atrial fibrillation at some time. In some, spontaneous reversion to sinus rhythm occurred but was usually soon followed by relapse. Unlike "lone" atrial fibrillation the ventricular rate was usually fast and ventricular extrasystoles were common (Fig. 9). As might be expected, atrial fibrillation was commoner in the older patients in the series. Atrial flutter was not encountered. Minor syncopal episodes and faint feelings occurred in a few patients and were associated with the onset of atrial fibrillation in two, while two others had first-degree heart-block.

Chronic Cough

This was common. A history of chronic bronchitis was obtained in one-third of the patients, all of whom were heavy smokers; indeed, almost all patients in the series were smokers. However, none had evidence of pulmonary heart disease, though bronchitis no doubt contributed to dyspnoea in many and was sometimes erroneously thought to be the primary cause of disability.

Symptoms Referable to Other Symptoms

These symptoms were of interest and importance from the diagnostic point of view, although rarely more than of nuisance value to the patient. *Excessive sweating*, especially at night, was common. This may have been due to heart failure; however, it was prominent in some when there was no obvious evidence of failure. Excessive sweating in heart failure was first reported by Haugen (1957). It is postulated that left heart failure causes an increased sympathetic tone, one manifestation of which is a stimulation of sweat glands, another being lid retraction, which we have often observed under the same circumstances. However, it seemed that nocturnal sweating was directly related to the excessive alcohol intake rather than to heart failure in these patients. In those who sweated excessively the skin was often warm, but hepatomegaly, pink palms, and spider naevi were uncommon and not associated with this symptom. *Anorexia* was common in the late stages. Four gave a history of previous peptic ulcer and three of the beer-drinkers had had gastrectomy. A mild *stomatitis* and glossitis occurred in a few patients. Pruritus was not uncommon. Only three gave a past history of *gout*.

Neurological Symptoms

These were never dominant, but, though slight, they were often pointers to the diagnosis. Aching in the legs and, less commonly, paraesthesiae suggested mild peripheral neuritis in a few patients, but clear objective evidence of this was rare. Only eight patients had tender calves and/or absent deep reflexes, and none had a significant loss of sensation. Two had had delirium tremens in the past and one was said to have had an alcoholic dementia. Many showed some evidence of psychopathology: a "shifty" disposition, evasiveness, an aura of disarray or dirt, even when well dressed, while obvious lying and a past history of erratic employment were common. These patients appeared to have an exceptionally high tolerance for alcohol, for it seemed that drunkenness was rare. Indeed, we have come to the conclusion that frequent drunkenness, which at any one time imposes a limitation on the quantity consumed, is not associated with the development of cardiomyopathy.

Radiology

Cardiac enlargement was seen on x-ray examination in every patient. As in other forms of cardiomyopathy the left heart

FIG. 9.—E.C.G. of 56-year-old man with 20-year history of alcoholism. Atrial fibrillation, multifocal ventricular extrasystoles, and "local" T-wave inversions in lead V₄.

was mainly affected. Radiological signs clearly depended on the degree of myocardial damage and its resulting haemodynamic disturbance rather than the aetiology of the process. The least degree of enlargement was seen in those few patients who presented with a beriberi-like syndrome, and a return to normal or near normal heart size followed treatment (Figs. 1 and 2). Intermediate degrees of enlargement were seen in those patients in whom an arrhythmia appeared to be the main problem, and the greatest degrees of cardiomegaly were seen in patients with severe chronic low-output failure which showed little tendency to respond to treatment.

Some degree of pulmonary venous congestion was common but pulmonary oedema was not seen. Small pleural effusions were common as in other forms of congestive cardiac failure. There was a rather high incidence of chronic bronchitis, and patchy irregular streaking of lung parenchyma was associated with this in a few patients. Only two had recognized episodes of pulmonary infarction with associated radiological features.

Electrocardiography

A wide range of abnormality was found in the E.C.G.s of these patients. Progressive abnormalities were seen during the course of the disease in some, while in others spontaneous improvement was observed. The E.C.G. was abnormal in all but two at first presentation. These two normal tracings were from patients who had a subacute beriberi type of heart failure, which supports the conclusion of Schrire and Gant (1959) that a normal or near normal E.C.G. in heart failure of obscure origin is strongly suggestive of beriberi.

Arrhythmias were frequent and atrial fibrillation with relatively fast ventricular rates occurred in half of the patients at some time during the illness. Frequent ventricular extrasystoles were common and were recorded equally in patients in sinus rhythm or atrial fibrillation (Fig. 9). Nodal rhythm occurred in two patients; one subsequently developed atrial fibrillation and the other complete heart-block.

Abnormal P waves were present in 12 cases. This was usually the pattern of right and left atrial hypertrophy commonly seen in chronic heart failure associated with myocardial disease.

Conduction defects were present in 19 cases. Seven had a prolonged P-R interval; three patients in this group presented initially with cardiac beriberi, one of whom later developed complete heart-block. Left bundle-branch block was present in eight and right bundle-branch block in four. Pathological Q waves, presumably due to fibrosis, were present in four cases and in two of these necropsy confirmed the absence of coronary disease. Left ventricular hypertrophy shown by deep S waves in right precordial leads was seen in six cases.

Abnormalities of the T waves occurred in the majority of E.C.G.s recorded from these patients. A common finding was of atrial fibrillation with T-wave abnormalities unaccompanied by abnormalities of the QRS. Evans (1959) emphasized the frequency and diagnostic importance of a sharply inverted ("dimple") T wave in this condition; we have recorded this in some patients, but in view of the wide range of abnormalities encountered in this series and in coronary artery disease we are reluctant to attach diagnostic significance to any particular pattern in this disorder. The E.C.G. findings are due to the site and the extent of muscle damage rather than to the nature of its cause. Thus a small area of damage strategically placed may cause a significant conduction defect whereas a similar lesion deep in the muscle mass might not be "seen" electrically or at the most produce a local and minimal T-wave abnormality.

Other Investigations

The haemoglobin concentration was raised above 100% in 39 patients; the average level was slightly higher in those with

atrial fibrillation than in those without. This was thought to be due to long-standing low-grade heart failure. Haemoglobin concentration was low, presumably due to haemodilution, in the three beer-drinkers who had gross oedema, venous hypertension, and evidence of a relatively high cardiac output. Treatment of the heart failure in these patients was associated with a rapid rise in the haemoglobin concentration (see Case 35). Leucocyte counts were within the normal range. The E.S.R. was normal or low. Mild to moderate proteinuria was common in the untreated patients but rapidly disappeared with treatment of heart failure. Liver-function tests revealed slight abnormalities in many, and in four cases the albumin/globulin ratio was reversed.

Serum cholesterol estimations were made in 23 cases, and were lower than the average for the patients' age and sex and much lower than the average range found in patients with coronary disease (Fig. 10). Only five patients exceeded 250 mg./100 ml., and 14 of the 23 had levels below 200 mg./100 ml. The cause of these low cholesterol levels is not known. However, dietetic deficiency and/or replacement of fat or carbohydrate by alcohol is the most likely cause. Low levels are usual in starvation and cachectic states (Manley and McKusick, 1960). Cholesterol also tends to be low in patients with chronic congestive heart failure, which was present in many when examination was made. Possibly liver damage interferes with cholesterol synthesis but none had clinical or post-mortem evidence of hepatic cirrhosis.

Yet another possibility concerns the relation between cholesterol metabolism and magnesium. It is known that excessive alcoholism leads to hypomagnesaemia (Flink *et al.*, 1954) and there is some evidence that this element is concerned in cholesterol synthesis. Unfortunately we were unaware of the increased excretion of magnesium by the kidney in alcoholics (Heaton *et al.*, 1962) when these patients were being investigated, so that we have no data on the levels in our patients. There was no occlusive coronary disease in the patients examined at necropsy. Howell and Manion (1960) have shown that the necropsy incidence of myocardial infarction in a large series of patients with portal cirrhosis (associated with alcoholism) was only 25% of that found in a control series. It is tempting to assume that this sparing of the vascular intima of the coronary circulation in alcoholic cirrhosis and in alcoholic cardiomyopathy is related to the hypolipidaemia.

Differential Diagnosis

Erroneous diagnosis was common. In six cases a firm diagnosis of *cardiomyopathy* was made but the history of

FIG. 10.—Serum cholesterol levels in patients with alcoholic heart disease tend to be lower than in patients with coronary disease. A=Alcoholic heart disease. B=Normal. C=Ischaemic heart disease.

alcoholism was either missed or ignored. There are many case histories in papers on such subjects as "idiopathic cardiac hypertrophy" and "primary myocardial disease" where alcoholism is noted but no causal relation recognized or discussed. *Thyrotoxicosis* was considered or suspected in five patients, four of whom had atrial fibrillation and the other had multiple extrasystoles. The combination of tremor, a warm skin, excessive sweating, and atrial fibrillation was highly suggestive of thyrotoxicosis, especially when there was tachycardia and a low blood cholesterol; however, the thyroid gland was not enlarged, appetite was poor, and thyroid-function tests were normal. Thyroidectomy had been performed on slender evidence in two patients. The possibility of *systemic hypertension* was seriously considered when the diastolic pressure was elevated in the presence of heart failure in a few patients. However, the natural history was different from that of hypertensive heart disease, no other evidence of hypertension existed, and pressures became normal when heart failure improved.

Cardiac infarction was considered in a few patients. None of these had cardiac pain at any time. Nine patients in the whole series came to necropsy and no significant coronary disease was found. Other patients were thought to have idiopathic paroxysmal atrial fibrillation or lone atrial fibrillation, cirrhosis of the liver, cor pulmonale from pulmonary embolism, or endomyocardial fibrosis, and, as in all forms of cardiomyopathy, constrictive pericarditis was occasionally considered, and erroneously diagnosed in two cases in this series. All of these diagnoses were discarded after investigation, operation, or necropsy.

Treatment

Routine treatment for congestive cardiac failure with short-term bed rest, digitalis, and diuretics produced a good response in 10 patients who were seen in the first attack of heart failure. These patients had the least abnormal electrocardiograms (T-wave abnormalities only). On the other hand, 10 patients, who had a long history of heart failure with signs of a low cardiac output and more severe abnormalities of the ventricular component of the cardiogram, responded poorly or not at all. Many patients fell between these extremes. Unfortunately none of the patients was treated by prolonged bed rest as advocated by Burch *et al.* (1963), who found that 11 out of 21 patients with unexplained cardiomegaly showed a return of heart size to normal after more than six months' bed rest.

Aneurin had little or no effect on the majority of patients. However, five had a good response and three others showed a doubtful response. Those who responded well to aneurin were in a first attack of heart failure and their electrocardiographic abnormalities were slight; two had had gastrectomy (of three in the series) and two had minor evidence of peripheral neuropathy.

Quinidine was used in nine patients who had atrial fibrillation. Five were converted to normal rhythm and four remained in atrial fibrillation. Three have since been converted to sinus rhythm by D.C. countershock. As might be expected, the "successes" occurred in patients with less severe degrees of myocardial disease than was evident in the "failures."

Withdrawal of alcohol has little or no influence in the late stages of the disease; however, it is known that recovery may be complete if total abstinence is practised after a first attack of failure with beriberi-like features. Three patients in this series who had gross oedema, raised venous pressure, and relatively normal cardiograms have continued in good health since discontinuing alcohol. It is obviously wise to advocate total abstinence in alcoholic heart disease, but it appears to us that irreversible damage had already occurred in many of our patients at the time of first presentation. Although the work of Burch *et al.* (1963) is based on series of patients with "large hearts associated with myocardial disease of unknown cause," approximately half of the males were thought to be chronic

alcoholics, and it may be that prolonged bed rest is particularly valuable in this group because of the additional factor of alcohol withdrawal. It appears, therefore, that the outlook for patients with cardiomyopathy in general and alcoholic cardiomyopathy in particular may be better than hitherto realized.

Pathology

Post-mortem examinations were performed in nine cases. The usual findings were of moderate hypertrophy of the left ventricle with dilatation of the right ventricle and both atria. There were small areas of macroscopic fibrosis in the left ventricle and in two there were mural thrombi with localized underlying endocardial fibrosis (Fig. 8). Microscopically small scattered areas of muscle degeneration were seen; some showed patchy fibrosis, while in other areas there was recent focal necrosis with a slight cellular reaction (Fig. 6). The remaining muscle fibres were hypertrophied. These small areas of muscle necrosis with or without a slight cellular reaction were present even in the long-standing cases, suggesting that there was a continuing disease process. These abnormalities were present in all chambers of the heart, but most obvious in the left ventricle. In two patients who died after a rather shorter history of heart disease than the others the pathology was similar, except that the hypertrophy of the left ventricle was only slight; there was less fibrosis, but there were many areas of recent muscle degeneration with interstitial oedema, particularly surrounding these areas. Benchimol and Schlesinger (1953) described similar features and found much hydropic degeneration and interstitial oedema. However, their patients had a poorer nutritional status, the natural history was shorter, and the whole disease process was probably more acute.

None of the nine necropsy cases showed evidence of valvular disease, and the coronary vessels were widely patent in all. The degree of atheroma in the aorta and coronary arteries was mild to moderate, probably representing an average amount for the age and sex. The kidneys were examined for evidence of hypertensive disease, but none was present and the findings in the other organs were those associated with congestive cardiac failure. Examination of the liver showed no evidence of disease other than that directly related to congestive cardiac failure.

Nature of the Lesion

Perusal of the literature on non-coronary myocardial disease and the study of these patients provide strong evidence that a long-standing high-level consumption of alcohol in some individuals is associated in a causal way with myocardial disease. However, the nature of the relationship and the pathogenesis of the lesions is obscure. The development of myocardial disorder is related not only to the amount of alcohol consumed and the duration of alcoholism but also to additional factors, some of which are known. Thus it seems that an adverse nutritional status due to socio-economic factors or gastrointestinal disease (and possibly gastrectomy) predisposes to the development of alcoholic heart disease, particularly of the beriberi type.

In beriberi the problem is concerned with the depletion of aneurin resources, which adversely affects myocardial metabolism, and in a few patients in this series vitamin B₁ therapy caused a remarkable improvement. However, in this country aneurin replacement is effective or partially effective in only a small number of patients with alcoholic cardiomyopathy, and most of these are patients who have another nutritional problem in addition to alcoholism. There seems to be a rather firm demarcation between aneurin-responsive disease and non-beriberi cardiopathy. However, it is possible that this distinction may not be as profound as it appears, for most of the unresponsive group with evidence of severe muscle disease do

not have a gravely defective nutritional status, and **flagrant** beriberi would not be expected to appear in patients who maintain a reasonably normal mixed diet. It is possible that the repetitive partial exhaustion of enzyme-vitamin systems is a recurring insult to the myocardium which leads to an accumulation of small lesions, and these may not affect the heart sufficiently in the early stages to produce a clinical problem.

It is possible that the muscle injury may be due to a direct toxic effect of the high blood level of alcohol; however, if this were so we might expect more frequent evidence of it in the form of acute cardiovascular disorders following isolated bouts of heavy drinking; furthermore, we would expect a much greater incidence of myocardial disease among alcoholics. Another possible mechanism concerns the effect of alcohol on other metabolic factors. The histological appearance of patchy myocardial necrosis closely resembles that caused by hypokalaemia (Follis *et al.*, 1942; McAllen, 1955), and there is evidence that acute hypomagnesaemia—which may be associated with cellular potassium depletion—may result from a large consumption of alcohol (Heaton *et al.*, 1962). Furthermore, Selye (1958) has shown that supplemental potassium and magnesium may protect animals against the development of focal myocardial necrosis caused by various noxious stimuli. Indeed, it has been shown that necrotizing cardiopathies produced by different agents are uniformly aggravated by deficiencies in potassium, magnesium, and chlorides (Bajusz, 1963).

The possibility that an autoimmune process, initiated by myocardial necrosis caused by alcohol in one way or another, might be responsible for perpetuation of the disease process must be considered. However, no patient showed any of the clinical manifestations of hypersensitivity such as persistent fever, raised E.S.R., serositis, or arthropathy, but in two patients out of 10 anti-heart antibodies were demonstrated using the tanned-red-cell technique as applied to the post-cardiotomy syndrome (Robinson and Brigden, 1963). As we are unable to relate this observation to any other factors in these cases its significance is obscure. It seems to us that while high alcohol consumption may cause myocardial damage some other factors must condition the process or determine that the site on which alcohol acts as a noxious agent is the heart rather than the nervous system or liver in a particular individual.

Summary and Conclusions

Fifty patients with evidence of myocardial disease and a long-standing high consumption of alcohol were seen over a ten-year period. The usual causes of myocardial disease were excluded as far as possible. All but one were male, and their ages ranged from the fourth to eighth decades. Three clinical syndromes which depend on the dominant derangement of circulatory function at any one time were recognized.

Cardiac beriberi (aneurin-responsive disease) was the least frequent and least serious disorder. It occurred in five heavy beer-drinkers (not averse to spirits as well) and two of these had had a previous gastrectomy, which was thought to provide an additional adverse nutritional factor. Therapeutic response to aneurin and withdrawal of alcohol was good in these patients, but relapse has occurred following resumption of previous habits in at least one, and another has cardiographic evidence of persistent myocardial abnormality.

A second, larger, group of patients presented with arrhythmia—especially atrial fibrillation—with or without varying degrees of heart failure. The ventricular rate tended to be fast and multifocal ventricular ectopics were common. Spontaneous return to sinus rhythm occurred in some, but usually relapse followed after a variable period. Fast heart rates, frequent extrasystoles, cardiomegaly, and abnormal QRST complexes on the cardiogram distinguished the condition from so-called idiopathic atrial fibrillation. Treatment with digitalis, diuretics,

and conversion of rhythm met with variable success in this group. Reasonable health has been maintained in some when total abstinence has been observed and when the disease process was not far advanced on first presentation. The development of an arrhythmia with accompanying palpitation may draw attention to alcoholic heart disease before irreversible damage has been done.

A third group of patients presented with hypokinetic heart failure, cardiomegaly, and electrocardiographic evidence of severe myocardial disease. Response to treatment was moderate at first but an episodic downhill course was usual.

The electrocardiogram showed a wide range of abnormality as in other forms of cardiomyopathy. There was a fairly close correlation between the degree of cardiographic abnormality and the severity of the myocardial disease as judged by heart size and response to treatment. Mild polycythaemia was observed in many patients, and was thought to be a response to low-grade chronic cardiac insufficiency. Serum cholesterol levels tended to be lower than average and were believed to be the result of dietary replacement by ethanol.

Diagnostic problems abound in these patients, especially when the story of alcoholism is missed or its significance overlooked. In our experience most of these men consumed far more than was admitted in the initial interrogation. "Fallen hypertension" and silent coronary occlusion were common diagnostic errors (there was no occlusive coronary disease in nine cases examined at necropsy). Atrial fibrillation, a fast ventricular rate, sweating, and tremor with a low serum cholesterol combined to produce a superficial resemblance to thyrotoxicosis. As in other forms of cardiomyopathy, constrictive pericarditis has been erroneously diagnosed in patients with severe heart failure, but attention to clinical detail and the electrocardiogram should indicate the correct diagnosis and prevent unwarranted surgery.

The pathological findings on nine necropsy cases are described and possible mechanisms of pathogenesis discussed.

It is concluded that the association of high alcohol consumption for a long time and myocardial disease, manifest by arrhythmias and heart failure, is not fortuitous but causal. However, we have no evidence on the pathogenesis of the process nor on the nature of individual susceptibility.

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