CLINICAL, LABORATORY AND ANGIOGRAPHIC STUDIES ON ADULT NIGERIANS WITH HEART MUSCLE DISEASE

A thesis submitted to the Faculty of Medicine, University of Ibadan

BY

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ABSTRACT

Heart muscle disease (HMD) is a common cardiovascular disease in Nigerians. It presents with cardiomegaly associated with myocardial failure. Some of the patients have mild, transient hypertension when they are in failure but this rapidly improves with treatment of heart failure and without hypotensive drugs. A number of them have incompetence of the mitral valve and sometimes of the tricuspid valve. There is no pathognomonic sign on the electrocardiogram and chest x-ray usually shows cardiomegaly and signs of heart failure. Cardiac angiography shows dilated, poorly contractile left ventricle.

The heart macroscopically is flabby, dilated and hypertrophied with focal areas of fibrosis. Intra-cardiac thromb are common. Histologically, the muscle fibres are hypertrophied, there are areas of myocytolysis and focal scarring with scattered lymphocytes.

A critical review of studies conducted at the University College Hospital, Ibadan, Nigeria and aimed at finding the cause of HMD showed that there was very little evidence to incriminate malnutrition and anaemia as the cause of the disease although they may make the heart more susceptible to other injurious factors. There was strong evidence that hypertension could be an aetiological factor though a number

of questions remained unanswered. Thiamine deficiency was present in a significant number of Nigerians with HMD and might produce reversible myocardial damage. It could also act as a catalyst to other factors producing myocardial injury.

These suggested aetiological factors are, however, just a few of the disorders known to cause myocardial damage. Other disorders that have been incriminated in causing myocardial damage were therefore reviewed. A study was then undertaken, using a multifactorial approach, to assess the role of these disorders in the aetiology of HMD.

50 Nigerians with HMD were studied. Initial assessment included a comprehensive history and physical examination. A wide range of investigations was also carried out. The patients were treated on admission with digitalis and frusemide and maintained on the same dose of drugs on discharge from hospital. Thiazides, and when necessary, alpha methyldopa were substituted for frusemide if at any stage there was no improvement and if the blood pressure remained elevated. Each patient was followed up for at least 1 year.

Of the 50 patients, 6 were found on left ventricular angiography to have organic mitral incompetence. 18 of the remaining 44 patients presented with a normal blood pressur (diastolic blood pressure below 90 mmHg) and 26 with a diastolic blood pressure of 90 - 100mmHg. Of the 18 normotensive patients, 12 remained normotensive throughout the entire observation period. Their heart failure was controlled with digoxin and frusemide both as in-patient and in the subsequent out-patient follow-up. The heart failure of the remaining 6 patients was controlled while in hospital but they developed elevated blood pressures and relapsed into heart failure during out-patient follow-up on digoxin and frusemide. They needed antihypertensive therapy in the form of thiazides or methyldopa with thiazide to keep them out of heart failure. 20 patients with initiall raised blood pressures responded to in-patient treatment with a fall in blood pressure and remission of their cardiac failure. During out-patient follow-up the blood pressure became elevated again and cardiac failure reappeared. These patients needed antihypertensive therapy to produce a fall in blood pressure and relief of their heart failure. 6 other patients who presented with elevated blood pressures did not respond even as in-patients until antihypertensive therapy had been instituted. Those who needed antihypertensive

treatment to improve their heart failure had significantly enlarged aortic shadows on plain chest x-ray and on angiography. Many of them had small kidneys on intravenous pyelography and one of the patients who died had bilaterall contracted kidneys.

20 of the 44 patients with HMD were also alcoholics. All but one of the patients in the high socio-economic group were alcoholics. Many of the patients with HMD had a background of protein malnutrition as reflected in their significantly low serum albumin. They were also signifi-cantly thiamine deficient, only 1 patient had a high cardiac output reversed by thiamine administration. There was no significant difference between their serum potassium and controls.

There was also no significant difference in the frequency of toxoplasma infection between patients with HMD and controls. Two female patients with HMD had toxoplasma cardiomyopathy. They became ill in early puerperium and had very high titres against toxoplasma gondii.

Patients with HMD had a significantly higher incidence of infection from Coxsackie B viruses than controls. They also had higher levels of antibody titres. Antibodies to Coxsackie viruses B2, B3 and B6 were also more commonly

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Fig. 25: Case 2. Left ventricular angiogram during systole (A) and diastole (B) showing a slightly dilated left ventricle, good myocardial contraction in systole and moderate mitral incompetence.

CHAPTER 1

HEART MUSCLE DISEASE IN IBADAN

INTRODUCTION

There are various descriptions from many geographical areas of the world of obscure forms of heart disease which primarily affects the heart muscle (Fejfar, 1968). These descriptions have been published under various names such as idiopathic cardiomegaly (Reesinger and Blumenthal, 1941), nutritional heart disease (Gillanders, 1951), cardiovascular collagenosis (Becker et al, 1953), idiopathic hypertrophy of the heart (Altman and Stein, 1956), cardiomyopathy (Brigden, 1957), cryptogenic heart disease (Higginson et al, 1960), primary myocardial disease (Mattingly, 1961), heart muscle disease (Edington and Jackson, 1963) and a cardiac disorder of unknown aetiology (Stuart and Hayes, 1963). The common feature of these descriptions is that patients affected present with congestive cardiac failure and cardiomegaly, the cause of which is not readily apparent. The disease is particularly common in the tropical and sub-tropical countries and in these countries constitute one of the major clinical and health problems

(World Health Organisation (W.H.O.), 1965).

For want of a better name, this condition has been traditionally called heart muscle disease (HMD) at the University College Hospital (U.C.H.) Ibadan, Nigeria. This name will be retained in the discourse that follows.

PREVALENCE AT U.C.H., IBADAN

Most of the studies aimed at defining its prevalence in Ibadan have shown that HMD is the commonest cause of cardiac failure encountered either in the wards or at autopsy. Lauckner et al.(1961) in an analysis of medical admissions to the UCH in 1958 found that HMD was the most common disorder, accounting for over 30% of the patients who suffered from cardiovascular diseases. Edington and Jackson (1963) also analysed 1828 necropsies performed at the U.C.H., Ibadan and found that cardiovascular disease, excluding congenital conditions, accounted for 3.6 per cent of the necropsies. Of this percentage, HMD was the commonest cardiovascular condition. In a 12-month survey of new patients presenting in heart failure between 1967 and 1968, Brockington (1974) also found that HMD was the commonest cardiovascular disease. It

formed 21% of the 322 new cardiac patients. Also in an 8-year review of autopsies, Brockington (1974) found that HMD was responsible for 7% of cardiac deaths and was the fourth most frequent cause of cardiac death.

However, in a clinical prospective study of adult cases presenting at the cardiac unit, U.C.H., Ibadan between 1968 and 1969 (a year after Brockington conducted his 12 month survey) Carlisle and Ogunlesi (1972) found that HMD constituted 14% and was second to hypertensive heart failure (HHF) in percentage frequency. These workers used more rigorous criteria in separating HHF from HMD and this probably accounted for the lower incidence obtained.

Studies in children have also demonstrated its relatively frequent occurrence. Antia et al. (1972) in a prospective study of acquired heart disease in Nigerian children from birth to age 5 years for a period of $4\frac{1}{2}$ years found that HMD was second to rheumatic heart disease in frequency. It formed 25% of a total of seventy-two children studied.

PATHOLOGY:

The first published account from Ibadan of the pathology of HMD was in 1963 by Edington and Jackson.

This description was later amplified and relabelled as idiopathic cardiomegaly in 1968 (Edington and Hutt, 1968).

Macroscopically, there is a n increase in the heart size and weight as a result of dilatation and hypertrophy of both the right and the left ventricles (fig. 1). Dilatation tends to be predominant and therefore the left ventricular wall thickness may not be increased. The myocardium is soft in consistency and focal areas of fibrosis are present. There may be thinning of the wall of the apex of the left ventricle. The mitral and the tricuspid valve rings are usually dilated. The endocardium of the ventricular cavities usually shows a lacework pattern due to stretching of the trabeculae carnae. The papillary muscles are usually flattened. Intra-cardiac thrombi are frequent and are often found at the atrial appendages.

Histologically, there is hypertrophy of the muscle fibres and an increase in the connective tissue of the heart. The muscle fibres vary in size and have bizarre shapes. Anitschkow's myocytes may be seen. Focal scarring is always found and may be extensive. This scarring may follow obvious foci of myocytolysis (fig. 2) but elsewhere there is atrophy of the fibres with

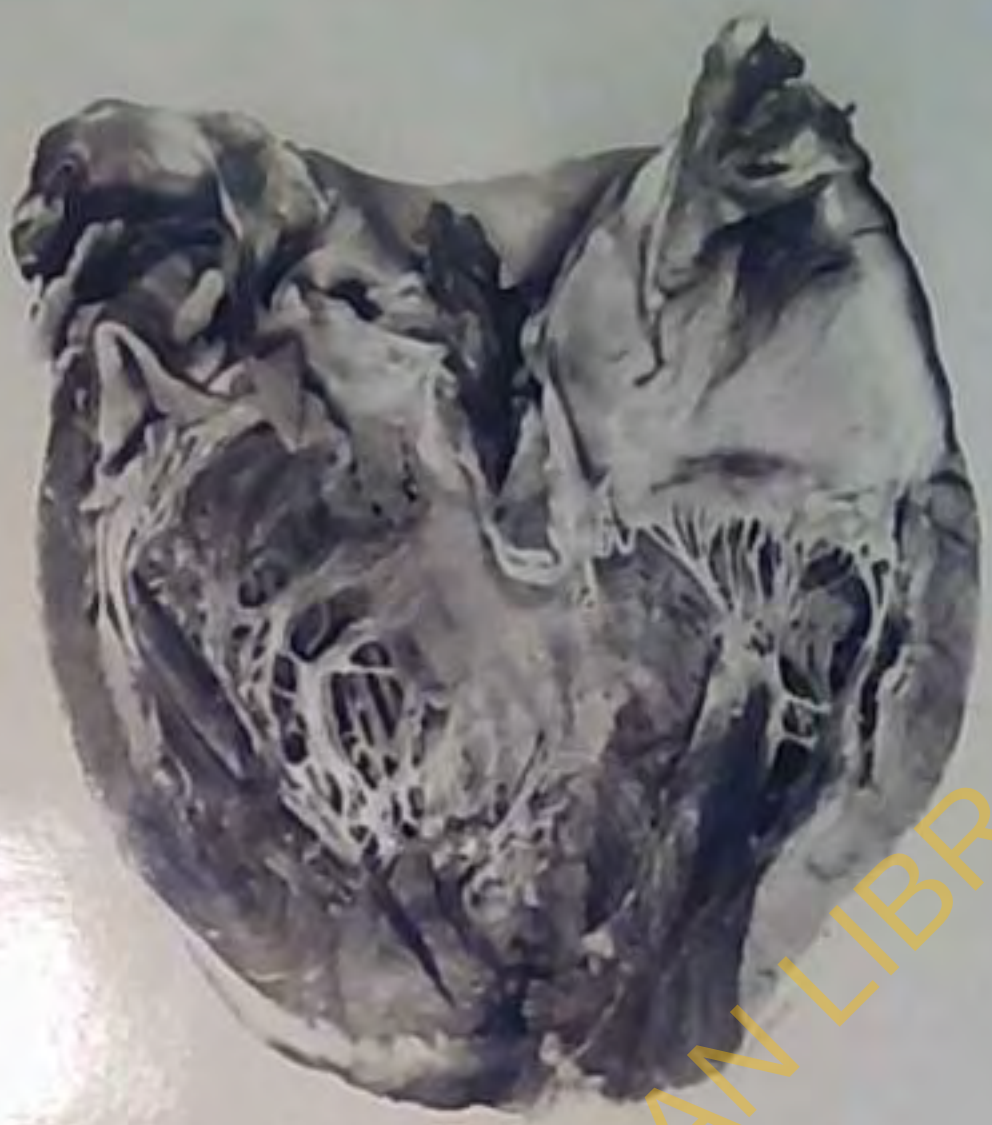

Fig. 1 A typical heart with heart muscle disease. It shows a dilated heart with hypertrophy of the ventricles.

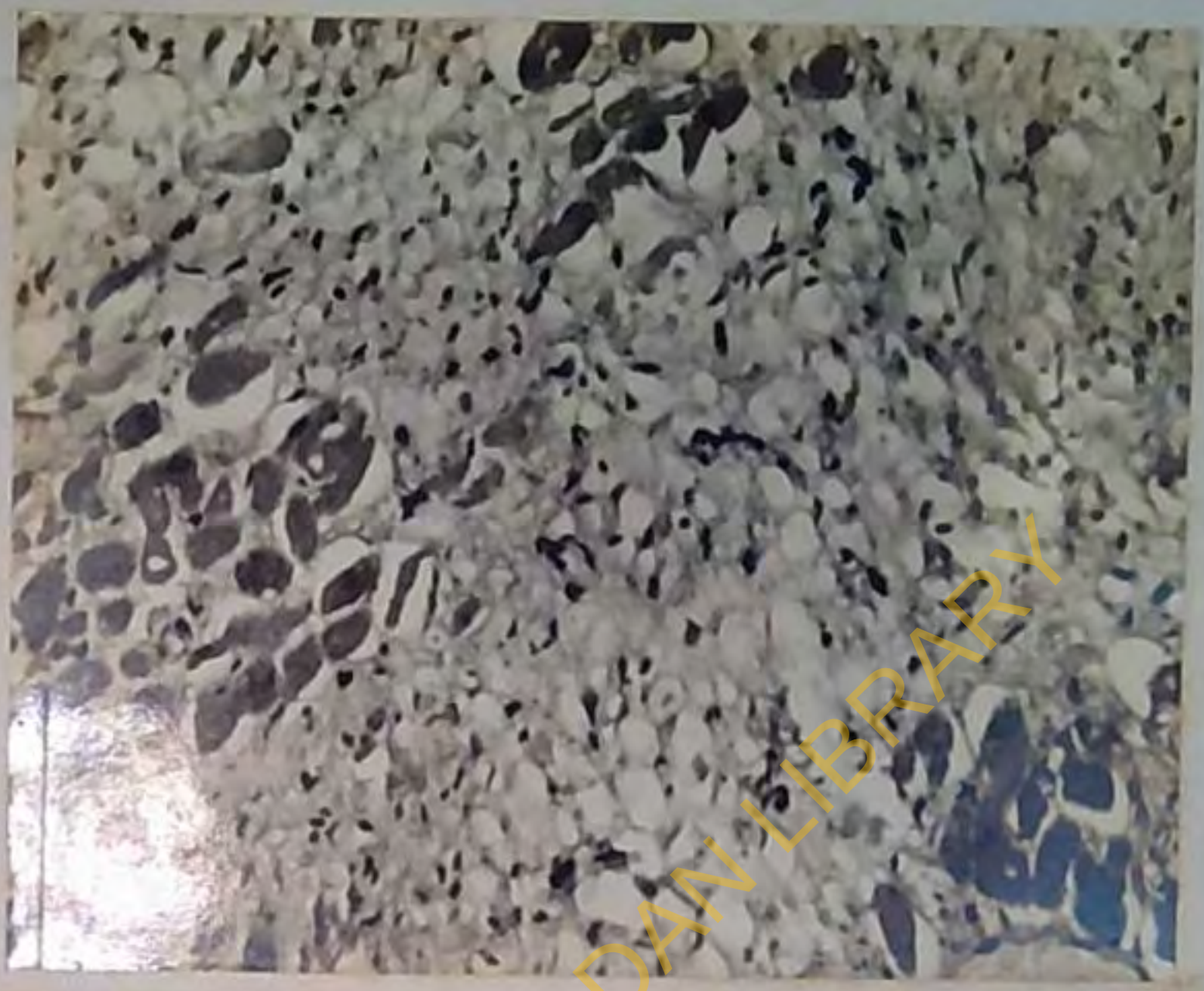

Fig. 2 Histology of a heart with heart muscle disease showing extensive areas of myocytolysis and moderate hypertrophy of the muscle fibres.

fibrotic replacement. Scattered lymphocytes and occasional histiocytes may be present especially in areas of myocytolysis. The coronary arterial vasculature is usually normal.

The changes in other organs include chronic venous congestion especially of the liver. There may be minute embolisation of the glomerular capillaries and lung vasculature. Occasionally, infarcts may be present in the lungs, kidneys, spleen and the brain. Rarely coronary artery embolus may occur.

CLINICAL FEATURES:

These have been well described by Parry and Ikeme (1966), Parry (1968) and recently by Brockington (1974). The following description is based on these papers.

It is a disease of middle-aged patients although adolescents, young adults and children (Antia et al, 1972) may be affected. There is a preference for men (Brockington, 1974) and it has no respect for social class (Parry, 1968).

The patients usually present with cardiac failure dominated either by acute left ventricular failure or systemic venous congestion or more commonly both. Only very few patients complain of fever in contrast to the

situation in children where fever is common (Antia et al, 1972).

The physical signs depend on the degree of failure and include commonly an easily palpable left ventricle, displaced apex beat and a raised jugular venous pressure. A prominent 'a' wave is easily discernible on the jugular venous pulse but in more severe cases with tricuspid incompetence, a prominent systolic wave is present. Occasionally there may be rapid 'x' and 'y' descents. The right ventricular impulse is commonly heaving and other signs of venous congestion such as hepatomegaly, ascites, and peripheral oedema are present.

On auscultation, an apical pansystolic murmur of mitral incompetence is present together with a loud third sound. A murmur of tricuspid incompetence may also be present. Incompetence of these valves are usually considered as functional.

The blood pressure is often raised when these patients are in heart failure and diastolic levels of up to 130 mm Hg have been recorded (Parry and Ikeme, 1966; Akinkugbe, 1972; Brockington, 1974). This hypertension in the typical case is mild and transitory the blood pressure becoming normal with treatment and staying normal without sustained treatment

by diuretics or hypotensive agents. It has been referred to as "reactive hypertension" (Akinkugbe, 1972; Brockington, 1974) and is thought to be due to intense peripheral vasoconstriction occurring in cardiac failure (Parry and Ikeme, 1966).

The arterial pulse varies from a low to a full volume pulse. Sustained arrhythmias are not common (Parry and Ikeme, 1966; Parry, 1968). The ocular fundi may show "minor arterial changes" (Parry, 1968).

ELECTROCARDIOGRAM:

There is no pathognomonic pattern on the electrocardiogram. A low voltage may be present but often there is left ventricular hypertrophy. There may be left atrial hypertrophy and the T waves are often generally inverted or flat. Abnormal intraventricular conduction (most commonly left bundle branch block) may occur.

RADIOGRAPHIC FINDINGS:

This shows a large heart with a prominent left ventricle (Cockshott et al, 1967). There may be signs of pulmonary oedema and cardiac movements are reduced on screening. Pleural effusions occur frequently. Ventricular angiography usually shows large ventricular

chambers with little change in size and shape throughout the cardiac cycle and with persistence of contrast. Mitral incompetence is present in some cases.

DIFFERENTIAL DIAGNOSIS:

HMD has to be distinguished from patients with hypoalbuminaemia, cirrhosis of the liver or chronic renal failure with a nephrotic picture (Parry, 1968). It also has to be distinguished from hypertensive heart failure although this is difficult. Persistence of the abnormally high blood pressure indicates that the patient has hypertensive heart disease (Parry, 1968). The presence of florid retinopathy may also help in the diagnosis of hypertensive heart disease although arterial changes may be present in HMD (Parry, 1968).

Patients with organic mitral incompetence also constitute an important group in the differential diagnosis. In most cases of HMD, the pansystolic murmur at the mitral area gets much less or disappears after treatment of cardiac failure (Parry, 1968; Brockington, 1974). If the murmur persists, mitral valve disease is possible and rheumatic mitral incompetence, left ventricular endomyocardial fibrosis or a submitral left ventricular aneurysm must be considered. Also most

patients with HMD are over the age of 40 years and diastolic murmurs, common in rheumatic mitral incompetence are rare (Brockington, 1974). The presence of mild hypertension in HMD also helps in distinguishing it from rheumatic mitral incompetence as it is rare in the latter (Brockington, 1974).

Cor pulmonale is also an important condition in the differential diagnosis. The diagnostic criterion that patients with HMD must have evidence of left ventricular enlargement and failure seeks to establish its distinction from cases of pulmonary heart disease (Brockington, 1974). This distinction is not always clear, however, for a grossly enlarged left ventricle may not appear so on the chest x-ray and left ventricular failure may itself occur in cor pulmonale (Brockington, 1974).

Ischaemic heart disease may also mimic HMD although this is rare in Nigerians (Parry, 1968; Brockington, 1974; Falase et al, 1973).

Occasionally constrictive pericarditis may present difficulties, especially when patients with HMD present with signs of cardiac constriction (Parry, 1968). Rarely, exploratory thoracotomy may be

necessary (Parry, 1968).

PROGNOSIS:

Of 127 patients studied by Brockington (1974), 4 continued to attend and remained asymptomatic without therapy. 34 patients improved and remained well on drugs for up to 2 years. 29 patients defaulted for up to one month and came back in heart failure. 19 relapsed while still attending the clinic and receiving medication. In 5 patients, there was a delayed recovery followed eventually by improvement on therapy. 10 patients continued to have signs of considerable left ventricular enlargement and pulmonary hypertension although they did not go into heart failure. 26 patients remained in chronic heart failure. 5 patients were known to have died. He thought the remainder died at home.

PERIPARTUM CARDIAC FAILURE:

This well-recognised entity of cardiac failure of unknown cause occurring in women in relation to child-birth has also been reported at Ibadan (Parry and Ikeme, 1966; Brockington, 1971). Brockington (1971) reported 50 cases from Ibadan seen over a period of 10 years and noted that hypertension was present on admission in 84%

of the patients. He argued that this entity was more compatible with a hypertensive origin than with intrinsic myocardial disease and was probably a special form of acute hypertensive heart failure. The clinical picture is similar to HMD (Parry and Ikeme, 1966; Davidson and Parry, 1974), except that it occurs during late pregnancy or after delivery. Patients with peripartum cardiac failure also tend to recover fully and quickly. Cardiac size usually returns to normal on recovery, in contrast to patients with HMD.

STUDIES FROM OTHER PARTS OF NIGERIA:

Reports from Lagos, Zaria and Benin have shown that HMD is common in other parts of Nigeria. Okuwobi (1968) reported a prevalence of 29% to 36% from Lagos in a paper analysing the pattern of heart disease at the Lagos University Teaching Hospital. HMD was the commonest and there were two peak incidences between the ages of 20 to 30 years and 50 to 70 years.

HMD is also commonly seen at Ahmadu Bello University, Zaria (Ladipo, 1976) but peripartum cardiac failure is particularly common among the Hausa women (Davidson et al, 1974) accounting for a

substantial percentage of female medical admissions. It appears to occur more commonly in Zaria than in Ibadan (Davidson et al, 1974).

Oviasu (1973) in a study of 225 patients presenting in heart failure at the University of Benin Teaching Hospital found that HMD occurred in 36 patients (30%). These 36 patients were made up of 22 males and 14 females Their ages ranged between 10 years and 59 years, the highest incidence occurring between 20 years and 49 years.

SUMMARY

HMD is a common cardiovascular disease in Nigerians. It presents with cardiomegaly associated with myocardial failure. Some of the patients have mild, transient hypertension when they are in failure but this rapidly improves with treatment of heart failure and without hypotensive drugs. A number of them have incompetence of the mitral valve and sometimes of the tricuspid valve. There is no pathognomonic sign on the electrocardiogram. The chest x-ray shows cardiomegaly and signs of heart failure. Cardiac angiography shows dilated, poorly contractile left ventricle.

The heart macroscopically is flabby, dilated and hypertrophied with focal areas of fibrosis. Intra-cardiac thrombi are common. Histologically, the muscle fibres are hypertrophied, there are areas of myocytolysis and focal scarring with scattered lymphocytes.

Similar diseases have been reported from elsewhere in Nigeria (Lagos, Benin and Zaria).

CHAPTER 2

THE AETIOLOGY OF HEART MUSCLE DISEASE - REVIEW OF HYPOTHESES FROM IBADAN

A few studies have been conducted at Ibadan aimed at determining the cause of HMD. This chapter critically reviews the findings.

MALNUTRITION:

Abrahams and Brigden (1961) studied 50 Nigerians with mitral incompetence and pulmonary hypertension and found that over half of them presented in congestive cardiac failure. A number of them had tricuspid incompetence in addition. Many had ventricular extrasystoles but none was hypertensive. 16 had signs suggestive of an active carditis. All the patients were anaemic and had a background of chronic malnutrition. Their average serum albumin was 2.5 gm/ 100 ml.

13 of the patients came to necropsy. Some of these 13 patients had endomyocardial fibrosis, some had rheumatic carditis while the rest had "non-specific myocarditis".

They concluded that some of the patients were cases

of HMD and that considering their background, protein malnutrition and anaemia may have a part to play in its aetiology.

Earlier in 1951, Gillanders described a syndrome seen in Africans in Johannesburg characterised by severe heart failure, tachycardia gallop rhythm, low cardiac output, mild peripheral neuropathy, a dilated and hypertrophied heart and mural thrombi. Histologically the hearts showed intracellular oedema and hydropic degeneration of muscle fibres with focal interstitial fibrosis. The pathogenesis was thought to be a metabolic myocardial dysfunction leading to cardiac dilatation and hypertrophy with secondary mural thrombosis.

He regarded this condition as a manifestation of chronic malnutrition. Many of the patients improved in hospital on a well-balanced diet of wholesome food but relapsed on discharge home. Their condition deteriorated when they were fed in hospital on a poor diet they took at home. A number of the patients had hepatic abnormalities such as fatty liver, cytosiderosis, portal scarring, and cirrhosis. All these were regarded as due to malnutrition.

Protein malnutrition occurring naturally in man or experimentally induced in monkeys may result in cardiac abnormalities (Ramalingaswami, 1974). Histologically, however, this is different from HMD. The hallmark is cardiac atrophy in contradistinction to the overweight heart of HMD. Kwashiorkor, common among Nigerian children, also gives rise to an atrophic heart with clinical evidence of a low output state. ECG abnormalities are common and cardiac failure may occur as a result of associated anaemia (Wharton et al, 1969). In Chile, a high incidence of myocardial destruction, cardiac dilatation and congestive cardiac failure have been reported in children dying from protein-calorie malnutrition (Piza et al, 1971). However there is no study that has shown that the myocardial damage sustained in childhood due to malnutrition may later on manifest as adult HMD. In fact, follow-up studies carried out in Capetown (Smythe et al, 1962), Kingston (Garrow and Pike, 1967) and Kampala (Cook and Hutt, 1967) on children treated successfully for kwashiorkor some 2 - 10 years previously did not show any evidence of cardiac sequelae.

Gillanders' patients however resemble those with HMD clinically and pathologically. Shaper (1968) has critically analysed Gillanders' evidence for a nutritional aetiology in this condition and found it inadequate. Higginson (1958) has also pointed out that the experiment showing recurrence of heart failure on reversion to a poor diet has never been repeated. It has also been suggested that these patients are no more under-nourished than the rest of the population (Isaacson, 1966) and siderosis has been shown to be common in the Bantu (Bothwell and Isaacson, 1962). Shaper (1968) has also raised the possible role of alcohol in the aetiology of heart failure of the patients described by Gillanders because in a later paper from the same hospital, Grusin (1957) described some cases of acute reversible heart failure in Africans in whom alcoholism was a significant feature and in whom a response to thiamine was obtained in some cases.

In Nigeria, Brockington (1974) compared the socio-economic status of patients with HMD with patients with other types of heart diseases and found no difference between the two groups. Parry (1968) had earlier noted

that no social class was exempt from HMD.

The evidence for protein malnutrition as the cause of HMD thus remains tenuous. Although Abrahams and Brigden noted that their patients had a background of chronic malnutrition, the majority of patients attending UCH, Ibadan belong to the low socio-economic class (Falase, et al, 1973) and their observations may be a reflection of the whole population. Protein malnutrition may, however, be a conditioning factor, allowing infection to be more virulent (Woodruff and Kilbourne, 1970) and increasing the susceptibility of the heart to other injurious agents.

Anaemia produces a high output failure as opposed to the low output failure of HMD. Although some patients with anaemia may on rare occasions have a low cardiac output failure (Knight, 1974) they are unmistakenly different from HMD. In addition, there has been no long-term study that shows that patients with chronic anaemia can progress to the chronic myocardial failure of HMD. It is however possible, in view of suboxygenation and consequent myocardial impairment anaemia produces, that it makes the heart more susceptible to other injurious factors such as infections.

ENDOMYOCARDIAL FIBROSIS (EMF)

Edington and Jackson in 1963 studied 29 hearts of patients who died in congestive cardiac failure not due to rheumatic carditis. They divided the hearts into three groups. Group I subjects had hearts which were similar to HMD. Group III patients had endomyocardial fibrosis (EMF). The hearts of the patients in Group II were intermediate between the hearts of those in the other two groups. They resembled the hearts in group I but differed in that they had more ante-mortem thrombi and patchy endocardial thickening.

They therefore contended that HMD was an early form of EMF in which degeneration of muscle fibres was seen microscopically and the heart enlarged with early visible fibrosis of the trabeculae carnae. At a later stage thrombi became adherent to the endocardium particularly between the fibrotic trabeculae. In the fully developed cases the sheet of collagenous tissue at the apex was the result of thickening of the endocardium together with organisation of thrombus. Fibrotic trabeculae were then incorporated in the thrombus, the fibrotic process later on extending up the inflow path and involving

the papillary muscle, chordae tendinae and the valve cusps of the mitral or tricuspid valve. They therefore concluded that HMD and EMF were stages in one pathological process. They agreed that no conclusions could be drawn from their study regarding the aetiology of HMD and EMF in Nigeria. However, they contended that if their hypothesis that the two conditions were the outcome of one and the same process was correct, the investigational field could be narrowed.

Since then, there has been no study confirming that HMD could progress to EMF but there is some evidence that these two conditions are probably unrelated. HMD is commonly seen in the northern part of Nigeria where EMF is rare (Ladipo, 1976). Furthermore, if HMD progresses to EMF, the latter would be expected to occur in the older age group and HMD in the younger. However, the reverse is the case. More than two-thirds of autopsied subjects with EMF are below the age of 35 years (Hutt and Edington, 1968) while HMD is commoner in adults over the age of 35 years (Parry, 1968).

Most authors now classify HMD and EMF as two distinct disease processes (Oakley, 1972; Korb, 1974).

Edington, in two later publications (Edington and Hutt, 1968; Edington and Giles, 1969) described HMD separately from EMF. There has also been no further suggestion in these papers that both diseases are the result of the same process. It seems therefore unlikely that HMD and EMF are the outcome of one and the same process and at present both diseases are best regarded as two distinct aetiological entities.

HYPERTENSION:

Brockington (1974) in a thesis on HMD in Nigeria compared the epidemiology, clinical picture, course, pathology, aortic measurement, retinal appearances and the renal changes at necropsy of patients with HMD and HHF. His cases consisted of patients admitted to the wards or seen in the out-patient clinic and a retrospective case note study. He also reviewed necropsies over an 8 year period.

He found that both diseases were similar in age distribution, sex ratio and geographical distribution (although there was an excess of young patients with high blood ureas in HHF especially in the necropsy series).

There was no difference in the duration of

symptoms or presenting complaints. All the signs of clinical severity were found in HHF and these did not seem less severe than HMD.

At necropsy, there were more dilatation, thrombus formation and endocardial fibrosis in HMD. In addition there were more attenuation and smooth muscle hypertrophy histologically.

The proportion showing signs of right and left ventricular disease after recovery from failure was lower in HHF. Studies of the course of the first episode showed a steadily poorer outcome with lower presenting blood pressure. More patients came back after more than one default. The survival time of patients with HHF was longer, more of them dying from non-cardiac causes. HMD seemed to be more severe, not in its overall clinical picture at the time of presentation but in its less rapid and complete recovery from failure.

The electrocardiogram showed considerable left ventricular hypertrophy in HMD though less than in HHF. There was less left ventricular thickening in HMD probably due to the greater ventricular dilatation in this disease.

The aortic width was intermediate between that of HHF and normotensive controls. Arteriolar narrowing in the retina was absent in HMD. 18 of 36 patients with HMD whose kidneys were examined at necropsy had arterial changes of chronic hypertension.

Brockington also found that there was a general tendency for the blood pressure of patients with HHF to fall at subsequent presentations. This was illustrated by 5 patients who initially had hypertension without heart failure but who subsequently presented in heart failure but with only a mildly raised blood pressure.

He therefore concluded that HMD and HHF are similar and that HMD is the late stage of untreated chronic HHF. However, he admitted that in about 3% of the cardiac necropsies, it was difficult to find any evidence of chronic hypertension. He thought these cases may have subacute hypertensive failure.

In another study on 50 cases of peripartum cardiac failure seen over a 10 year period, Brockington (1971) noted hypertension on admission in 84% of the patients. He related the disorder to the phenomenon of symptomless postpartum hypertension (Stout, 1934)

and suggested that a proportion of those developing transient postpartum hypertension were liable to progress to hypertensive heart failure. He therefore concluded that peripartum cardiac failure could be a special form of acute hypertensive heart failure. Recently, from Zaria, there has been a suggestion that a proportion of the patients seen there with peripartum cardiac failure might have HHF (Fillmore and Parry, 1976).

A transient elevation of the blood pressure limited to the period of congestive cardiac failure is a recognised feature of HMD (Parry and Ikeme, 1966; Parry, 1968) and similar diseases described elsewhere in the world (Reesinger and Blumenthal, 1941; Brigden, 1957; Stuart and Hayes, 1963; Fowler, 1964; WHO, 1965; Tobin et al, 1967). With response to treatment of the heart failure, the diastolic pressure returns to normal and stays normal without any hypotensive drug. This transient elevation is called 'reactive hypertension' in Ibadan but is more widely known as 'Sahli's Hochdruckstauung' (Brockington, 1972). This concept of 'reactive hypertension' holds that the elevation of the blood pressure is as a result of the

heart failure and not the cause of the heart failure (Fishberg, 1940; Davies et al, 1951; Fowler, 1964; Harvey et al, 1964; Massumi et al, 1965; Akinkugbe, 1972).

It is also well-recognised that there is increased catecholamine secretion and sodium retention, factors which tend to raise the blood pressure, in heart failure (Oram, 1971). However, elevation of blood pressure in heart failure tends to occur more commonly and decidedly more pronounced in HMD (Massumi et al, 1965; Brockington, 1972). Brockington (1974) analysed the case notes of 118 patients presenting in heart failure other than HHF or HMD in a 12 month survey and showed that hypertension was absent when they were in heart failure. The average presenting blood pressure was 127/88 mm Hg for cor pulmonale, 114/74 mm Hg for endocardial disease; 182/61 mm Hg for aortic incompetence, 128/63 mm Hg for anaemic heart failure and 114/71 mm Hg for 29 other patients. In those who were over the age of 40 years, the average presenting blood pressure for patients with endocardial diseases such as EMF or rheumatic heart disease was 122/74 mm Hg.

Fahr (1923) in his work on the hypertensive heart

believed that 'chronic myocarditis' was hypertensive in origin. He found that at necropsy, his patients showed hypertrophy and dilatation with a histological appearance of diffuse and focal fibrosis and that these changes occurred in patients with a pure pressure load (e.g. chronic asthma, congenital pulmonary stenosis) and could not be produced experimentally by the injection of microorganisms. He also found, that 70% of the patients with 'chronic myocarditis' had hypertension of at least 170/100 mm Hg or the pathological findings of atherosclerotic kidneys, and most also had 'Sabot-shaped' hearts on the chest x-ray. Furthermore, he noted that patients with a lower blood pressure had a history of hypertension or renal findings suggesting chronic hypertension and that it was well known that the blood pressure not infrequently fell in 'hyperpiesis' when cardiac insufficiency set in.

Laurie et al. (1960) and Foster (1965) working in different parts of Africa have also all suggested that hypertension was the agent of unexplained heart failure in their respective countries.

Ikeme et al. (1975) studied sixty Ugandan patients in heart failure without any obvious associated causes

except a raised blood pressure in some. They classified them into three groups, according to the level of the diastolic blood pressure on admission i.e. (1) idiopathic cardiomegaly (ICM) with heart failure, diastolic blood pressure $<$95 mm Hg (35 cases); (2) mild to moderate hypertension with heart failure, diastolic blood pressure 95-114 mm Hg (15 cases) and (3) hypertensive heart failure diastolic blood pressure $>$ 114 mm Hg (10 cases). They found it difficult to distinguish one group from the other on clinical grounds except on the basis of the blood pressure. The 35 patients who presented with what was regarded traditionally as ICM showed evidence suggestive of the existence of hypertension such as aortic arch dilatation before the onset of heart failure. Some of them manifested hypertension on recovery from heart failure. The 15 patients who were admitted with moderately raised blood pressures also exhibited considerable increase of the blood pressure on recovery from heart failure. The remaining 10 cases with a diastolic blood pressure above 114 mm Hg required hypotensive therapy from the outset, combined with the antifailure regimen given to all the subjects in the study.

They concluded that hypertension was an important causative factor in many of the cases of the ICM and that the extent of the associated myocardial damage in them, the cause of which was so far uncertain, may determine the tendency to a fall in the blood pressure when they present in overt cardiac failure.

The question therefore is whether the mild, transiently raised blood pressure seen in HMD is the cause of it or a result of heart failure. There is strong evidence as outlined above to show that hypertension is the cause of the heart failure but some questions remain unanswered. For example, why is the hypertension transient, why does the pressure respond to treatment of heart failure only and why does it remain normal without hypotensive drugs when the patients are out of heart failure? In addition can such mildly raised blood pressure occurring transiently as it does be responsible for biventricular failure? Furthermore, why do certain people with mild or moderate hypertension develop dilated and hypertrophied hearts and cardiac failure whereas others living in the same area are able to sustain prolonged severe hypertension without these effects?

There is little agreement at present on what level of hypertension can be considered the cause of rather than a consequence of myocardial failure and in Ibadan where HMD and HHF are both common, it is often difficult in clinical practice to find a clear dividing line between the two conditions. However, a close look at Brockington's figures (1974) yielded some interesting findings.

He defined HHF as a mean presenting blood pressure of 135 mm Hg and above (the mean blood pressure was defined as the diastolic pressure plus one third of the pulse pressure). He also stratified HMD into three different groups. The first group had a mean presenting blood pressure of 121 - 135 mm Hg, the second 106 - 120 mm Hg, while the third group had a mean presenting blood pressure below 106 mm Hg. The actual presenting blood pressure for each patient seen clinically was not given but the blood pressures of those who came to necropsy were available in the thesis. A close look at the presenting blood pressures of these patients (calculation mine) showed that those with HHF below the age of 40 years (10 patients) had systolic blood pressures ranging between 170 and

250 mm Hg with a mean of 205.2 mm Hg. Their diastolic blood pressures ranged between 120 and 165 mm Hg (mean = 144.5 mm Hg).

10 other patients with HHF who were above the age of 40 years had a systolic range of 150-240 mm Hg (mean 197.7 mm Hg) and a diastolic range of 113-180 mm Hg (mean = 133.3 mm Hg).

Patients with HMD with a mean blood pressure of 121-135 mm Hg (8 patients) had systolic blood pressures between 145 and 190 mm Hg (mean = 156.3 mm Hg). Their diastolic blood pressures ranged between 105-120 mm Hg (mean = 112.5 mm Hg).

The remaining groups of HMD i.e. those with mean presenting blood pressure of 106-120 mm Hg and those with mean presenting blood pressure below 106 mm Hg were further divided by him into two subgroups - those with good or fair evidence of chronic hypertension and those with little or no evidence of hypertension.

In those with mean presenting blood pressure of 106-120 mm Hg, those with chronic hypertension (12 patients) had systolic blood pressures ranging from 117 mm Hg to 160 mm Hg (mean = 142.2 mm Hg). Their diastolic blood pressures ranged from 90 - 110 mm Hg (mean = 97.7 mm Hg). Those with no clear evidence of chronic

hypertension (10 patients) had the following systolic and diastolic blood pressures respectively 130-160 mm Hg (mean = 140 mm Hg) and 95 - 113 mm Hg (mean = 102.8 mm Hg).

In the last group of patients with HMD, the systolic and diastolic blood pressures of those with good evidence of chronic hypertension (15 patients) were respectively 80-130 mm Hg (mean 116.5 mm Hg) and 70-93 mm Hg (mean = 81.75 mm Hg). The remaining sub-group (17 patients) with no evidence of chronic hypertension were 100-135 mm Hg (mean = 112.3 mm Hg) for systolic pressures and 70-95 mm Hg (mean = 82.6 mm Hg) for diastolic pressures.

In the study, Brockington (1974) found that all the patients with mean presenting blood pressures between 121 and 135 mm Hg closely resembled HHF (i.e. those with mean blood pressure greater than 135 mm Hg) in their tendency to remain hypertensive, their aortic size and their very low necropsy index. They differed from HHF only in the lack of ECG evidence of left ventricular hypertrophy and retinal changes. As stated above, some of the patients with mean presenting blood pressure of 120 mm Hg and below had evidence of chronic hypertension and others did not.

The above therefore implies that those with a mean diastolic blood pressure of about 112.5 mm Hg resembled HHF while those with 102.88 mm Hg and below were in the grey zone. This therefore emphasises the importance of the presenting blood pressure. Most definitions of the presenting blood pressure compatible with HMD are arbitrary. Although some workers have suggested diastolic levels of up to 130 mm Hg as compatible with HMD (WHO, 1965; Brockington, 1974) many physicians would at the present time probably regard this figure as too high and ascribe failure to hypertension alone. Most of these patients would almost certainly receive hypotensive drugs. This has also been well illustrated by Brockington's study outlined above which showed that patients with diastolic blood pressure levels between 100 mm Hg and 130 mm Hg resembled hypertensives with higher diastolic blood pressures. Selection of more of these patients in any study will certainly lead one to conclude that HMD is HHF.

However, the fact that some of his patients with lower diastolic blood pressures were hypertensives and others, possibly, were cases of "subacute HHF" is

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However, the fact that some of his patients with lower diastolic blood pressures were hypertensives and others, possibly, were cases of "subacute HHF" is

interesting. Also interesting is the fact that some patients who had hypertension without failure subsequently came back in heart failure with a lower blood pressure.

Brockington presented some of his findings in a debate on whether HMD is really hypertensive heart disease (HHD) in disguise at a symposium held in London in 1971 (Dickinson et al, 1972). His contention that HMD is a form of HHD was supported by Oakley. She argued that a failing left ventricle cannot achieve an increase in mean blood pressure and that there are well documented hypertensives who lose the need for hypotensive drugs at the same time as their hearts got larger and failed. She also pointed out that HMD was common in areas in which hypertension was common and the lack of hypertensive changes in the arteries was as a result of lack of sustained hypertension caused by the failure of the left ventricle to maintain output.

The view that HMD is HHF in disguise was challenged by Goodwin (1972). He showed that the heart in HHD is different structurally from the heart in HMD. The heart in the former was more hypertrophied than dilated while that of the latter showed more

cavity dilatation than hypertrophy. Coronary artery disease was common in hypertension but rare in HMD. The ECGs of both diseases were different and the phase of hyperfunction or hypertrophy described by Meerson (1962) in his experimental work on cardiac hypertrophy was not seen in HMD. Systemic hypertension in HMD was rare in cases seen in Britain.

From all the above, the evidence is strong that hypertension may have some part to play in the aetiology of HMD but a number of questions remain unanswered.

THIAMINE DEFICIENCY

In 1972, we (Basile et al, 1973) examined the thiamine status of 22 consecutive and unselected Nigerians with congestive cardiac failure and compared them with 33 Nigerian blood donors and 16 Nigerian elite (i.e. doctors and other senior members of staff of U.C.H., Ibadan). 8 of the 22 patients had HMD while the remaining 14 patients had other forms of heart failure. The thiamine status was determined by the erythrocyte transketolase method (Brin et al, 1960).

We found that patients with HMD were significantly deficient of thiamine (mean TPP effect in % hexose =

35.5). Those with other forms of heart failure had a normal mean TPP effect of 11.9. The mean TPP effect of the Nigerian blood donors and Nigerian elites were 10.9 each. The mean age of the patients with HMD was 44.5 years while those with other forms of heart failure was 45.4 years. None of the patient was an alcoholic and only one patient had transient hypertension.

Unfortunately, the response to treatment with thiamine was not determined. The cardiac outputs of the patients were also not measured although clinically they all seemed to be in low-output heart failure.

The relationship of thiamine deficiency to obscure forms of heart failure called congestive cardiomyopathy (CC) has been extensively investigated in South Africa. Brandt et al in 1965 found that 18% of the patients with CC were thiamine deficient and labelled them atypical beri-beri heart disease. Brink et al (1966) found that 25% of 54 patients with congestive cardiac failure were thiamine deficient. The thiamine deficient patients were all from the Cape coloured or Bantu groups whose diet consisted largely of carbohydrate and little protein and fat.

In two other papers from South Africa (Seftel et al, 1972; Seftel, 1972), two main forms of CC were recognised - beriberi heart disease which was of high output and reversible by administration of thiamine and idiopathic cardiomyopathy (IC) which was much commoner and in which cardiomegaly or myocardial failure was usually persistent or progressive. Acute pernicious beriberi (Shoshin type) also occurred.

Some of the patients with IC had associated high output beriberi heart failure. They responded to treatment with thiamine but cardiomegaly tended to persist after recovery. The other group of patients with IC were not thiamine deficient and showed no response to thiamine administration. Alcoholism was very common among the patients and was considered the major cause of CC. The other cause of CC was thought to be chronic malnutrition.

Beriberi heart disease on the other hand is virtually non-existent in Great Britain (Goodwin and Oakley, 1972) and in the United States of America. It is now generally accepted that the myocardial disease found in many alcoholics is not a consequence of thiamine deficienoy since they always maintain an

adequate diet without clinical evidence of a vitamin deficiency (Mitchell and Cohen, 1974).

The classical picture of the beriberi heart is a high output failure, a situation totally different from that of HMD. A patient with low output heart failure caused by beriberi has, however, been reported by McIntyre and Stanley (1971). Their patient subsequently had high output on the administration of thiamine. Low output heart failure has also been reported by Blackenhorn (1945) and Walters (1953) but their diagnosis of beriberi was made by exclusion and not all their cases responded to thiamine administration.

There are conflicting reports as to whether thiamine deficiency can cause permanent myocardial damage. Crawford (1952) described a case with permanent myocardial damage presumed to have beriberi heart disease. The patient was an alcoholic in congestive cardiac failure who had a blood pressure of 130/90, a mitral systolic murmur and ECG changes suggestive of diffuse myocardial damage. He was apparently not in high output failure and response to thiamine was not determined. At necropsy, the patient had an enlarged, soft flabby heart and histologically degenerative cellular changes,

interstitial fibrosis and focal areas of necrosis in the septum and the left ventricle. Crawford (1952) considered these histological changes to be due to thiamine deficiency. He quoted other workers who had found similar changes in the hearts of patients presumed to have beriberi heart disease but who were also alcoholics. He also quoted experiments on animals made thiamine deficient. The hearts of such animals were dilated. Extensive microscopic alterations were seen as early as the thirty-seventh day of deficiency. Focal and diffuse areas of necrosis were also seen throughout the myocardium. Scar tissue was present in animals who had suffered several episodes of thiamine deficiency.

Crawford's case was atypical for beriberi heart disease and resembles a cardiomyopathy probably due to alcohol which is now well-recognised as one of the causes of myocardial damage (Burch and De Pasquale, 1968 and 1969).

Walters (1953) also reported that irreparable damage may persist in spite of recovery from the acute stage of cardiovascular failure caused by beriberi. Most of his cases similarly resembled HMD, some of

them were alcoholics and his diagnosis of beriberi heart disease was made by exclusion. Thus his claim remains not completely proven.

Wenckebach (1935) noted sarcolysis of muscle fibres giving an appearance of swelling and liquification in a seven month study of beriberi among the "Tropical Wonders of Java and Sumatra". A deficiency of thiamine in the diet was the cause of beriberi in his patients. He did not, however, consider the alterations he found specific for beriberi heart disease.

Conversely, Griffith (1952) has noticed that patients who survive the acute stages of beriberi and who are properly treated do not have residual clinical heart disease. Among patients who recovered from beriberi, the incidence of cardiovascular disease from other causes was no higher than would normally be expected. In those who die, the myocardium was normal histologically (Vedder, 1938). McIntyre and Stanley (1971) also noted that their two patients with beriberi heart disease had no residual myocardial impairment after recovery. Bryne-Quinn and Fessas (1969) described two cases who recovered completely after treatment. We have also described an

alcoholic with high output beriberi heart failure who had no residual damage following treatment with thiamine (Falase et al, 1977).

It therefore seems that chronic myocardial damage has been seen only in cases of possible beriberi heart disease who are alcoholics or who have features quite like HMD. This tallies well with the observations in South Africa where patients with pure beriberi heart disease had a reversible disease but those in which myocardial damage was present had, in addition, idiopathic cardiomegaly thought to be caused by alcohol or chronic malnutrition.

The role of thiamine deficiency in the aetiology of HMD thus remains speculative. Thiamine deficiency itself may produce reversible myocardial damage and by imposing a greater strain on an already damaged heart and causing metabolic acidosis (Jeffcy and Abelmann, 1971) may be accelerating or worsening myocardial injury produced by other factors. It may also be the factor that eventually tilts such hearts into failure.

SUMMARY AND COMMENTS:

A critical review of studies conducted at Ibadan

and aimed at finding the cause of HMD has been undertaken. There is very little evidence to incriminate malnutrition and anaemia as the cause of the disease although they may make the heart more susceptible to other injurious factors. There is strong evidence that hypertension may be an aetiological factor though a number of questions remain unanswered. Thiamine deficiency is present in a significant number of Nigerians with HMD and may produce reversible myocardial damage. It may also act as a catalyst to other factors producing myocardial injury.

The above-named factors are just few of the disorders known to cause myocardial damage (Fowler, 1964; Oakley 1972). Several workers have also emphasised the fact that HMD (or similar diseases described in other countries) is unlikely to be due to a specific pathogenesis or aetiology (WHO, 1965; Edington and Hutt, 1968; Hutt, 1974).

The next chapter therefore reviews the other disorders that have been incriminated in causing myocardial damage.

CHAPTER 3

REVIEW OF OTHER KNOWN CAUSES OF MYOCARDIAL DAMAGE

(1) FAMILIAL OR CONGENITAL

HYPERTROPHIC CARDIOMYOPATHY (HOCM):

Two forms of this disease are known to exist, one with, the other without obstruction at the outflow tract (Oakley, 1972). It was first described by Schminke in 1907 and later reported by Mahaim in 1945 as "diffuse tumours of the myocardium". Teare (1958) called it asymmetrical hypertrophy in a report of 8 cases. It was called hypertrophic obstructive cardiomyopathy by Cohen et al. (1964) and idiopathic hypertrophic subaortic stenosis by Brockenbrough et al. (1961).

Its main feature is inappropriate hypertrophy of the left ventricle. Occasionally, the right ventricle may also be affected. It is usually acquired after birth but the predisposition is genetically based (Oakley, 1972).

Two families have been reported with many members affected (Hollman et al, 1960; Pare et al, 1961). Of 14 patients reported by Braunwald et al. (1960) 3 were siblings, 2 were mother and son. Brent et al.

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(1960) also reported 2 families with HOCM.

HOCM has also been associated with other inborn anomalies such as lentiginosis (Polani and Moynaha, 1972), Friedreich's ataxia (Soulie et al, 1966) and Noonan's syndrome (Phornphutkul et al, 1973). It has similarly been reported in association with other congenital cardiovascular lesions (Shem-Tov et al, 1971) and in newborn children (Neufeld et al, 1960).

On electron microscopy, severely disorganised bundles of muscle cells are seen (Ferrans et al, 1972).

Commonly it presents with dyspnoea, angina pectoris, syncopal attacks or sudden heart failure. Arrhythmias are common and older patients tend to have more severe symptoms (Shah et al, 1974). Congestive cardiac failure occurs only in a minority of cases. Mitral incompetence is often present. Familial cases often resemble each other though they may differ in severity (Oakley, 1972). They also often have inflow difficulty without obstructive murmurs.

HOCM has to be differentiated from HMD especially if congestive features are present. By this time, the left atrium, the right ventricle and the right atrium will all be dilated, giving rise to some increase in heart size which may sometimes be considerable

(Oakley, 1972).

There has been no report of HOCM at Ibadan although two cases have been reported from Lagos (Okuwobi, 1974).

FAMILIAL CARDIOMYOPATHY:

In 1949, Evans described two families with cardiac enlargement of unexplained origin and called it "familial cardiomegaly". Autopsy performed on a single member of each family showed myocardial fibrosis with hypertrophy of the remaining muscle fibres producing great cardiac enlargement. Intramural thrombosis was present.

Clinically the patients presented with palpitations, momentary giddiness and frank Stokes-Adams attack. Some died suddenly and in some, heart failure was precipitated by the onset of paroxysmal tachycardia. Physical examination revealed irregularity of the pulse due to extrasystoles, paroxysmal tachycardia, atrial fibrillation or heart block. The heart was usually enlarged but the blood pressure was normal. There were usually no murmurs but a third sound was present in some cases. The electrocardiogram (ECG), in addition to confirming the above arrhythmias, showed wide QRS complexes and T wave inversions. Chest x-ray showed

cardiomegaly and their prognosis was dependent on the extent of cardiac fibrosis and associated cardiac enlargement.

A similar illness has been reported by Battersby and Glenner (1961). They described a sibship of which five members had an identical cardiomyopathy. Hudson (1969) also described a youth of 18 years who was the last survivor of 5 brothers, all of whom died young, 2 at least from heart failure. He also described another family where severe myocardial scarring was found at necropsy in a father aged 32 years, his son aged 12 years and in his daughter aged 10 years. He mentioned a third example of a woman of 28 years who died of puerperal heart failure after the birth of her second child. A few years later, her first child, a daughter, died at the age of 7 years and at autopsy her heart resembled her mother's.

FIBROELASTOSIS:

Although this disease is usually classified as one of the primary cardiomyopathies, some believe it is not an entity but a nonspecific reaction of the heart to congestive heart failure with cardiac dilatation of long duration (Black-Shaffer, 1957). Patchy

endocardial fibroelastosis is found in many adult patients who die after long-standing congestive heart failure associated with cardiomyopathies (Fowler et al, 1961) or other causes of persistent cardiac dilatation. In children, primary endocardial fibroelastosis may result from the same mechanism and may actually be a complication of primary cardiomyopathy (Fowler, 1964).

Some writers, however, believe that this disorder results from a familial metabolic defect (Kelly and Andersen, 1956) or from foetal endocarditis and is distinct from the secondary varieties which may occur in children with aortic stenosis, pulmonary stenosis, coarctation of the aorta and other varieties of congenital heart disease (Andersen and Kelly, 1956).

Examples of fibroelastosis have been reported in adults (White and Fennell, 1954). In 90% of instances of fibroelastosis, however, congestive heart failure causes death within the first 2 years of life (Blumberg and Lyon, 1952) and children with primary endocardial fibroelastosis usually die before the age of 6 years.

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features were important. One was the early onset of congestive cardiac failure. In 85% of patients, heart failure occurred before the age of 8 months and seldom after 1½ years. Secondly, the ECG pattern of left ventricular hypertrophy was found in 86% of patients with this disease. This helped to distinguish it from patients with myocarditis.

DYSTROPHIC CARDIOMYOPATHIES AND FRIEDREICH'S ATAXIA

DUCHENNE'S MUSCULAR ATROPHY:

Cardiac involvement is well-recognised in Duchenne's muscular atrophy. This occasionally results in heart failure (Wahi, 1963; Slucka, 1968). Severe circulatory failure usually develops only a short time before death (Slucka, 1968) which rarely occurs above the third decade (Walton and Natrass, 1954). Microscopically, there is usually atrophy of the cardiac muscle fibers and hypertrophy of connective tissue which is sometimes extensive though without signs of either inflammation or changes in the coronary vessels (Slucka, 1968; Gilroy et al, 1963). ECG abnormalities are frequent (Weisenfeld and Messinger, 1952; Wahi, 1963; Welsh et al, 1963; Gilroy et al, 1963; Slucka, 1968).

LIMB-GIRDLE MUSCULAR DYSTROPHY:

Cardiomyopathy is less common in the limb girdle muscular dystrophy group. Subtle quadruple gallop rhythm was found by Perloff et al. (1966). One patient had heart failure while Welsh et al. (1963) found 3 cases of heart failure out of 26 patients.

DYSTROPHIA MYOTONICA:

Church (1967) reviewed 300 cases of myotonia atrophica in the literature and 17 cases seen at Columbus, Ohio, U.S.A. Electrocardiographic abnormalities were common, usually with conduction defects leading to atrial arrhythmias or rarely Stoke-Adams attacks. 37 had T wave abnormalities while 34 had cardiomegaly but without heart failure. One case described by Cannon (1962) died of chronic heart failure.

FACIO-SCAPULO-HUMERAL MUSCULAR DYSTROPHY:

Cardiac involvement is rare in facio-scapulo-humeral muscular dystrophy (Brain and Wilkinson, 1969). Wahi (1963) found no cardiac involvement in 6 cases with this disease. Welsh et al. (1963) similarly found no ECG abnormalities in their cases. Perloff et al. (1966) found only quadruple gallop rhythms in some of

FRIEDREICH'S ATAXIA:

Over 55% have cardiac abnormalities (Boyer et al, 1962). The heart commonly shows a diffuse change, enlargement being caused by thickening of the muscle and diffuse fibrosis. Microscopically, there is fatty degeneration of the muscle fibres with slight chronic inflammatory infiltration and fibrosis (Russell, 1946; Boyer et al, 1962).

Heart failure, non-specific heart murmurs, atrial dysrrhythmias, heart block and other ECG abnormalities may occur (Evans and Wright, 1942; Tyrer and Sutherland, 1961; Boyer et al, 1966).

TUBEROSE SCLEROSIS:

This disease may rarely be associated with cardiac dysrrhythmias. Intermittent partial heart block of the Wenckebach type and both ventricular and atrial extrasystoles, or multifocal extrasystoles, may occur (Oram, 1971). An associated cardiac tumour (rhabdomyoma) has been described (Critchley and Earl, 1932) although some authorities believe that the cardiac infiltration is due to glycogen (Oram, 1971).

THE MUCOPOLYSACCHARIDES:

Myocardial lesions have been reported in up to 85% of necropsies of patients with gargoylism (Steen,

1959). Biventricular hypertrophy may be present with all the four valves thickened and rigid due to dense poorly-cellular fibrous tissue. Chest x-ray may show cardiomegaly but there is no specific ECG pattern. The ECG more commonly is normal. Death occurs usually in the first two decades with about two-thirds of the patients dying from congestive cardiac failure.

PSEUDOXANTHOMA ELASTICUM:

Huang et al. (1967) reported a case of pseudoxanthoma elasticum who presented with arrhythmia, cardiomegaly and congestive cardiac failure during pregnancy. The patient died suddenly and autopsy revealed an enlarged, flabby heart with an area of endomyocardial fibrosis in the left ventricle. Histology showed thickening of the endocardium and changes in the elastic fibres. A review of the literature showed that myocardial involvement is not common in this condition. The most common cardiac lesion is diffuse endocardial fibrosis with valvular involvement. The endocardial thickening may involve the conduction system and dysrrhythmias may occur. Involvement of the coronary arteries, including calcification, may give rise to angina pectoris.

(2) NUTRITIONAL

The relation between malnutrition, th'amine deficiency and HMD has been examined in the last chapter and will not be further considered here.

ALCOHOL:

There are various reports suggesting that alcohol itself can cause myocardial failure and many 19th century physicians had postulated that overindulgence in alcohol could lead to heart disease. Brigden and Robinson (1964) described 50 patients with unexplained myocardial failure and a history of long-standing alcohol consumption. 5 had aneurin-responsive cardiac beriberi in addition. Burch and De Pasquale reviewed the whole subject of alcoholic cardiomyopathy in 1968 and 1969 and made a strong case for its existence as an entity. Tobin et al.(1967) studied 39 alcoholics and emphasized the importance of alcohol in the genesis of myocardial failure. They also pointed out that those who abstained from further drinking had a much better cardiac prognosis than those who continued to drink. Asokan et al.(1972) performed haemodynamic studies in 9 alcoholics with normal ECGs and normal cardiothoracic ratios as shown by chest radiographs.

They found that the mean left ventricular end-diastolic pressure was elevated, the mean cardiac output was low and there was depressed myocardial contractility. They concluded that true functional cardiac impairment may exist in these patients prior to the development of abnormal clinical parameters such as cardiomegaly.

Blomquist et al.(1970) also reported the acute effects of alcohol on the haemodynamics in normal subjects. They found that mechanical efficiency was decreased. Regan et al.(1969) demonstrated that administration of alcohol to patients with fatty livers due to alcohol caused a depression of left ventricular function resulting in raised left ventricular end-diastolic pressure and diminished stroke work in response to an induced increase in aortic pressure than in normal control subjects. They also studied the effects of chronic administration of lcohol in man. Daily consumption of 500 ml of whisky for $5\frac{1}{2}$ months by a patient who had been an alcoholic and previously been in congestive heart failure caused tachycardia with a third sound, an increase in heart size and an increase in circulation time and venous pressure. All these effects returned to control values within seven weeks after cessation of alcohol intake.

They also showed a significant elevation of potassium, phosphate and glutamic-oxaloacetic transaminase in the coronary sinus blood of alcoholic patients receiving 375 ml of whisky. A decline of free fatty acid extraction by the myocardium was also demonstrated. Similar changes were also found in normal dogs after acute administration of ethanol (Regan et al, 1966).

Wendt et al.(1965) found that in patients with chronic alcoholism, intramitochondrial enzymes isocitric dehydrogenase and malic dehydrogenase were released by cardiac muscle, both at rest and on exercise, even in those patients with no clinical evidence of heart disease. In 1966, Wendt et al, also showed that acute ethanol ingestion in chronic alcoholic patients caused a fall in the myocardial extraction of free fatty acid but no change in the myocardial extraction of triglyceride despite a significant increase in arterial blood levels. In many patients, an increase in isocitric dehydrogenase occurred in coronary sinus blood.

Other studies in animals have also shown that alcohol can damage the myocardium (Webb and Degerli, 1965; Regan et al, 1966; Maines and Aldinger, 1967, Burch et al, 1971; Miezwiak et al, 1972).

Electron-microscopic and histochemical changes have also been found in animals and patients dying of alcoholic cardiomyopathy (Hibbs et al, 1965; Burch et al, 1971; Ferrans et al, 1965) but these are not considered to be specific. Prolonged ethanol intake in the absence of evident malnutrition has also been found in dogs to produce intraventricular conduction abnormalities and morphologic alterations which were related to duration of ingestion. This was considered to be consistent with a cumulative toxic effect of alcohol (Ettinger et al, 1976).

Shaper (1967) has argued that alcohol might have played a more prominent role than malnutrition alone in the patients described by Gillanders (1951) as nutritional heart disease. More recently Seftel et al (1972) and Seftel (1972) have shown that alcohol is an important aetiological factor in their South African patients with obscure forms of heart failure.

In Ceylon, Nagaratnam (1970) found that 27 out of 80 alcoholics had unexplained heart failure, 2 had hepatic cirrhosis and 2 acute alcoholic hepatitis. A form of heart failure common in palm-wine tappers has also been described from the Gambia (Harling et al, 1965).

Schenk and Cohen (1970) reviewed 2,100 necropsies and found that 15 out of 97 alcoholics had unexplained heart failure and 87 had diffuse interstitial fibrosis and myofibre vacuolation. Male alcoholics have also been shown to have a greater abnormal myocardial function than female alcoholics (Wu et al, 1976).

There is therefore a lot of evidence implicating alcohol as a cause of myocardial failure. Some however feel that alcohol may be but one of many conditioning factors which lowers the resistance of the myocardium to noxious agents yet unknown or a contributing factor to myocardial damage which operates in concert with other as yet unknown damaging factors. Goodwin and Oakley (1972) found no difference in the drinking habits of patients with congestive cardiomyopathy compared with patients with other forms of heart disease, and did not think that alcohol was the cause of congestive cardiomyopathy in majority of their patients (Goodwin, 1972). It is pertinent to note here that Brockington (1974) also did not think alcohol was a cause of HMD in Nigerians.

MUCOVISCIDOSIS:

The commonest cardiac lesion in patients with fibrocystic disease of the pancreas is cor pulmonale

secondary to pulmonary disease (Oram, 1971). However, a cardiomyopathy may also occur consisting of myocardial fibrosis. The children present with dysrhythmias, cardiomegaly and ECG abnormalities and usually die in congestive cardiac failure. Autopsy usually shows biventricular dilatation and hypertrophy with scar tissue replacing degenerating muscle fibres. There may be endocardial fibroelastosis of the atria.

(3) INFLAMMATORY (MYOCARDITIS)

VIRAL AND RICKETTSIAL DISEASES:

MEASLES:

Electrocardiographic abnormalities have been reported in measles (Ross, 1952) and recently in Nigerian children with this disease (Jaiyesimi, 1976). Permanent cardiac damage is not a recognised sequela However, Giustra (1954) reported a child of $5\frac{1}{2}$ years who was normal until he developed measles. This was associated with disorders of the cardiac rhythm consisting of "bizzare arrhythmias", supraventricular tachycardias and conduction blocks. During a subsequent 3 year observation, the patient continued to have paroxysmal attacks of these arrhythmias and finally died during a convulsive seizure which accompanied

an attack of tachycardia. Autopsy showed generalised subendocardial sclerosis and focal fibrosis in the left bundle branch. The dilatation and hypertrophy of the heart was more pronounced on the right side but there were no myocardial changes.

RUBELLA: Ainger et al.(1966) studied 47 infants with congenital rubella syndrone and found that 10 had ECG evidence of myocardial damage. Autopsy performed on 4 who died showed myocardial necrosis but no evidence of an interstitial inflammatory response or cellular infiltration. Rubella virus has been isolated from the myocardium in a few instances (Sever and Monif, 1965).

MUMPS: Myocarditis due to mumps has been reported by Gore and Saphir (1947), Bland (1949) and Bengtsson and Orndahl (1954). In 564 cases studied by Bengtsson and Orndahl (1954), ECG changes were found in 4.4%. No heart failure was reported. Mohammed and Carlisle (1971) reported a doubtful case in an adult of 40 years in Ibadan. She presented in heart failure with a 2-week history, soon became uraemic and four weeks later developed parotid swelling. No other evidence was available. The diagnosis was based on the parotid

swelling which the patient had and this does not seem enough. It is noteworthy that parotitis with swelling occasionally complicates terminal renal failure.

POLIOMYELITIS: Saphir and Wile (1942) found 6 cases of myocarditis in 7 patients with poliomyelitis while Ludden and Edwards (1949) in their series of 35 cases of fatal poliomyelitis found 14 cases of myocarditis. Gore and Saphir (1947) have also reported cases of myocarditis complicating poliomyelitis.

CHICKEN-POX: Hackel (1953) described focal interstitial inflammatory lesions in the hearts of 7 patients who had chicken-pox at the time of death. A control group of 6 healthy people who died suddenly of traumatic causes had no similar lesions. He therefore suggested that myocardial lesions may occur without clinical manifestation in non-fatal cases of chicken-pox.

SMALL-POX: Anderson et al.(1951) reported 5 fatal cases of myocarditis due to small pox. All of them had tachycardia, soft heart sounds and irregularity of the heart during their illness. They died in acute heart failure. Saphir (1952), too reported a case with myocarditis who also died in acute heart failure.

INFECTIVE HEPATITIS: Saphir et al. (1956) reported

4 cases of myocarditis in 6 patients dying of acute viral hepatitis. 3 of the 4 patients died after a relatively short course of the disease and 2 had ECG abnormalities. At autopsy, the myocardium showed minute foci of necrosis and a more diffuse serous inflammation. The bundle of His was involved in 3 of the 4 cases and showed necrosis of isolated fibers, haemorrhage and an acute inflammatory exudate.

Nagaratnam et al.(1971) recently reported four cases of myocarditis due to infective hepatitis. ECG abnormalities were also common in their cases and autopsy findings were similar to those of Saphir et al.(1956).

YELLOW FEVER: Cannell (1928) described myocardial changes in 29 patients with yellow fever in West Africa and in 9 monkeys experimentally infected. The changes found included cloudy swelling, granular and fatty degeneration. He concluded that these changes were not specific for yellow fever.

INFECTIOUS MONONUCLEOSIS:

A fatal case of acute myocarditis complicating infectious mononucleosis reported by Fish and Barton (1958) showed at autopsy numerous areas of necrosis in the heart with mononuclear infiltration. The

patient's ECG which previously had been normal showed T wave changes during his illness. Terminally, he developed right bundle branch block.

RABIES: Ross and Armentrout (1962) described a patient with rabies who had evidence of myocarditis. Her ECG showed non-specific ST - T changes. At autopsy, the cardiac chambers were not enlarged but there were faint, diffuse, reddish-brown mottling prominent over the subendocardial regions of the anterior and posterior walls of the heart. Histology showed an acute exudative myocarditis with chronic inflammatory cell infiltration. Similar changes were also found in two cases reported by Cheetham et al (1970) from Britain.

INFLUENZA: Myocarditis caused by influenza viruses has been described by Silber (1958), Clough (1958), Oseasohn et al (1959) and Coltman (1962). Myocarditis was present in a third of the fatal cases described by Oseasohn et al (1959). Coltman (1962) suggested that a prolonged elevation of serum amino transferase may be of assistance in making a diagnosis of myocarditis in influenza.

CYTOMEGALOVIRUS: Fatal myocarditis in children has been reported by Seifert (1965) and also in two adult

women aged 60 and 43 years who also had chronic myocardial failure with myocarditis (Wilson et al, 1972; Waris et al, 1972.

DENGUE: Hyman (1943) found bradycardia and extrasystoles in troops who had dengue in the South Pacific between 1942 and 1943. Obeyesekere and Hermon (1972, 1973) recently suggested that arbovirus myocarditis may be a cause of cardiomyopathy in Sri Lanka. They studied and followed up 35 patients who developed cardiac symptoms after dengue-like fever. They all had high titres to dengue or chikungunya viruses. Three patients died and three others developed heart failure. One patient who had two episodes of fever separated by 18 years had cardiomegaly following the first attack and heart failure after the second. Other causes were however not excluded.

EPIDEMIC HAEMORRHAGIC FEVER:

Hullinghorst and Steer (1953) found mononuclear cellular infiltration of the myocardium in 61 cases who died of epidemic haemorrhagic fever. Subepicardial haemorrhages were common especially in the right atrium.

SCRUB TYPHUS: Sayen et al, (1946) found pathological, clinical and ECG evidence of myocarditis in a series of patients with scrub typhus. Autopsied cases showed

extensive myocardial damage. Sokolow and Garland (1945) and Levine (1945) in follow-up studies of scrub typhus concluded that the heart of a patient who survives the acute phase of the disease eventually shows complete return of function. Woodward and Bland (1944) studied 30 patients with typhus fever and concluded that peripheral rather than central circulatory collapse was the main clinical problem.

Q-FEVER: Sheridan et al. (1974) described 2 cases of myocarditis complicating Q-fever. Their evidence was based on ST-T changes on the ECG. None of the cases had heart failure.

OTHER RICKETTSIAL DISEASES: Myocarditis has been reported in other rickettsial diseases such as epidemic typhus and Rocky Mountain spotted fever (Gore and Saphir, 1947).

PSITTACOSIS: Jannach (1958) reported a case of myocardial psittacosis in an infant. Vosti and Roffwarg (1961) described a 48 year old woman who died from systemic embolism arising from left ventricular mural thrombus after her myocarditis had been successfully treated with tetracycline. Sutton et al.(1967) in an immunological study, found

evidence of psittacosis in 9 of 599 suspected cases of acute perimyocarditis. The same team in 1971 found high chlamydial antibody titres in 40 of 139 patients with primary myocardial disease.

COXSACKIE A VIRUSES:

Coxsackie A viruses are increasingly being reported as causes of myocarditis or pericarditis or as causes of sudden death in which myocarditis was suspected as being responsible (Grist and Bell, 1969). Coxsackie A1 viral myocarditis has been reported by Movitt et al. (1958) and Grist and Bell (1968); Coxsackie A4 by Gold et al. (1961), De Goes et al.(1959), Grist (1966) and Bell and Grist (1968); Coxsackie A9 by Hosier and Newton (1958), Grist (1966), Helin et al.(1968), and Christodoulopoulou and Havredaki (1968). Coxsackie A16 has been implicated as a cause of myocarditis by Magoffin et al.(1961) and Wright et al.(1963). Coxsackie A23 (formerly called echovirus 9) has also been reported as a cause of myocarditis by Cherry et al.(1967) and Monif et al.(1967).

ECHOVIRUSES: Echoviruses are not considered as important causes of cardiac disease (Grist and Bell, 1969) although a few cases of myocarditis due to these

viruses have been reported (Lerner and Wilson, 1973). Echovirus 9 was found to be responsible for an acute virulent myocardiopathy in a 34 year old dentist admitted to hospital with pyrexia and heart block (Monif et al, 1967). At autopsy, an echovirus was isolated from the heart. A homotypic neutralising antibody titer of 1 in 8 was found in the serum. Autopsy showed discrete mottling of the myocardium. Many discrete, slightly raised, ovoid, greyish-white plaques, often rimmed by haemorrhages were seen. The largest lesions were soft and necrotic. Histology showed focal and diffuse inflammatory cell infiltrates and massive focal necrosis of cardiac muscle fibres.

Echovirus 9, however, has now been reclassified as Coxsackie A23 virus following the finding of its pathogenicity for suckling mice (Sickles et al, 1959).

COXSACKIE B VIRUSES: are established causes of viral myocardiopathy (Lerner and Wilson, 1973). Sainani et al.(1968), Ornius (1968) and Smith (1970) have studied adult heart diseases suspected to be caused by group B coxsackie viruses and their findings were similar.

Sainani et al.(1968) studied 22 patients (13 men and 9 women) aged 15-66 years. Of these 22 patients, 10 had clinically pericarditis, 10 myocarditis and 2 myocarditis and pericarditis. All of them had abnormal ECGs, 12 had cardiomegaly and 8 pleural effusions. Leucocytosis with a shift to the left was found in 15 and raised erythrocyte sedimentation rates in 19. 14 patients had increased serum enzymes and serological tests strongly suggested a Coxsackie B aetiology in 19 of the 22 cases. Type B4 was thought to be causative in 9 of the 22 cases, B2 in 6, B3 in 3 and B1 in one case.

Congestive cardiac failure, cardiomegaly and abnormal ECGs persisted in 5 patients and elevated erythrocyte sedimentation rates and ST-T changes in 2 others. Symptoms recurred in 7 patients and concomitant with their virus cardiomyopathies, mitral incompetence appeared for the first time in 3 patients. One patient died during the acute illness of ventricular tachycardia.

Burch and Colcolough (1969a) reported the case of a 45 year-old man who developed acute pancarditis and aortic incompetence. He had consequent severe heart failure and died a year later. During his illness, a rise in neutralising antibodies (1/4 to 1/256) to

Coxsackie B4 virus was observed. At autopsy, Coxsackie B4 antigen was found within degenerating myocardial cells. Coxsackie B4 virus paticles were also demostrated around the tubules of the sarcoplasmic reticulum on electron microscopy. Coxsackie B4 antigen was also present in the kidney.

Burch et al. (1968) have also localised Coxsackie B virus antigens in the hearts of 9 of 29 patients with interstitial myocarditis of varying severity found among 50 consecutive routine autopsies.

Bates (1970) found Coxsackie B3 antigen in the heart of a stillborn infant delivered in the 8th month of gestation. He had cardiac failure and generalised oedema. Histology showed extensive endocardial, subendocardial and interstitial myocardial fibrosis along with areas of degenerating muscle fibres.

Three other patients (a 55 year old man, a 5 year old girl and a 3 day old infant) with acute virulent cardiomyopathy and valvulitis were shown by immunofluorescent techniques to have Coxsackie B1, B4 and B5 antigens respectively in their hearts (Burch et al, 1967). Sutton (1967) described a 42 year old executive who had an apparently mild, nonspecific , febrile illness which lasted several days. Subsequently,

he felt fatigued and began a conditioning programme. He swam daily after work. About a month later he died of sudden pulmonary oedema. At autopsy, Coxsackie B4 virus was isolated from the ventricular myocardium.

Sainani et al.(1975) studied 55 patients with heart disease suspected to be of viral origin at Nagpur over a period of 2 years. A viral aetiology of the heart disease was proven in 19 patients. Of these 19, 5 had acute myocarditis, 5 acute myopericarditis, 3 acute pericarditis and 3 congestive cardiac failure of obscure origin. 2 had pleuropericarditis and the remaining one developed post-partum heart failure with cardiogenic shock. All of them had ECG abnormalities. 13 had cardiomegaly, 1 had a right sided pleural effusion and 2 had pericardial effusion.

Follow-up studies up to 10 weeks after discharge showed that 8 patients were clinically normal but 4 of these 8 had persistent ST-T changes. Of the remaining 11 patients, 3 had persistent chronic heart failure, 3 vague symptoms of precordial pain but no abnormal signs, and 5 patients were lost to follow-up.

Coxsackie B viruses have been reported to cause valvulitis and lesions suggestive of rheumatic heart

disease. Coxsackie B4 virus produced Aschoff - like bodies and Anitschkow myocytes when injected intravenously into cynomolgus monkeys (Burch and Colcolough, 1969b). Moreover, the monkeys developed aortic and mitral valvulitis. Coxsackie B4 virus has also been found to produce mitr ' and aortic incompetence in humans (Burch and Colcolough, 1969a; Burch et al, 1967).

Experimentally, Coxsackie A9 produced a mild, focal, inflammatory response in the hearts of adult mice while Coxsackie B3 virus caused a virulent, diffuse, necrotic and inflammatory lesion involving 25-50% of the myocardium (Wilson et al, 1969). Exercise (Gatmaitan et al, 1970), adrenal corticoids (Wilson et al, 1969), ingestion of alcohol (Morin et al, 1969), special genetic susceptibility of certain strains of mice (Grunberg and Prince, 1964), unusual virulence of the infecting virus (Brunberg and Prince, 1963), pregnancy (Farber and Glasgow, 1970), chronic undernutrition (Woodruff and Kilbourne, 1970) led to an increased severity of virus infections and particularly myocarditis.

VIRAL ANTIBODIES IN HEART FAILURE OF OBSCURE ORIGIN:

Fletcher et al (1968) performed a controlled viral

survey of 34 patients with heart failure of obscure origin. The determined serum viral antibody levels to Coxsackie viruses B1 - 6, echoviruses 6 and 9, influenza A and B, mumps, herpes simplex and psittacossis. They found no difference in the incidence of elevated viral antibody titres between the patient and control groups. Subdivision of the patients by race, sex or age also revealed no difference in viral antibody titres. They pointed out, however, that previous viral infection no longer reflected by elevated antibody titres could not be ruled out as an aetiologic factor in these patients.

BACTERIAL INFECTIONS:

DIPHTHERIAL: Gore (1948) found myocarditis in 143 (70%) of 205 fatal cases of diphtheria. Pathologically, the hearts were dilated with flabby, pale or mottled musculature. Histologically, there was p imary toxic degeneration of the myocardial fibers with an inflammatory response secondary to muscle injury. He noticed clinically that in one-third of the patients myocarditis appeared when they seemed to have recovered.

Boyer and Weinstein (1948) found ECG abnormalities in 61 of 93 patients with diphtheria. These consisted

of ST-T changes, prolongation of the Q-T interval, complete atrioventricular block, ventricular tachycardia and widened QRS complexes.

The only report of chronic myocardial failure due to diphtheral infection occurred in a patient reported by Griffith and Herman (1952). He had persistent ECG abnormalities with low voltage QRS complexes, various conduction defects and other arrhythmias. He survived for 12 months despite a complicating hepatitis and died in cardiac asystole. Autopsy showed degenerative changes in the myocardium.

TYPHOID: ECG changes due to myocarditis have been found by Rachmilewitz and Braun (1948) and Fine et al. (1950) in patients with typhoid. One of the patients studied by Fine et al.(1950) died and autopsy showed toxic degeneration of the muscle fibres and interstitial myocarditis.

BRONCHOPNEUMONIA, LOBAR PNEUMONIA: Saphir and Amromin (1948) found that 26 out of 67 autopsied patients with bronchopneumonia had myocarditis. Six of the 26 patients had ECG abnormalities.

Myocarditis and ECG abnormalities complicating pneumonia have also been reported by Stone (1922), Master et al.(1931) and Saphir (1948).

MYOCARDIAL ABSCESSES: Sanson et al.(1963) studied 23 autopsied cases of myocardial abscesses. The incidence was 1.5% of 1,251 autopsies performed over a period of 7 years. Myocardial abscesses were often associated with abscesses in other organs and almost always there was evidence of generalised pyaemia. Staphylococcus aureus and Escherichia coli were the most common aetiological agents. Previous surgical procedures were responsible for inducing or disseminating the pyaemic process in almost half of the patients.

ECG changes were frequent, though nonspecific. The myocardial abscesses were often clinically silent and their presence obscured by manifestations of an overwhelming pyaemic process.

PHARYNGITIS AND TONSILLITIS: Gore and Saphir (1947b) reported 35 instances of fatal myocarditis due to acute nasopharyngeal and tonsillar infections. All the patients died in heart failure although heart disease was suspected in life only in 3 cases. 15 of them died suddenly.

Clinically, they had disproportionate pulse rate and temperature, hypotension, feeble pulse and retrosternal

discomfort. Cyanosis, dyspnoea and orthopnoea were frequent. Significant enlargement of the heart was present in many cases.

Histologically, their hearts showed inflammatory process with muscle degeneration. Cellular reaction was predominantly mononuclear.

MENINGOCOCCAL MENINGITIS: Saphir (1936) in a series of ten autopsies on patients who died of meningococcal infection found two instances of myocarditis caused by actual seeding of the organisms in the myocardium. Lowe and Diamond (1948) reported the case of a girl who had meningococcal meningitis and associated pericarditis, cardiac enlargement and failure. Levin and Painter (1966) found in a clinical series of 28 consecutive patients with meningococcal meningtitis that 11 had hypotension and pulmonary oedema while 13 patients had gallop rhythm. Those with hypotension had ECG abnormalities while those who were normotensive had no such abnormalities. Those with hypotension were believed to have had myocarditis as a complication of their meingitis.

TUBERCULOSIS: Wallgren (1947) in his paper on tuberculous heart disease concluded that this was a

rare phenomenon and that pericarditis associated with tuberculous heart disease was often a tuberculous - allergic phenomenon. Auerbach and Guggenheim (1937) however in 10,165 autopsies on adult patients with tuberculosis found the myocardium involved in 0.28%. In 973 children, the myocardium was involved in 3.9%. Gore (1946) in a study of 581 autopsies found heart lesions in 1.5%. Schnitzer (1947) reported a case of myocardial tuberculosis complicated by paroxysmal ventricular tachycardia. The patient died and at autopsy, he had miliary tuberculosis with extensive involvement of the myocardium.

OTHER INFECTIONS: Gore and Saphir (1947) in a series of 1,402 autopsy cases found that myocarditis was caused by Streptococcal septicaemia in 11 patients, staphylococcal septicaemia in 34 and pneumococcal septicaemia in 9 cases.

Myocarditis has been reported in tetanus (Murphy, 1970) but apart from occasional gumma (Sohval, 1935) myocardial lesions in syphilis is now attributed to arterial disease.

Bryceson et al. (1970) found ECG abnormalities in a study of 62 cases of louse-borne relapsing fever in Ethiopia. All the patients were febrile, cardiac

output was usually high but none of them presented in chronic heart failure..

PARASITIC INFECTIONS:

Meleney (1925) found Leishman - Donovan bodies in the hearts of patients with Kala-azar but without clinical effects. Sidorov (1935) has also reported a case of granulomatous myocarditis due to balantidiases with parasites in the myocardium.

SCHISTOSOMIASIS: Lima (1969) found schistosomal myocardial granulomata in 10 out of 544 patients. Alzahawi and Shukri (1956) described a case considered to be bilharzial myocarditis. The boy, aged 13 years, was in heart failure with mitral systolic murmur and an emphysematous lung. He died 16 hours after admission and at autopsy, his myocardium contained 'healthy' eggs of Schisostoma haematobium with an inflammatory reaction around them. These myocardial lesions were considered to be allergic in nature.

MALARIA: Myocardial sludging has been thought to occur with Plasmodium falciparum infection although this view has generated some controversy (Maegraith, 1948). Spitz (1946) studied the hearts of 50 patients and found no evidence of thrombosis in the vessels of the heart. Gore and Saphir (1947) however, reported 5 cases

of myocarditis attributed to malaria in their collection of 1,402 autopsies.

CYSTICEROSIS: The myocardium in this disease may harbour a large number of cysts (Castellani and Acanfora, 1938; Menon and Veliath, 1940) but in only one case did they have any possible clinical effect.

ECHNOCOCCOSIS: Di Bello and Menedez (1963) reviewed the literature and found 101 of 269 cases of intracardiac rupture of hydatid cysts. 29 of the patients died suddenly. Cysts of the right ventricle ruptured more frequently than those of the left ventricle. The effects of these intracardiac ruptures included emboli and metastatic visceral echinococcosis.

AFRICAN TRYPANOSOMIASIS: Myocarditis has been reported with Trypanosoma rhodesiense infection in man (e.g. Raadt and Koten, 1968) and in monkeys (Peruzzi, 1928). Raadt and Koten (1968) found that heart signs were usually scanty although 2 of their 6 patients had cardiac enlargement. Manson-Bahr and Charters (1963) reported two patients who had congestive heart failure with cardiac enlargement and who responded rapidly to treatment of their trypanosomiasis. They thought the underlying lesion was myocarditis.

Myocarditis has been described in Trypanosoma gambiense infection which is the type seen in Northern Nigeria (e.g. Bertrand et al, 1967). Collomb and Bartoli (1967) reported 5 cases of sudden death with dilated ventricles. One case reported by Francis (1972) was that of Tiv woman from Gboko who presented in acute heart failure at UCH, Ibadan and responded to a course of Mel B.

TRICHINOSIS: Terry and Work (1940) reported a fatal case who at autopsy had cardiac and skeletal muscle involvement. The patient did not present in heart failure and no cardiac enlargement was noticed. Chase (1957) also reported another case who had no cardiomegaly or heart failure but who at autopsy had focal disseminated myocarditis consisting of collections of inflammatory cells of which eosinophils predominated. The changes were thought to be due to a hypersensitivity reaction.

Gray et al.(1962) and Spink (1935) noted that ECG changes were common in trichinosis but that the vast majority of the patients recovered. Heart failure was rare.

TOXOPLASMOSIS: Toxoplasmic myocarditis have been reported in patients on treatment with steroids,

cytotoxic drugs, irradiation or during immunosuppresive therapy following kidney transplantation (Vitezke et al, 1968; Reynolds et al, 1966) and in one case with acute lymphocytic leukaemia, myocarditis dominated the picture and was responsible for the patient's death (Wertlake and Winter, 1965).

In overwhelming congenital infection, the clinical manifestations are those of meningoencephalomyelitis but at autopsy, next to the central nervous system the myocardium is found to be the most frequently involved (Zuelzer, 1944; Callahan et al, 1946). Antemortem, cardiomegaly on chest x-ray and peripheral oedema have been noted in some infants and pathologic examination subsequently revealed inflammatory changes and parasites in their heart muscle.

Acquired forms may have minimal symptoms or may be completely asymptomatic, the latter being the case in the majority of toxoplasma infections (Theologides and Kennedy, 1969). It can, however, produce severe and fatal disease with a wide spectrum of clinical manifestations. The disease may start as a generalised infection and then become localised in the myocardium (Theologides and Kennedy, 1966). Pathological findings of myocarditis have been observed in almost

all cases of acquired disseminated infection reported (e.g. Vietzke. et al, 1968; Wertlake and Winter, 1965; Pinkerton and Weinman, 1940) although in most instances the myocarditis was not suspected antemortem. Cardiomegaly on chest x-ray has been reported (Pinkerton and Henderson, 1941; Tomlinson, 1945; Kass et al, 1952; Hooper, 1957) although one case showed a normal sized heart (Strom, 1951). ECG abnormalities include low voltage (Sexton et al, 1953), left ventricular hypertrophy (Corpening et al, 1952), atrial fibrillation and later ventricular fibrillation (Wertlake and Winter, 1965), interventricular conduction defect (Budzilovich, 1961), non-specific ST-T changes (Strom, 1951; Adams, 1962) and pericarditis (Wertlake and Winter, 1965).

Isolated toxoplasma myocarditis may occur and the symptoms and signs are related to heart disease and at autopsy only the heart is infected (e.g. Nakkila et al, 1958; Paulley et al, 1956, Cathie, 1955). The course of myocarditis was acute in one case (Potts and Williams, 1956). The usual clinical picture is that of chronic cardiomyopathy (Theologides and Kennedy, 1969) in which congestive heart failure, cardiomegaly, gallop rhythm, arrhythmias and systolic murmurs may be present. The temperature may be normal or raised.

Chest x-ray in isolated myocarditis may be normal (e.g. Shee, 1964) but cardiomegaly is present in all other cases. ECG changes as described previously may be present.

Pathologically, the heart may be grossly normal or may show hypertrophy and dilatation. A yellowish mottling and subendocardial petechial haemorrhages may be present. Histology shows focal interstitial infiltrates, with central necrosis. No toxoplasma organisms are seen within the cellular infiltrates. Areas of fibrosis may be present if the disease has been of long duration. Myocardial fibres may show myocardial degeneration and necrosis. The toxoplasma organisms are usually seen as minute basophilic masses with a "pseudocyst" in normal or damaged myocardial fibers. Trophozoites may be seen especially during the acute phase.

Experimentally, myocarditis has been produced in mice (Henry and Beverley, 1969) and in rabbits (Henry et al, 1973). In the latter, histological changes were more severe with the low-virulence strains of toxoplasma gondii. ECG abmormalities were detected only when the infection was being cleared from the.

heart, when toxoplasma antigen had been mostly removed and when areas of active inflammation were being replaced by fibrous tissue.

Ludlam and Somers (1966) investigated the incidence of toxoplasma antibodies in 4 groups of Ugandans - blood donors, patients with EMF, congestive cardiomyopathy and rheumatic heart disease. They found no significant difference between these groups and concluded that toxoplasma infection was not an important cause of cardiomyopathy.

CHAGAS DISEASE: This is a common cause of chronic myocarditis in Latin America. Prata et al.(1974) found it in 10% of all their necropsies. It was the most frequent cause of cardiac failure and death in their rural population. The clinical manifestations of cardiac involvement in the acute phase were those of chronic myocarditis, frequently accompanied by a pericardial effusion (Prata et al, 1974). Cardiac arrhythmias were rare in the acute phase although some patients developed congestive cardiac failure. In the chronic phase, cardiac failure was frequent although some were asymptomatic without cardiomegaly (Prata et al, 1974). In these asymptomatic patients, first degree heart block,

right bundle branch block or primary ST-T changes were commonly found on the ECG. Other patients presented mainly with arrhythmia and myocardial failure, when present, was mild to moderate in degree. The incidence of sudden death was high in such patients and advanced degrees of atrioventricular block were present in 10% of them (Andrade and Andrade, 1968; Andrade and Andrade, 1971). Another group of patients presented with chronic heart failure. ECG abnormalities included low voltage QRS complexes, Q waves and ST-T changes. Atrioventricular conduction disturbances were common. Complete right bundle branch block commonly associated with left anterior hemiblock were also common (Prata et al, 1974).

(4) DRUGS AND TOXINS

Amitryptiline has been reported to cause sudden death (Moir et al, 1972) probably as a result of arrhythmia. An overdose of paracetamol taken by a girl of 15 years and a woman of 26 years caused focal myocardial necrosis (Sanerkin, 1971; Pimstone and Uys, 1968). Methyl salicylate caused death in 3 patients reported by Ojiambo (1974). Autopsy revealed myofibrillar necrosis in the subendocardial area of the

left ventricle. Their ECGs showed evidence of hyperkalaemia.

Myocarditis is a well-known complication of emetine therapy. Turner (1963), reported 3 fatal cases and noted that ECG changes were common. 1 other case of emetine myocarditis was reported by Speer et al. (1963). 4 cases were noticed in a 12 month necropsy survey at U.C.H., Ibadan, by Brockington (1974). Dehydroemetine has also been shown to be cardiotoxic though less so than emetine (Lister, 1968); Motte et al, 1970; Dempsey and Salem, 1966). It is a myocardial depressant (Salako and Durotoye, 1974).

Argemone has been reported to be responsible for epidemics of " dropsy" in Calcutta (Sarkar, 1926). This has been confirmed by experiments on human volunteers (Chopra et al, 1939) but there is disagreement as to whether heart failure is a factor in producing the oedema, hepatomegaly and dyspnoea seen in these cases (Sanghvi et al, 1960). The venous pressure is not raised the circulation time is not increased and the heart is not greatly enlarged on the chest radiograph. The active component is sanguinerine, and it causes capillary dilatation and telangiectasia

leading to oedema without hypoproteinaemia. The heart is affected by the same changes. Balani et al.(1968) have, however, reported that heart failure occurred in 7 out of 27 patients in Bombay.

Large toxic doses of digitalis have been found to produce areas of myocardial necrosis in animals (Dearing et al, 1943). Digitalis induced myocardial lesions have also been reported in the presence of experimental hyperthyroidism in cats (Dearing et al, 1950). Kyser et al. (1946) have shown that the cardiotoxic effect of digitalis in dogs is due to vagal stimulation which causes coronary vasoconstriction.

ECG changes have been reported in 34 of 45 patients with scorpion stings (Poon King, 1963). One patient died in pulmonary oedema but had a normal myocardium histologically (Gueron et al, 1967).

Mercurial diuretics have caused sudden death (Kaufman, 1948) possibly due to ventricular fibrillation.

HEAVY METALS:

Antimony compounds often cause ECG changes and have been reported to cause death (Honey, 1960). Lithium caused fatal myocarditis in a 65 year old woman (Tseng, 1971). Lead poisoning caused myocarditis in 5 children,

2 of whom died of acute heart failure (Kline, 1960).

Over 2,000 beer drinkers had arsenic poisoning in 1900. Heart failure was the apparent cause of death (Reynolds, 1901) although selenium was suggested as an alternative agent (Tunnicliffe and Rosenheim, 1901).

Cobalt used as a foaming agent was responsible for heart failure in beer drinkers in Quebec, Belgium, Omaha, Minneapolis and Leuven (Bonenfant et al, 1967; McDermott et al, 1966; Alexander, 1969; Kesteloot et al, 1966). Dilatation of the ventricles occurred in 25 hearts studied at necropsy. The myocardium showed moderate hypertrophy and occasionally ventricular mural thrombi were present. Histological changes included myocardial degeneration and focal fibrosis (Bonenfant et al, 1967). Experimental studies in animals have confirmed the cardiotoxic effect of cobalt (Mohiuddin et al, 1970).

CARBON MONOXIDE: Anderson et al.(1967) described seven cases of carbon monoxide poisoning. Two patients died, one five days after poisoning of what appeared clinically to be an acute myocardial infarction. Autopsy showed a mural thrombus in the left ventricle with coronary embolisation.

ECG abnormalities were frequent and occurred immediately or after the acute episode had subsided.

CATECHOLAMINES:

Myocardial changes consisting of multiple sites of focal myocarditis, subpericardial haemorrhages, oedema and degeneration of myofibrils have been found in patients treated with noradrenaline for shock (Szakacs and Cannon, 1958). Similar changes have been described in patients with phaeochromocytoma (Watkins, 1957; Szakacs and Cannon, 1958; Kline, 1961). Adrenaline also produces myocarditis in rabbits (Samson, 1932). Wenzel (1967) found that isoprenaline, adrenaline, noradrenaline, phenylephedrine, ephedrine, tyramine and methamphetamine alone or in combination with other drugs caused necrotic myocardial lesions in rats. These effects were blocked by alpha but not beta blockade.

(5) CONNECTIVE TISSUE DISORDERS AND HYPERSENSITIVITY REACTIONS

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE):

The cardiac lesion in SLE is most commonly a pericardial effusion, hypertension or Libman-Sacks endocarditis. Myocardial lesions were present in 44%

of the patients seen at necropsy by Harvey et al, (1954). Congestive cardiac failure is however rare (Oram, 1971).

POLYARTERITIS NODOSA: Involvement of the heart in polyateritis nodosa is common (Churg and Strauss, 1951; Mowrey et al, 1954; Rose and Spencer, 1957) and is usually due to coronary arteritis. The heart is enlarged, both ventricles being involved (Churg and Strauss, 1951). Patchy myocardial scarring and in some cases endocardial fibrosis with mural thrombi were common. The most constant lesion was interstitial eosinophilic inflammation.

In the review of 230 cases by Mowrey and Lundberg (1954), myocardial infarction occurred in 17%. Heart failure was the most common cause of death. T wave changes and conduction defects on the ECG were common. Hypertension was also common and its development was closely associated with the healing stages of renal polyarteritis or glomerulitis (Rose and Spencer, 1957).

POLYMYOSITIS: Lynch (1971) described a patient with complete heart block. He also mentioned 3 others in the the literature with fibrosis.

RHEUMATOID ARTHRITIS: 3-10% of patients with rheumatoid arthritis have granulomata in the pericardium, myocardium or the valves (Sokoloff, 1953; Schwartz, 1967). These granulomata are similar to those found in the joints and subcutaneous tissue and are associated with diffuse arteritis. 2 patients died in chronic heart failure in a review of 62 cases by Lebowitz (1963). Congestive cardiac failure, disproportionate to the severity of valve lesions may be found in rheumatoid arthritis and is attributed to myocardial disease (Oram, 1971).

RHEUMATIC HEART DISEASE: Heart failure occurs in acute rheumatic fever and myocardial dysfunction due to low-grade inflammation and fibrosis can occur in the chronic disease. Hildner et al. (1972) using single plane ventriculography found impaired myocardial function in 39 of 71 patients including 6 out of 16 patients with pure mitral stenosis.

ANKYLOSING SPONDYLITIS: Lone aortic incompetence occurs in up to 5% of the patients with ankylosing spondylitis (Oram, 1971). Takkunen et al.(1970) found that 32% of 55 patients had left ventricular failure.

REITER'S DISEASE: The cardiac complications in Reiter's disease are similar to those seen in ankylosing spondylitis although some may have pericarditis. Myocardial involvement is rare. The ECG may show prolonged P-R interval, widening of the QRS and non-specific ST-T changes (Neu et al, 1960).

SYSTEMIC SCLEROSIS: D'Angelo et al.(1969) found excess myocardial fibrosis in 81% of 58 autopsy cases with systemic sclerosis compared with 55% of matched controls. 53% had pericardial fibrosis compared with 14% of controls; 17% had concentric intimal hypertrophy in the small coronary arteries compared with 2% of matched controls. Minor mitral valve abnormalities and nodular thickenings of the free edge of the mitral valve were found but were considered clinically insignificant. Sackner (1966) found severe fibrosis in only 3 of 25 patients he studied. He concluded that chronic pericarditis, cor pulmonale and hypertension were the most important cardiac effects. The most common cause of heart failure is cor pulmonale (Oram, 1971) although some can have myocardial infarction from involvement of their coronary arteries (Fowler, 1964).

OTHER COLLAGEN AND AUTO-IMMUNE DISORDERS: Sub-clinical myocardial lesions have been found in patients with dermatomyositis (Smith, 1955; Lutier, 1962). Levene and

Madden (1957) reported on fatal case of myocarditis caused by Wegnener's granulomatosis. Mendelow and Genkins (1955) found that 5 of 12 consecutive patients with myaesthenia gravis had myocardial necrosis. One of them had fibrosis which did not have any clinical effects.

HEART DISORDERS ASSOCIATED WITH OTHER SENSITIVITY PHENOMENA:

Myocardial lesions have been reported with serum sickness, sulphonamides, penicillin, neoarsphenamine, tetanus toxin and injection of foreign protein. The basic pathology is widespread vascular damage including the heart (Auer and Lewis, 1910; Boughton, 1917; Clark, 1938; Waugh, 1952). ECG changes are common (Shookoff and Lieberman, 1933; Fox and Messeloff, 1942; Goodman, 1948; Lilliengeld et al, 1950; Felder and Felder, 1950; Binder et al, 1950; McManus and Lawlor, 1950; Gulotta, 1951; Neustadt, 1953; Goldman and Lau, 1954; Roussak, 1954; Glotzer, 1954; Contro and Mond, 1956) and include non-specific ST-T changes which disappears in 3-21 days (Contro and Mond, 1956). Conduction distrubances have been described including first degree atrioventricular block (McManus and Lawlor, 1950), atrioventricular dissociation (Foster and Layman, 1952) and right bundle branch block (Lilliengeld et al, 1950; Foster and Layman, 1952). Some may have myocardial infarction (Roussak, 1954).

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Changes at autopsy included necrotising arteritis, myocarditis (Clark, 1938; Wells and Sax, 1945), myccarditis with coronary arteritis (Clark and Kaplan, 1937) and pericarditis (Contro and Mond, 1956).

Injection of foreign protein experimentally produced acute haemorrhages into the myocardium (Auer and Lewis, 1910), interstitial myocarditis (Longcope, 1915), verrucous endocarditis, lesions closely resembling Aschoff bodies (Rich and Gregory, 1943), generalised arteritis (Longcope, 1915) and periarteritis nodosa (Rich and Gregory, 1943).

The common denominator in both human and experimental pathology of sensitivity reactions is focal or diffuse myocardial involvement (Contro and Mond, 1956). No permanent myocardial damage has been reported.

Other forms of eosinophilic myocarditis not associated with drug reactions have also been reported. Some had associated blood eosinophilia (Buhler, 1954) while others did not (Reinhart, 1946).

LOEFFLER'S FIBROPLASTIC PARIETAL ENDOCARDITIS WITH EOSINOPHILIA

Loeffler (1936) described a group of patients with blood eosinophilia, parietal endocardial thickening and myocardial disease in whom there were features of

chronic congestive heart failure. Three patients were also reported from South Africa (Brink and Weber, 1963) and recently from Britain (Bell et al, 1976). It resembles EMF morphologically and in a review of 75 cases, Brockington and Olsen (1973) have shown that distinction between both diseases cannot always be made. Roberts et al.(1970) have also suggested that Loeffler's endocarditis, eosinophilic leukaemia and Davies EMF are the same disease at different stages.

6. IRRADIATION

Radiation - induced heart disease had been found to be more frequent than diagnosed (Stewart and Fajardo, 1971). They found an incidence of 6.6% in patients radiated for Hodgkin's disease and 4.5% in patients radiated for breast carcinoma. The hallmark of the late lesions in the pericardium and myocardium is fibrosis. The incidence of pericarditis is related to dose.

Animal studies also showed that the pathogenesis of the myocardial fibrosis was related to capillary endothelial cell injury leading to a quantitative loss of capillaries, failure of microcirculation and ischaemia (Stewart and Fajardo, 1971).

7. FIEDLER'S MYOCARDITIS

In 1899, Fiedler described four cases of acute interstitial myocarditis with autopsy findings. Since then, there have appeared in the literature many case reports which have been reviewed by Scott and Saphir (1929) and Saphir (1958). The incidence of Fiedler's myocarditis is 0.1 - 0.2% of routine autopsies (Kline and Saphir, 1960; Whitehead, 1965). The patients present with acute, subacute or chronic myocardial failure (Simon and Wolpaw, 1935) and the course is progressively downhill. In acute cases, fever and constitutional symptoms are frequent. Rapid progressive heart failure develops and sudden death is common. Emboli are common and may be the presenting symptom (Oram, 1971). Pathologically, there are two main groups - simple acute or chronic inflammation and granulomatous inflammation sometimes with various types of giant cells. Myocardial hypertrophy and dilatation are present without pericarditis or endocarditis. Mural thrombi are common. The aetiology is unknown.

8. ENDOCRINE DISEASES

THYROTOXIC HEART DISEASE: There is no form of myocardial disease specific for thyrotoxicosis, though young adults

may develop congestive cardiac failure as a complication (Fowler, 1964). In some of these patients, the heart failure subsides on successful treatment for thyrotoxicosis and there is no evidence of residual heart disease (Graettinger, et al, 1959).

MYXOEDEMA: There has been some controversy as to whether or not myxoedema produces heart failure. Fahr (1925), Hallock (1933) and Wood (1960) suggested that myoxoedema eventually leads to heart failure. On the other hand, catheter studies by Ellis et al.(1952) and Graettinger et al.(1958) on myxoedematous patients showed an increase in the cardiac output on exercise without any increase in the intracardiac pressures. Both groups of workers concluded that cardiac failure was not present in myxoedema. Blumgart et al.(1955) in fact showed that patients with intractable heart failure benefit if they are made myxoedematous. McBrien and Hindle (1963) in a study of twenty patients with myxoedema found that only one was in heart failure. Kern et al.(1949) also showed that pericardial effusion was common and was responsible for the ECG changes and the chest x-ray findings in myxoedema. Oram (1971) however stated that cardiac dilatation may occur to the extent of causing functional murmurs of mitral and

tricuspid incompetence.

ACROMEGALY: Myocardial failure occurs in patients with acromegaly (Pepine and Aloia, 1970; McGuffin et al, 1974). 13 of the 57 patients studied by McGuffin et al.(1974) had hypertension, 9 had symptomatic heart disease, 4 had arrhythmias and 3 hyperthyroidism. Seven patients had congestive cardiac failure, two of whom had coronary heart disease, two cardiomyopathy and two arrhythmia. Cardiomegaly, although uniformly present at necropsy, was detected clinically only in patients with hypertension or congestive cardiac failure.

9. MYOCARDIAL INFILTRATION

AMYLOID:

Cardiac involvement is more frequent in the primary and the senile varieties (Symmers, 1956; Buerger and Braunstein, 1960; Pomeranoe, 1965). In an analysis of 145 patients, Symmers (1956) found that the heart was involved in 90 cases and was directly responsible for death in most cases. Primary amyloidosis involves, in addition to the heart, the blood vessels of the tongue, gums and rectum (Symmers, 1956). It involves the liver, spleen, kidney,

lymphnodes, adrenal cortex and the peripheral nerves less frequently than the secondary form. The diagnosis of primary amyloidosis is usually not evident on physical examination (Fowler, 1964).

The effect of amyloidosis on the myocardium is to make it stiff and less contractile. Pressure tracings at cardiac catheterisation are therefore restrictive in type, resembling that of constrictive pericarditis (Hetzel et al, 1953; Garcia and Saeed, 1968).

Patients commonly present with intractable congestive cardiac failure (Lindsay, 1946; Garcia and Saeed, 1968). Cor pulmonale may occur; arrhythmias and conduction disturbances may be present (Lindsay, 1946). The liver may be normal in the primary type but is more involved in secondary amyloidosis.

The senile variety affects the heart alone and occurs in people over the age of 70 years. Pomerance (1965) found it in 10% of patients over the age of 80 years and 50% of those over 90 years.

SARCOIDOSIS: is commoner in Negroes (Poon and Forbes, 1959; Fowler, 1964; Gozo et al, 1971; Fleming, 1974) though other races can be affected (Gozo et al, 1971).

It is, however, rare in Nigerians (Francis, personal communications). Myocardial involvement is not rare (Kirchheiner, 1960; Porter, 1960; Fleming, 1974) and in some autopsy series has been estimated at about 20% (Longcope and Freiman, 1952; Freiman, 1948; Branson and Park, 1954). About 20-35% of patients with sarcoid die from cor pulmonale (Branson and Park, 1954). Death attributable to primary parenchymatous myocardial sarcoid is rare (Porter, 1960).

Conduction disturbances are the most common clinical manifestation of sarcoid heart disease (e.g. Salvesen, 1935; Schaumann, 1936; Cotter, 1939; Bates and Walsh, 1948; Ricker and Clark, 1949; First, 1949; Fleming, 1974) and these result from granulomatous involvement of the conducting system of the heart. Arrhythmias, frequently paroxysmal, are the next most frequent accompaniment of sarcoid heart disease. Minor ST-T changes accompanied by extensive involvement of the myocardium, papillary muscle and interventricular septum have been reported (Bates and Walsh, 1948; Fleming, 1974). Q waves may occur (Gold and Cantor, 1959). Sudden death is common (Porter, 1960; Fleming, 1974), Adam-Stokes attacks being responsible for a proportion of them.

Congestive cardiac failure due to cardiac sarcoidosis without cor pulmonale is less frequent than conduction disturbances (Botti and Young, 1959). Cardiac involvement has been described in two patients who had complete heart block but did not show any of the other manifestations of sarcoidosis (Fowler, 1964).

IRON: Chronic congestive cardiac failure occurs frequently in patients with primary haemochromatosis and transfusion haemosiderosis (Bothwell et al, 1952; Lewis, 1955; Engle et al, 1964; Buja and Roberts, 1971). The heart is usually enlarged, murmurs are absent and blood pressures are normal (Lewis, 1955; Engle et al, 1964). There is a high incidence of arrhythmias (Lewis, 1955; Engle et al, 1964) and T wave changes may be present. The heart is usually brownish in colour, mild hypertrophy and mural thrombi are frequent (Lewis, 1955). There is usually excessive deposit of haemosiderin pigment; degenerative changes in the cells with replacement fibrosis are frequent. Iron deposits are usually present in other organs particularly the liver. Iron deposits are also present more in the ventricular than in the atrial myocardium (Buja and Roberts, 1971). Supraventricular arrhythmias correlate well with the extent of iron

deposition in the atria myocardium. Iron deposits in the cardiac conduction tissue are usually minimal and always less than the myocardium (Buja and Roberts, 1971). Some patients with transfusion haemosiderosis may have pericarditis with percardial effusion (Engle et al, 1964).

GLYCOGEN: Myocardial lesions have been reported in Pompe's disease (Ehrlers et al, 1962) and McArdle's disease (Ratinov et al, 1965). Glycogen storage disease of the heart is a rare cause of heart failure in infancy and survival beyond a few years is rare (Oram, 1971).

TUMOUR METASTASES: Hanfling (1960) reviewed the literature and reported 127 cases of metastatic tumours in the heart. The overall incidence over a 7 year period was 18.3%. There was paucity or complete absence of symptoms in most cases despite extensive involvement of the heart by tumour. Tumour metastases were more common in lymphoma and leukaemia (36%) than in other tumours (12.6%).

Burkitts lymphoma can metastasise to the heart (Burkitt and Wright, 1970; Cole et al, 1975) and in a case reported from U.C.H., Ibadan, produced complete atrioventricular block (Cole et al, 1975). The

patient was in congestive cardiac failure although he was also anaemic.

10. MISCELLANEOUS

ISCHAEMIC HEART DISEASE: There are case reports of patients with occlusive disease of the coronary arteries presenting as primary congestive cardiomyopathy (Raftery et al, 1969; Burch et al, 1972). None of the 4 patients described by Raftery et al.(1969) had any chest pain. 3 patients who had angiographic studies had poorly-contractile left ventricles and severe obstructive disease of their coronary arteries. The fourth patient had autopsy confirmation.

71 (15%) of 1,338 cardiac autopsies performed by Himbert et al.(1970) had painless heart failure. Of these 56 had hypertension or some other heart disease in addition. The remaining 15 patients had no explanation for their heart failure except ischaemic heart disease.

ELECTROLYTES: Hyperkalaemia causes disintegration of myofibrils (Emberson and Muir, 1969). Hypokalaemia caused myocardial necrosis and fibrosis in rats (French, 1952). Microscopic myocardial changes have been described in some patients dying of chronic

diarrhoea (Keye, 1952; Tu et al, 1960). McAllen (1955) reported 2 cases of prolonged and severe potassium deficiency. He found widespread myocardial fibrosis in their hearts.

OTHER INBORN MYOCARDIAL DISEASES: Myocardial lesions have been reported in rhabdomyomatosis (Batchelor and Mann, 1945) and infantile xanthomatous cardiomyopathy (Kauffman et al, 1972). Heart lesions have been described in Rousy - Levy polyneuropathy (Lascelles et al, 1969) and Fabry's disease (Ferrans et al, 1969).

COMMENT

The review shows that there are many other disorders apart from those discussed in the last chapter that are known to cause myocardial damage. However, some of these disorders, for example endocardial fibroelastosis, muscular dystrophies and Friedreich's ataxia occur in the younger age groups these patients rarely surviving to adulthood. Such diseases probably have little or no role to play in the causation of adult HMD.

Some disorders produce ECG changes without clinical effect while others cause heart failure but only in the acute phase. Such disorders are not

known to produce the type of chronic myocardial failure seen in HMD.

Some of the disorders that can produce myocardial damage are easily recognisable clinically as they are part of well-known clinical syndromes and therefore have unmistakable diagnostic signs.

There remain a few disorders that can cause chronic myocardial damage and heart failure and which do not have signs that make them easily recognisable clinically. These disorders can therefore produce the clinical picture of HMD. Some of them include alcohol heart disease, haemochromatosis, primary amyloidosis, Coxsackie B virus cardiomyopathy, toxoplasma cardiomyopathy and Chaga's disease. The role of such disorders in the aetiology of HMD has not been assessed clinically at Ibadan. The aim of the studies reported in the chapters that follow is to assess the role of these disorders and further evaluate the importance of malnutrition, hypertension and thiamine deficiency in the aetiology of HMD.

CHAPTER 4

MATERIALS AND METHODS

THE PATIENTS:

The patients were obtained from two sources - referrals from the General Out-patient Department of U.C.H., Ibadan and direct referrals from general practitioners in Ibadan. Those referred from the General Out-patient Department were either admitted directly to the medical wards or seen initially at the Medical Out-patient clinic before admission. The patients were unselected and constituted a consecutive series. The study was conducted between January 1974 and December 1976.

DIAGNOSIS:

A diagnosis of HMD was made if a patient had congestive cardiac failure and cardiac enlargement confirmed by plain radiograph of the chest and if the known causes of heart failure or enlargement such as anaemia, congenital heart disease, organic valvular disease, endomyocardial fibrosis, hypertrophic obstructive cardiomyopathy and myocardial diseases with known causes have been clinically excluded.

Patients with mitral incompetence and in some cases additional tricuspid incompetence were included in the

series if it was considered clinically that their incompetence was functional and not organic. Patients with other murmurs were excluded.

PRESENTING BLOOD PRESSURE:

As mentioned in chapter two, a transient hypertension occurs when the patients are in failure and remits with treatment of the heart failure. As analysed in the same chapter, Brockington's (1974) results showed that all the patients who presented with a diastolic blood pressure above 100 mm Hg resembled hypertensive heart failure (HHF). Some of those with presenting diastolic blood pressure of 100 mm Hg and below had some evidence of chronic hypertension while the rest had no evidence of hypertension. It was therefore argued that a study that has more of the patients presenting with a diastolic blood pressure above 100 mm Hg will lead one to conclude that HMD is HHF. Therefore in this study, only patients with a presenting diastolic blood pressure of 100 mm Hg and below were included in the series. Patients with higher diastolic blood pressures were diagnosed as hypertensive heart failure.

HISTORY: (Appendix 1)

In addition to obtaining the usual complaints of

series if it was considered clinically that their incompetence was functional and not organic. Patients with other murmurs were excluded.

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HISTORY: (Appendix 1)

In addition to obtaining the usual complaints of

the patient, I administered prepared questionnaires to all the patients (appendix 1). Enquiries were made of chest pain before or during the illness. If the patient had chest pain further attempts were made to determine whether it was anginal, pleuritic or just a vague, non-specific pain. Each patient was also asked if he had paraesthesiae of hands and feet before or during the illness.

A history of symptoms of heart failure and mode of treatment in the past was also obtained. In addition, a history of drug ingestion or a febrile illness prior to the onset of the illness was obtained from each patient.

Attention was also paid to the dietary history and an attempt was made to determine the socio-economic status of each patient by assessing their annual income, property owned, job type and the number of wives and children they had. Their assessment using these parameters proved very difficult and it was also later realised that these variables could not accurately determine their socio-economic groups. Therefore, those whose annual income was less than one thousand naira were arbitrarily classified as belonging to the low socio-economic group while those whose annual income was

higher than this figure were regarded as belonging to the high socio-economic group.

An enquiry was also made from each patient about alcohol ingestion and family illness. Further confirmation of these histories was obtained from the relatives and, occasionally, friends of each patient. These relatives and friends were interviewed separately without the prior knowledge of the patients. This was thought to be necessary because many of the patients were reluctant to disclose any information about their family and often played down or simply lied about their alcoholic habits. Consumption of at least 2000 mls of beer or palm-wine or about 375 mls of spirits daily for over five years was considered a heavy and prolonged intake of alcohol.

A history of previous pregnancy and abortions was also obtained from each female patient. In addition each female patient was asked whether she had symptoms of heart failure during any of her pregnancies or within six months of delivery.

PHYSICAL EXAMINATION:

A detailed cardiovascular examination was performed as in the proforma (Appendix 1). A neurological examination was also performed to rule out any

neuromuscular disease and find out if the patient had peripheral neuropathy. Careful examination of the patients were also made to detect any systemic disease that may be the cause of the patient's heart failure. The skin was examined for onchocerciasis, exfoliation, angular stomatitis and other evidence of vitamin deficiencies. The eyegrounds were carefully examined in a dark-room using a Keeler ophthalmoscope. Blood pressures were recorded in the semi-recumbent position after 3 minutes rest, using a mercury sphygmomanometer. The first and the fifth Korotkoff sounds were used as measures of the systolic and diastolic blood pressures. All blood pressures were taken by the author only to eliminate observer variation.

INVESTIGATIONS:

HAEMATOLOGICAL: The packed cell volume (PCV), the leucocyte count and the blood film appearance were routinely checked. An erythrocyte sedimentation rate (ESR) and an Hb Genotype were obtained on each patient. The serum iron, total iron binding capacity and the percentage saturation were estimated by the one-tube method described by Williams and Conrad (1966).

BIOCHEMISTRY:

The serum sodium and serum potassium were measured

by flame photometry and the serum urea as described in Varley (1969). Total serum proteins were measured by the Biuret method (Gornall et al, 1949) and protein fractions by electrophoresis on cellulose acetate paper in barbitone buffer (Dyke, 1960). Blood for total serum proteins was drawn on admission with the patient recumbent. The serum cholesterol was measured as described by Searcy and Bergquist (1960). The liver function tests were also measured by standard techniques (Varley, 1969). Albuminuria was detected by albustix and glycosuria by clinistix (Ames).

Thiamine deficiency was assessed by the erythrocyte transketolase method (Brin et al, 1960). Transketolase is an enzyme that requres thiamine pyrophosphate (a phosphorylated form of vitamin B_1) for activity. It functions in the metabolism of pentose phosphate sugars. In the assay, haemolysed erythrocytes are incubated with ribose-5-phosphate, both with and without added thiamine pyrophosphate (TPP). In thiamine deficiency, the disappearance of pentose is reduced, as is the formation of hexose phosphate (fructose-6-phosphate and glucose-6-phosphate). In a thiamine - adequate person, the added TPP has little effect on enzyme activity. In thiamine - depleted individuals, however, the added TPP results in increased hexose formation or increased disappearance of ribose-5-phosphate, showing that the

transketolase enzyme was not saturated with thiamine pyrophosphate (Pearson, 1967). The effect of added TPP in percentage is referred to as the TPP effect. In this study, the hexose activity and its associated TPP effect was used for assessing thiamine status as this was more useful than pentose determination (Pearson, 1967). In a preliminary study done in the laboratory, there was an inverse relationship between the amount of hexose formed and the TPP effect. The higher the TPP effect, the lower the hexose formed per unit time. Therefore the results were not expressed in hexose formed in microgram per unit of time.

Fasting blood pyruvic acid was measured by the dinitrophenyl-hydrazine method (Friedemann and Haugen, 1943) and fasting lactic acid by the method of Barker and Summerson (1941).

The alcohol content of beers was determined from the specific gravity of distillate of the decarbonated beer using the Association of Official Agricultural Chemists methods of analysis (1970). Total carbohydrate was determined using phenol sulphuric acid reagent of Du Bois et al.(1951) and a glucose standard curve. Minerals were estimated using the atomic absorption spectrophotometry. Phosphorous was determined by the

method of Kitson and Mellon (1944). Protein was estimated by determining nitrogen using the Kjeldahl method and multiplying by 6.25.

A T_3-uptake test using Thyopac-3 supplied by the Radiochemical Centre at Amersham, England was used as a screening test for hypothyroidism and thyrotoxicosis. 0.1 ml. of standard reference serum was added to a T_3 test vial. The contents of each vial were mixed for 10 minutes and allowed to settle for 2 minutes. 1.0 ml of supernate was then removed from each test vial and each sample of supernate was counted. The counts of each patient's serum was expressed in terms of the reference standard. The normal values for this test lie between 92 and 117. Counts above 117 were regarded as hypothyroid and counts below 92 as hyperthyroid.

MICROBIOLOGICAL TESTS:

The blood film of each patient was examined for malaria parasites, microfilariae and trypanosomes. The stool was also examined for hookworm, ascaris or schisostoma ova and other parasites. The urine was spun down and examined for schisostoma ova, white cells, red cells and casts. Paired antibody titers were determined against Toxoplasma gondii in the serum.

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A latex slide agglutination test in kit form supplied by Italdiagnostic (Italy) was used to detect the Toxoplasma antibodies. For screening, equal sized drops (from droppers provided in the kit) of serum and of antigen suspension were placed on a black glass tile (one is provided) and gently mixed. After 2 to 5 minutes a reading was made in strong oblique lighting. When agglutination occurred, it was usually easily appreciated. Those sera reacting positively in the screening test were assessed quantitatively later on the same day. Doubling dilutions of test serum ranging from 1:2 to 1:1024 were made by a drop method and using the special diluent. One drop of each dilution was then mixed with one drop of antigen on the tile and observed as in the screening test.

A modified complement fixation test described by Kent and Fife (1963) was used to detect antibodies against Trypanosoma cruzi.

The Venereal Diseases Research Laboratory (VDRL) slide test as described in Crowley et al.(1969) was used to detect antibodies against syphilis . The anti-streptolysin-O titre (ASOT) was also determined for each patient (Crowley et al, 1969).

VIROLOGY:

All virus studies were undertaken in the Virus Research Laboratory, University of Ibadan.

Coxsackie B viruses were isolated from faecal specimen and from blood by inoculation into Verocells. Neutralisation test was carried out in Vero tissue culture.

VIRUS ISOLATION: About 1.2 gm of stool in 5 ml. Hanks BSS containing antibiotics and fungizone was emulsified with the aid of an applicator in a universal bottle. The suspension was centrifuged at 3,000 revolutions per minute for 20 minutes. The supernatant was removed and kept in the refrigerator and inoculated on the same day or it was kept at a temperature of - 20°C if it was not possible to inoculate on the same day. Whole blood was not treated before inoculation.

NEUTRALISATION TEST: A Coxsackie B 126 virus isolate was used in neutralisation tests. An initial titration was made in an attempt to determine the infectivity titre of the virus. Ten fold serial dilutions of viral suspension in Hanks BSS or maintenance medium were prepared and 0.1 ml. of each dilution was inoculated into 4 tubes of Vero cell cultures. The tubes were incubated at 36-37°C and examined daily for cytopathic effect for 7 days.

The end point was then calculated by the method of Reed and Muench (1938).

Virus neutralisation test was performed in Vero cell cultures. Sera were first screened by the constant - virus constant-serum method. The neutralising power of positive sera was determined by the constant virus varying serum technique. Three tenths aliquots containing 100 TCD_{50} of the virus were mixed with 0.3 ml. of diluted serum (1:4) previously inactivated at 56°C for 30 minutes. Serum virus mixtures were then incubated at 37°C for 2 hours. Duplicate tubes of Vero cells were inoculated with each serum-virus mixture, using 0.2 ml. of samples per tube. Test controls with ten-fold serial virus dilutions and serum controls were set up in parallel. All tubes were incubated at 36-37°C on the roller and read 24 hours post inoculation starting with the control tubes. Reading of tubes continued daily until 5 days post inoculation when the experiment was terminated.

RADIOLOGICAL EXAMINATIONS:

Each patient had plain radiographs of the chest taken in the postero-anterior and the left lateral positions. These radiographs were repeated at intervals during their follow-up.

Cardiac catheterisation was done when the patient improved and if the patient agreed to the procedure. Pressures were measured by a Statham pressure transducer Model P23DB and recorded by an Electronics for Medicine Multiple Channel Recorder. A point midway between the plane of the patient's sternum and the plane of the catheter table was taken as the zero pressure baseline. Angiograms were taken with an Elema-Schonander AOT rapid film changer. Right ventricular angiograms were performed in the antero-posterior positions while left ventricular angiograms were taken in the left oblique positions. Films were taken at the rate of 3 per second.

On each plain chest radiograph, the cardio-thoracic ratios and the total cardiac volumes were calculated as described by Lusted and Keats (1972). All these measurements were corrected for surface area. The aortic diameter was measured by the method of Brockington and Bohrer (1970).

The aortic diameter was also measured on the angiographic films at the root, mid-ascending and mid-descending levels. The left ventricular chamber volumes corrected for surface area were measured in

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The aortic diameter was also measured on the angiographic films at the root, mid-ascending and mid-descending levels. The left ventricular chamber volumes corrected for surface area were measured in

systole and diastole by the uniplane method described by Greene et al (1967). The ejection fraction was calculated from the formula $\frac{EDV - ESV}{EDV} \times 100$ where EDV = end-diastolic volume and ESV = end-systolic volume. The use of this fraction eliminates errors due to magnification or geometrical distortion (Gotsman et al, 1971).

The left ventricular wall thickness corrected for surface area was measured as described by Lusted and Keats (1972). The ratio of left ventricular cavity to left ventricular wall thickness was also determined.

Intravenous pyelography (IVP) was performed along the standard lines - pre-examination dehydration, mild laxative and suppository followed next day by the injection of the urographic dye. Focal film distance was 36 inches and centering point was the level of the 3rd lumbar vertebra. The length and width of the kidneys were measured as described by Noell (1961). Surface areas (in sq. cm.) were calculated using the formula for an ellipse $\frac{\pi}{4} \times$ length x width (Noell 1961).

CARDIAC OUTPUT:

The resting cardiac output of each patient was measured on admission. This investigation was repeated as necessary. Cardiac output was measured by the

dye-dilution method using tricarboncyanine (cardio-green) dye and a Waters densitometer model DCR-701 with a cuvette transducer. The equipment has an attached specialised analog computer designed to predict and display digitally the cardiac output from indicator dilution curves. The computer obtains its electrical input signals from the densitometer. It then integrates the area under the dye curve from its starting point on the down slope side at 75% of the peak. From 75% of the peak, the computer analyses the assumed exponential decay of the curve. At 50% of the peak normally well above second recirculation, the answer is predicted and the the direct readout of cardiac output is obtained.

The equipment was initially calibrated before use. A catheter was then advanced via a vein on the medial side of the antecubital fossa until it reached the axillary vein or the superior vena cava. Another catheter was inserted into a brachial artery and connected to the densitometer. The densitometer was then switched on and with controlled blood flowing through the cuvette, the densitometer balance button was pressed until the computer's digital display meter read 0.0. The recorder was then switched to record position and the dye injected as a bolus via the venous

catheter. The null - computer switch was then turned to compute. A direct readout of the cardiac output was made when the second function light came on. This light comes on usually at 50% of the peak.

5 mg of cardiogreen in 1 ml of water was usually injected. If the deflection was not good enough, 1½ ml and then 2 mls of the same dye concentration was used. 3 runs were made on each occasion and the average reading taken as the cardiac output.

ELECTROCARDIOGRAM (E.C.G.):

A standard 12-lead ECG was taken on each patient and at various periods during their follow-up with a Phillips Cardiopan machine model 531. The standardisation of the machine was always checked before any recording was done.

BIOPSIES:

A rectal biopsy was performed on each patient and examined under the microscope after haematoxylin-eosin and congo-red staining.

A liver-biopsy was performed if the congo-red stain on rectal biopsy was positive, if the serum iron was high or if there are other indications to warrant such a procedure. A liver biopsy was avoided if the patient was in congestive cardiac failure, if the prothrombin

time was prolonged or if the general state of the patient did not permit it.

TREATMENT:

Each patient on admission was given digoxin ranging 1 mg stat, then 0.5 mg twice daily followed by 0.25 mg twice daily. Each patient was also given frusemide 80 mg daily. The dose of frusemide was increased up to 240 mg daily if there was no improvement. Potassium supplements were also given to the patient. They also had a restricted salt diet and bed rest.

Frusemide was chosen because although it can lower the blood pressure (Anderson et al, 1971), its hypotensive action is low when compared with the thiazides (Anderson et al, 1971). If the patients are indeed hypertensives, it is possible that their improvement on treatment of their heart failure alone is due to the hypotensive and the diuretic actions of these diuretics. Since they were in congestive cardiac failure and therefore needed diuretics, frusemide was initially given because of its less pronounced hypotensive effect.

The patients were mainta ined on the same dose of drugs on discharge from hospital, Thiazides and when necessary alpha methyl dopa were substituted for frusemide if at any stage there was no improvement and if the blood pressure remained elevated.

FOLLOW-UP

Each patient was followed up for at least a year. To ensure that the patients received their drugs regularly from the Pharmacy Department their names were submitted to the Chief Pharmacist of the hospital to facilitate easy supply of drugs, they were exempted from hospital fees, given out-patient appointments not longer than a month, asked to report back if they did not receive the drugs and they were asked at each visit if they received their drugs and if they used them regularly.

At each out-patient appointment, the cardiovascular system of each patient was carefully re-assessed and the blood pressure recorded.

Following their recovery from heart failure, 20 patients (12 males and 8 females) were readmitted into hospital and observed on digoxin alone. Each of them was allowed liberal use of salt in his food. Their blood pressures and pulse rates were carefully monitored daily. Their treatment before admission was again resumed when they relapsed into heart failure.

Home visits were paid to those who defaulted for more than 3 months with the help from the Hospital Social Workers Division.

CONTROL GROUP: 52 patients attending the out-patient clinic without any heart disease were used as controls. Their sex, age and socio-economic status were assessed. A history of alcoholic consumption was also obtained and blood taken for determination of their thiamine status and serum albumin as described above. Paired antibody titres were also determined against Toxoplasma gondii, Coxsackie B viruses and Trypanosoma cruzi. The methods used were as described previously.

CHAPTER 5

RESULTS

A total of 50 patients made up of 28 females and 22 males were studied. Their age and sex distribution is shown in figure 3.

Organic Mitral Incompetence (MR):

Six (12%) patients were found, surprisingly, to have organic mitral incompetence or mitral regurgitation (MR) on left ventricular angiography. They had florid mitral incompetence although their left ventricles were only slightly dilated in diastole and showed good contraction in systole (figure 4).

Clinically their symptoms and signs resembled those of patients with HMD and functional mitral incompetence (tables 1-3). Both groups of patients presented in congestive cardiac failure and had third sounds and pulmonary hypertension. Both groups also had enlarged hearts confirmed by increased cardio-thoracic ratios (tables 48-51) on chest radiograph (e.g. figures 5 and 6). Left atrial and ventricular hypertrophy, ST-T changes and prolonged corrected Q-T interval (Q-Tc) beyond 0.44 seconds were not confined to either group (tables 41-43).

Despite these similarities, however, some changes which may make for easier clinical differentiation between the two groups were noticed on further analysis although the number

TABLE 1

SUMMARY OF THE SYMPTOMS AND SIGNS OF THE 6 PATIENTS WITH ORGANIC MITRAL INCOMPETENCE

Patient	Sex	Age	DOE	Ankle Swelling	Pulse Rate	Pulse Volume	JVP	Prominent (a) or (v) wave	Apical impulse	Apical impulse	Apical thrill	CCF	Apical S_1	Apical S_3	A_2	P_2	MR murmur	Character of murmur	Change treatment	TI	Change with treatment
									Location	Character											
L.L.	F	30	+	+	120	P	4 cm	'a'	D	H; L	-	+	N	+	N	+	+	Loud	None	-	-
G.K.	F	30	+	+	120	N	4 cm	'a'	D	H, L	+	+	N	+	N	+	+	Loud	None	-	-
A.O.	F	30	+	+	115	P	6 cm	a	D	H; NL	+	+	N	+	N	+	+	Loud	None	-	-
K. O.	M	35	+	+	100	P	5 cm	a	D	H; L	+	+	N	+	N	+	+	Loud	None	-	-
T.O.	M	17	+	+	108	N	10 cm	a,v	D	N, NL	-	+	N	+	N	+	+	Loud	None	+	None
M.O.	F	17	+	+	124	P	6 cm	a	D	H, NL	+	+	N	+	N	+	+	Loud	None	-	-

DOE = Dyspnoea on exertion.

MR = Mitral incompetence.

P = Poor.

S = Soft.

H = Heaving.

CCF = Congestive cardiac failure.

TI = Tricuspid incompetence.

D = Displaced

N = Normal

JVP = Jugular venous pressure.

MSM = Midsystolic murmur.

L = Localised

NL = Not localised.

NF = Not felt.

TABLE 2

SUMMARY OF THE FINDINGS AND SIGNS OF THE PATIENTS WITH HEART MUSCLE DISEASE AT HAD AUTOPSY(S) OR POST-MORTEM CONFIRMATION

Patient	Sex	Age	DCI	Ankle Swelling	Pulse Rate	Pulse volume	JVP	Prominent (a) or (v) wave	Apical impulse Location	Apical impulse Character	Apical thrill	CCF	Apical S_1	Apical S_3	A_2	P_2	MI murmur	Character of murmur	Change with Treatment	TI	Change with treatment
E. A.	F	60	+	+	100	F	10cm	a	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	-	-
A. O.	F	40	+	+	112	F	10cm	a, v	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]
Y. M.	F	60	+	+	100	F	4cm	a	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	-	-
M. T.	F	50	+	+	120	F	7cm	a	D	H, ML	-	+	H	+	+	+	-	-	-	-	-
M. A.	F	60	+	+	120	F	10cm	a	D	H, ML	-	+	3	+	H	+	[illegible]	3	[illegible]	-	-
B. L.	F	35	+	+	120	F	10cm	a	HF	HF	-	+	3	+	H	+	-	-	-	-	-
D. O.	F	63	+	+	100	F	4cm	a	D	H, ML	-	+	3	+	H	+	-	-	-	-	-
A. A.	F	40	+	+	108	F	10cm	a, v	D	H, ML	-	+	H	+	+	+	+	Loud	[illegible]	+	+
B. M.	F	40	+	+	100	F	6cm	a	D	H, ML	-	+	H	+	H	+	+	Loud	[illegible]	-	-
L. A.	M	60	+	+	90	F	10cm	a	D	H, ML	-	+	3	+	H	+	-	-	-	-	-
J. C.	M	60	+	+	110	F	10cm	a	D	H, ML	-	+	H	+	H	+	+	Loud	[illegible]	-	-
B. O.	M	48	+	+	80	F	4cm	a	HF	HF	-	+	H	+	+	+	+	Loud	[illegible]	-	-
*B. O.	M	67	+	+	130	F	6cm	a	HF	HF	-	+	3	+	H	+	-	-	-	-	-
J. U.	F	61	+	+	90	F	10cm	a	D	H, ML	-	+	3	+	H	+	-	-	-	-	-
B. E.	F	65	+	+	100	F	10cm	a, v	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]
A. T.	F	35	+	+	96	F	6cm	a	D	H, ML	-	+	H	+	+	+	+	Loud	[illegible]	-	-
B. A.	M	60	+	+	120	F	10cm	a	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	-	-
B. T.	M	62	+	+	92	F	4cm	a	HF	HF	-	+	3	+	H	+	+	3	[illegible]	-	-
*M. B.	M	26	+	+	90	F	10cm	a	HF	HF	-	+	3	+	H	+	+	3	[illegible]	-	-
J. F.	M	74	+	+	80	F	4cm	a	HF	HF	-	+	3	+	H	+	-	-	-	-	-
T. C.	M	35	+	+	80	F	6cm	a	HF	HF	-	+	3	+	H	H	[illegible]	3	[illegible]	-	-
C. C.	F	65	+	+	92	F	20cm	a	HF	HF	-	+	3	+	H	H	-	-	-	-	-
M. E.	M	54	+	+	108	F	10cm	v	D	ML	-	+	3	+	H	H	+	3	[illegible]	+	[illegible]
C. A.	F	55	+	+	90	F	10cm	a	D	H	-	+	3	+	H	+	-	-	-	-	-
B. M.	F	40	+	+	100	F	6cm	a	D	H; ML	-	+	H	+	H	+	+	Loud	[illegible]	-	-
C. C.	F	25	+	+	120	F	10cm	a	D	ML	-	+	H	+	H	+	+	Loud	[illegible]	-	-
T. I.	F	30	+	+	90	F	10cm	a	D	ML	-	+	H	+	H	+	-	-	[illegible]	-	-
A. I.	F	35	+	+	100	F	6cm	v	D	H	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]
								a	D	H, ML	-	+	3	+	H	+	+	3	[illegible]	-	-

* Heart muscle disease confirmed at post-mortem.

DCI = Dyspnoea on exertion. CCF = Congestive cardiac failure. JVP = Jugular venous pressure. MI = Mitral incompetence. TI = Tricuspid incompetence.

F = Poor. D = displaced HF = Not felt [illegible] = not localised H = Soft H = Normal H = Holosystolic [illegible].

TABLE 2

SUMMARY OF THE FINDINGS AND SIGNS OF THE PATIENTS WITH HEART MUSCLE DISEASE WHO HAD AUTOPSY OR POST-MORTEM CONFIRMATION

Patient	Sex	Age	DCE	Ankle Swelling	Pulse Rate	Pulse volume	JVP	Prominent (a) or (v) wave	Apical impulse		Apical thrill	CCF	Apical S_1	Apical S_3	A_2	P_2	MI murmur	Character of murmur	Change with treatment	TI	Change with treatment
									Location	Character											
E. A.	F	60	+	+	100	F	10cm	a	D	H, HL	-	+	3	+	H	+	+	3	[illegible]	-	-
A. C.	F	40	+	+	112	F	10cm	a, v	D	H, HL	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]
T. H.	F	60	+	+	100	F	4cm	a	D	H, HL	-	+	3	+	H	+	+	3	[illegible]	-	-
E. T.	F	50	+	+	120	F	7cm	a	D	H, HL	-	+	3	+	+	+	-	-	-	-	-
M. A.	F	60	+	+	120	F	10cm	a	D	H, HL	-	+	3	+	H	+	[illegible]	3	[illegible]	-	-
B. L.	F	35	+	+	120	F	10cm	a	HF	HF	-	+	3	+	H	+	-	-	-	-	-
D. O.	F	63	+	+	100	F	4cm	a	D	H, HL	-	+	3	+	H	+	-	-	-	-	-
A. A.	F	40	+	+	108	F	10cm	a, v	D	H, HL	-	+	H	+	+	+	+	Loud	[illegible]	+	+
B. M.	F	40	+	+	100	F	6cm	a	D	H, HL	-	+	H	+	H	+	+	Loud	[illegible]	-	-
L. A.	M	60	+	+	90	F	10cm	a	D	H, HL	-	+	3	+	H	+	-	-	-	-	-
J. C.	M	60	+	+	110	F	10cm	a	D	H, HL	-	+	H	+	H	+	+	Loud	[illegible]	-	-
B. O.	M	48	+	+	80	F	4cm	a	HF	HF	-	+	3	+	+	+	+	Loud	[illegible]	-	-
*D. O.	M	67	+	+	150	F	6cm	a	HF	HF	-	+	3	+	+	+	+	Loud	[illegible]	-	-
J. U.	F	61	+	+	90	F	10cm	a	D	H, HL	-	+	3	+	H	+	-	-	-	-	-
B. E.	F	65	+	+	100	F	10cm	a, v	D	H, HL	-	+	3	+	H	+	-	-	-	-	-
A. T.	F	35	+	+	96	F	6cm	a	D	H, HL	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]
B. A.	M	60	+	+	120	F	10cm	a	D	H, HL	-	+	H	+	+	+	+	Loud	[illegible]	-	-
B. T.	M	62	+	+	92	F	4cm	a	D	H, HL	-	+	3	+	H	+	+	3	[illegible]	-	-
*A. B.	M	26	+	+	90	F	10cm	a	HF	HF	-	+	3	+	H	+	+	3	[illegible]	-	-
J. P.	M	74	+	+	80	F	4cm	a	HF	HF	-	+	3	+	H	+	-	-	-	-	-
T. O.	M	35	+	+	80	F	6cm	a	HF	HF	-	+	3	+	H	H	[illegible]	3	[illegible]	-	-
O. O.	F	65	+	+	92	F	20cm	v	D	HL	-	+	3	+	H	H	-	-	-	-	-
I. E.	M	54	+	+	108	F	10cm	a	D	HL	-	+	3	+	H	H	+	3	[illegible]	+	[illegible]
O. A.	F	55	+	+	90	F	6cm	a	D	HL	-	+	3	+	H	+	-	-	-	-	-
I. M.	F	40	+	+	100	F	6cm	a	D	H; HL	-	+	3	+	H	+	+	Loud	[illegible]	-	-
O. O.	F	23	+	+	120	F	10cm	a	D	HL	-	+	H	+	H	+	+	Loud	[illegible]	-	-
T. I.	F	30	+	+	90	F	10cm	a	D	HL	-	+	H	+	H	+	-	-	-	-	-
A. I.	F	35	+	+	100	F	6cm	v	D	HL	-	+	3	+	H	+	+	3	[illegible]	+	[illegible]

* Heart muscle disease confirmed at post-mortem.

DCE = Dyspnoea on exertion. CCF = Congestive cardiac failure. JVP = Jugular venous pressure. MI = Mitral incompetence. TI = Tricuspid incompetence.

F = Poor. D = displaced HF = Not felt [illegible] = Not localised L = Left P = Parasternal [illegible]

Table 3

Summary of the symptoms and signs of the patients with heart muscle disease but with no definite aetiological confirmation

PATIENT	Sex	Age	DOE	Ankle Swelling	Pulse rate	Pulse volume	JVP	Prominent (a) or (v) wave	Apical Impulse Location	Apical Impulse Character	Apical thrill	CCF	Apical S_1	Apical S_2	A2	P2	MI murmur	Duration of murmur	Change with treatment	TI	Change with treatment
A. O.	F	55	+	+	90	P	5 cm	a	D	H, L	-	+	H	+	H	+	+	S	Yes	-	-
A. C.	M	50	+	+	90	P	10 cm	a	D	H, ML	-	+	S	+	N	+	H.S.	S	Yes	-	-
A. O.	F	61	+	+	80	P	4 cm	a	D	H, ML	-	+	S	+	H	+	+	S	Yes	-	-
J. A.	M	52	+	+	84	P	10 cm	a	D	H. ML	-	+	S	+	H	+	+	S	Yes	-	-
O. O.	F	50	+	+	80	P	4 cm	a	NF	N.F.	-	+	N	+	H	+	-	-	-	-	-
S. F.	M	75	+	+	92	P	3 cm	N	D	H, ML	-	+	S	+	H	H	H.M	S	None	-	-
M. E.	M	40	+	+	104	P	10 cm	a,v	D	H, ML	-	+	S	+	H	+	+	S	Yes	+	Yes
M. A.	F.	43	+	+	96	P	10 cm	a	NF	NF	-	+	S	+	H	+	+	S	Yes	-	-
L. O.	M	74	+	+	100	P	10 cm	a,v	D	H, ML	-	+	S	+	H	+	+	S	Yes	+	Yes
B. S.	F	45	+	+	100	P	5 cm	a	D	H, ML	-	+	S	+	H	+	-	-	-	-	-
J. S.	M	41	+	+	100	P	10 cm	a	NF	NF	-	+	S	+	H	+	-	-	-	-	-
O. O.	M	53	+	+	96	P	10 cm	a	D	H, ML	-	+	S	+	H	+	-	-	-	-	-
B. E.	F	65	+	+	120	P	6 cm	a	NF	NF	-	+	S	+	H	+	-	-	-	-	-
E. L.	M	64	+	+	60	P	20 cm	a,v	D	ML	-	+	S	+	H	H	+	S	None	+	None
O. F.	M	50	+	+	80	P	4 cm	a	NF	NF	-	+	S	+	H	H	-	-	-	-	-
T. A.	M	50	+	+	80	P	10 cm	N	NF	NF	-	+	S	+	H	+	-	-	-	-	-

DOE = Dyspnoea on exertion.
MI = Mitral incompetence.
P = Poor
ML = Not localised
NF = Not felt.

CCF = Congestive cardiac failure.
TI = Tricuspid incompetence.
D = Displaced
S = Soft

JVP = Jugular venous pressure.
MSM = Midsystolic murmur.
M = Moving
N = Normal

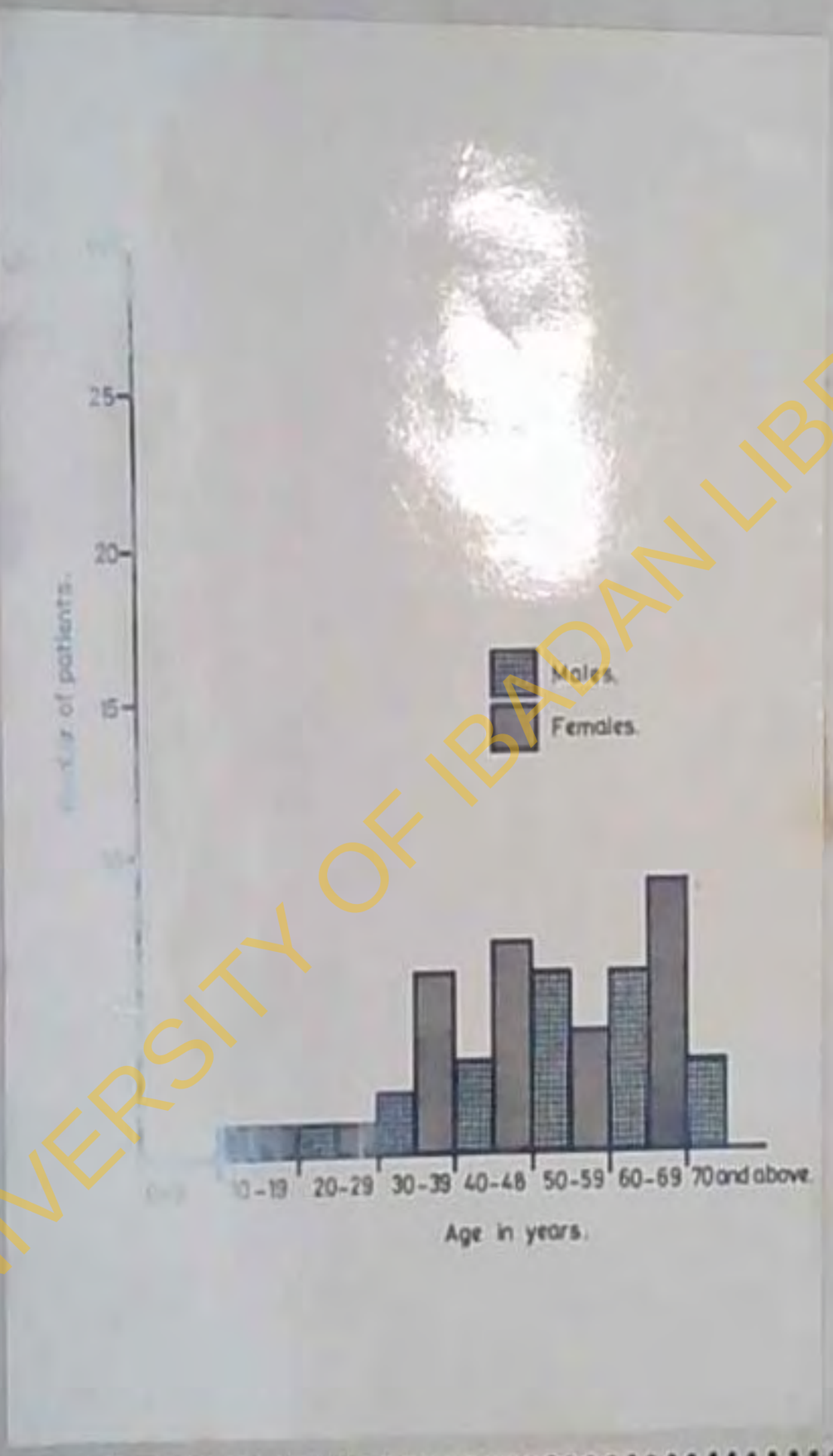
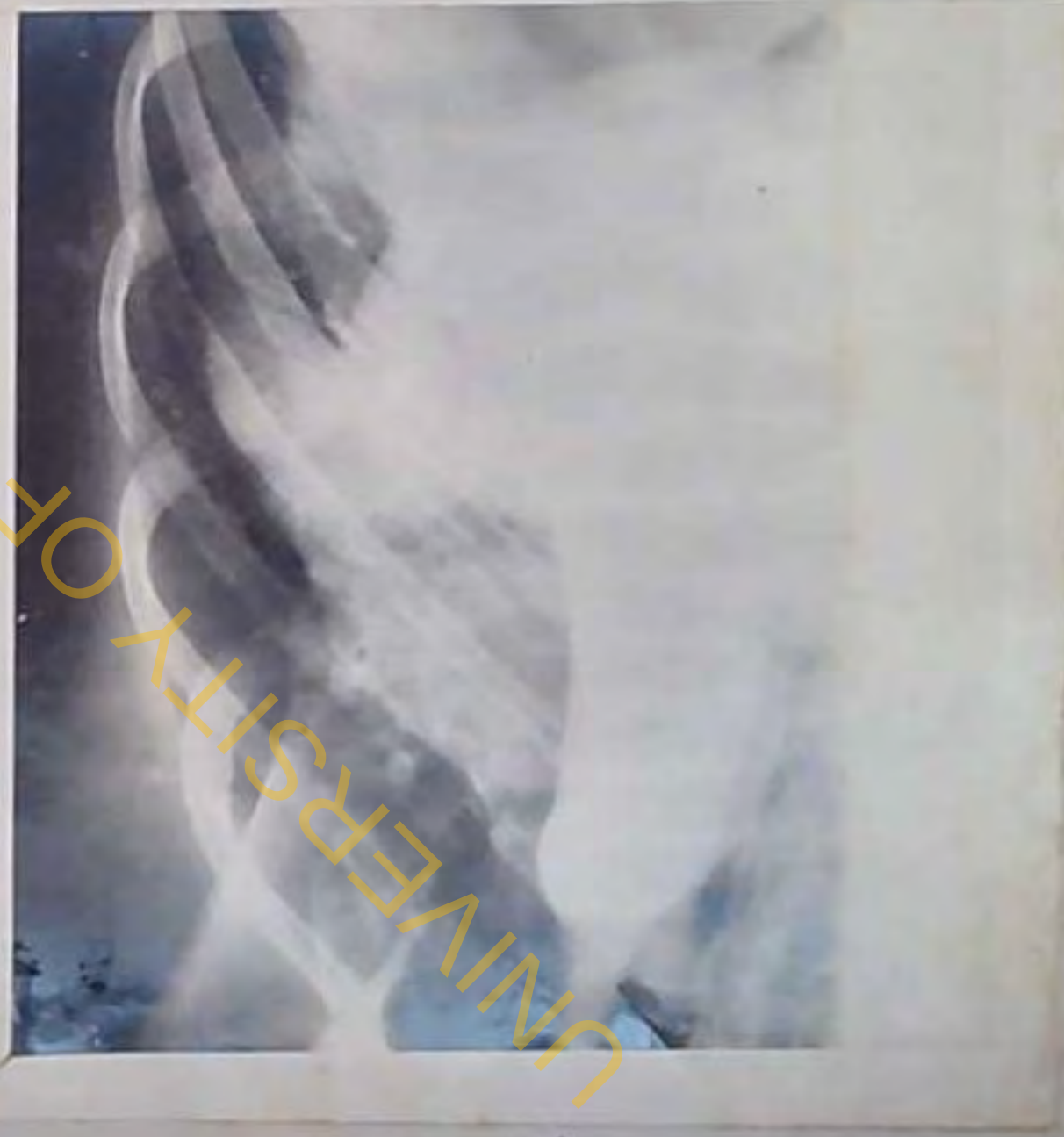


Fig. 3 The age and sex distribution of the 50 patients.



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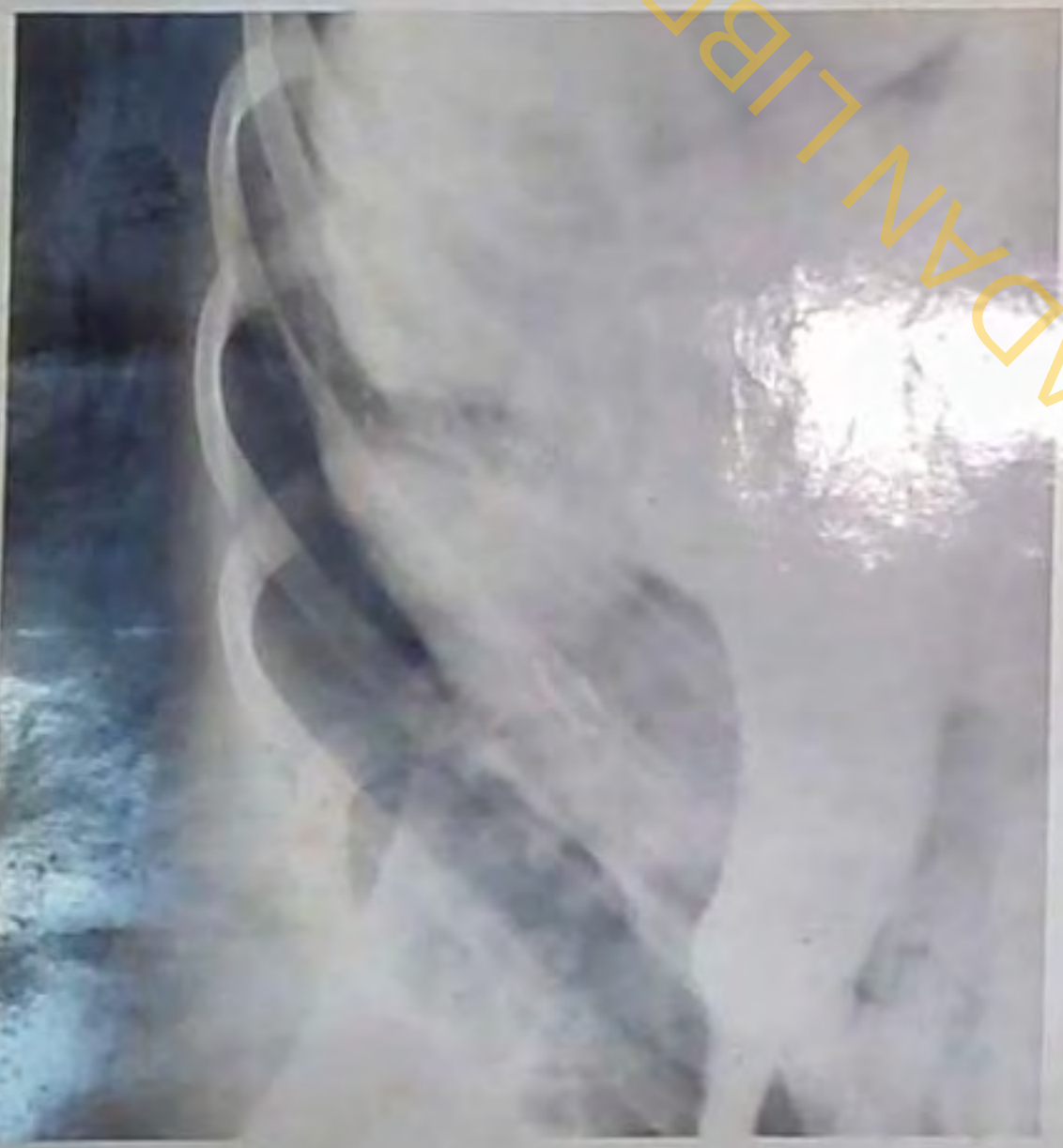
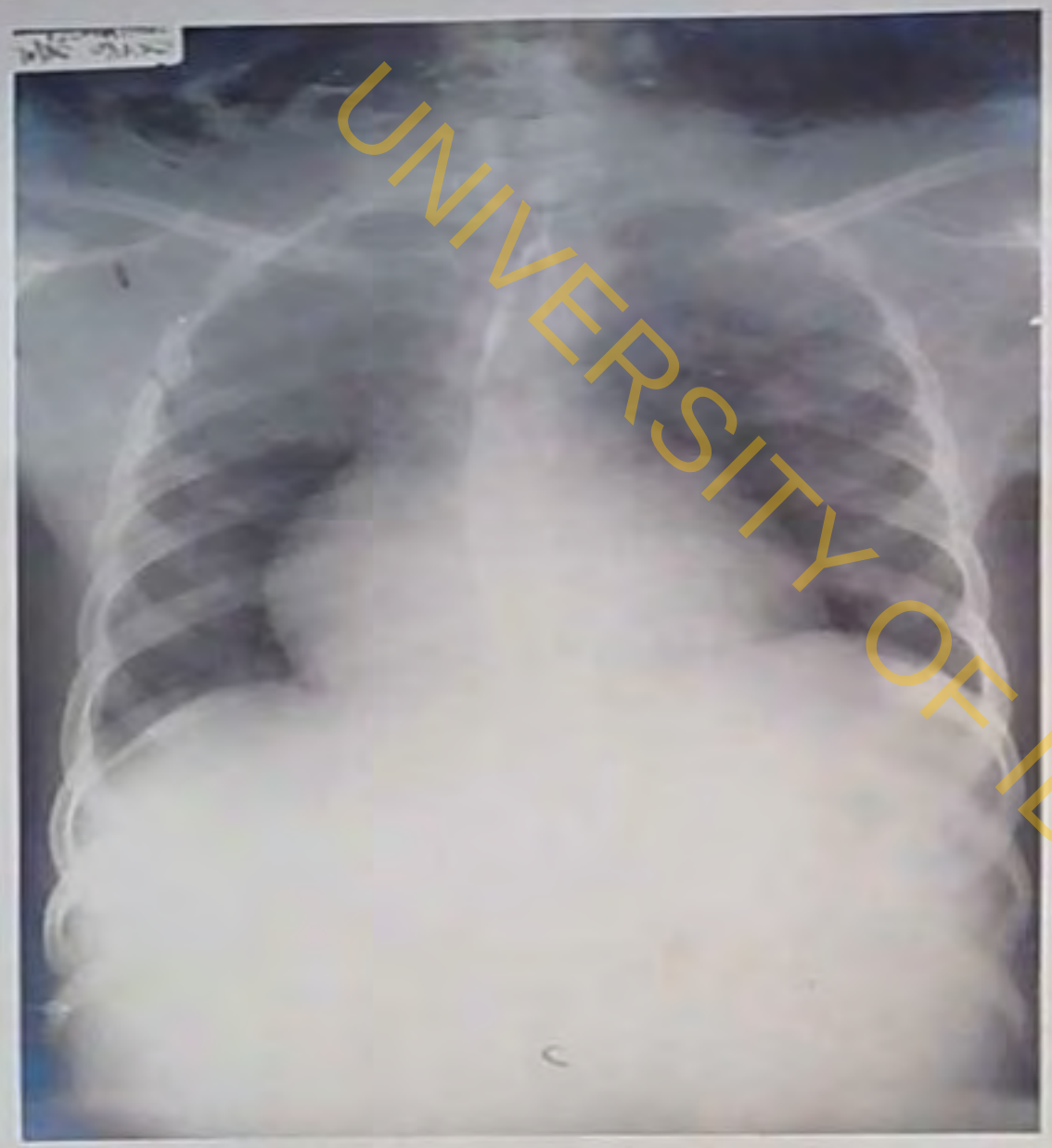


B

Fig. 4 Left ventricular angiogram of G.K. (table 1) showing a dilated left ventricle in diastole (B) with good contraction in systole (A). There is florid mitral incompetence.



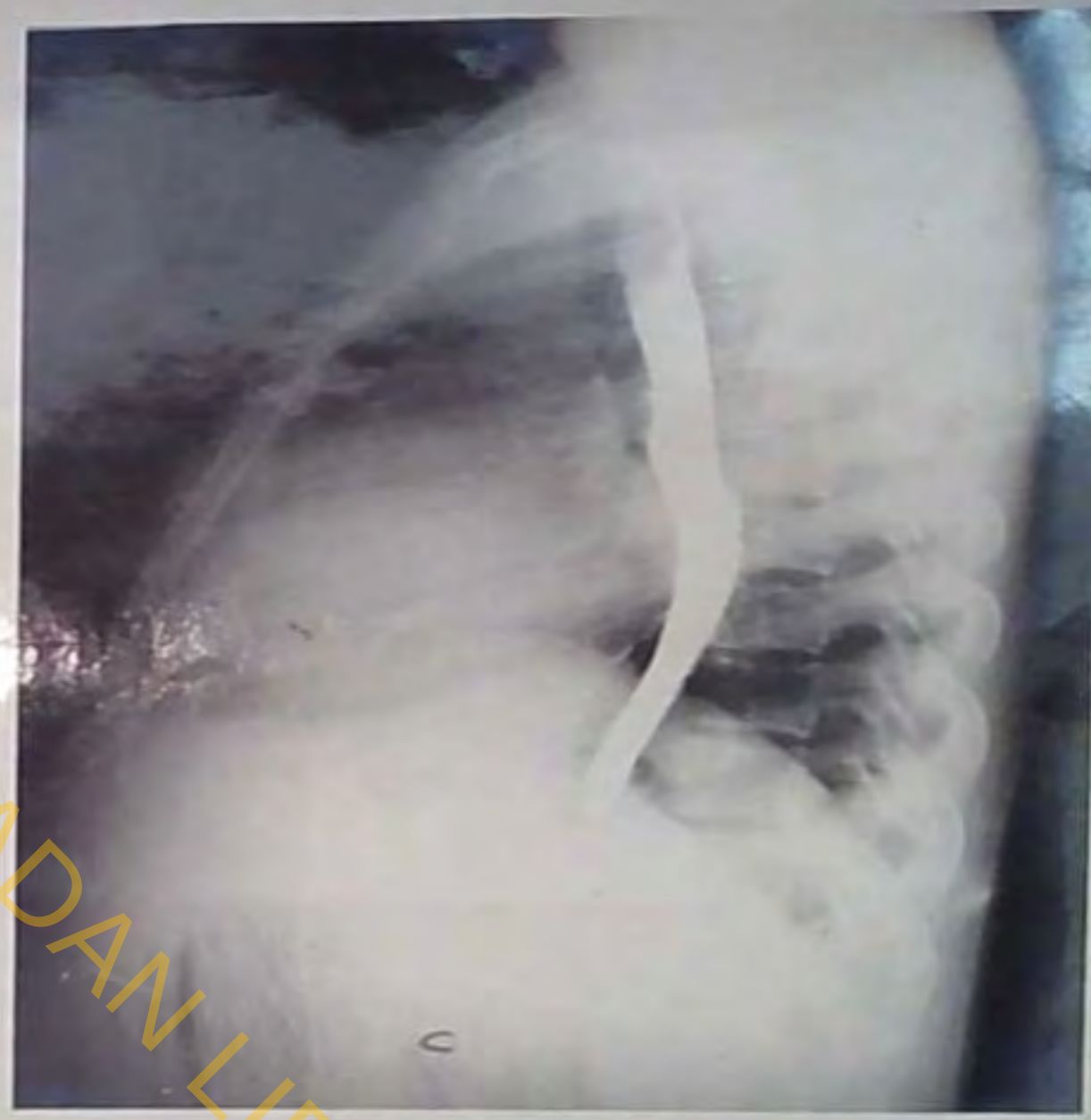
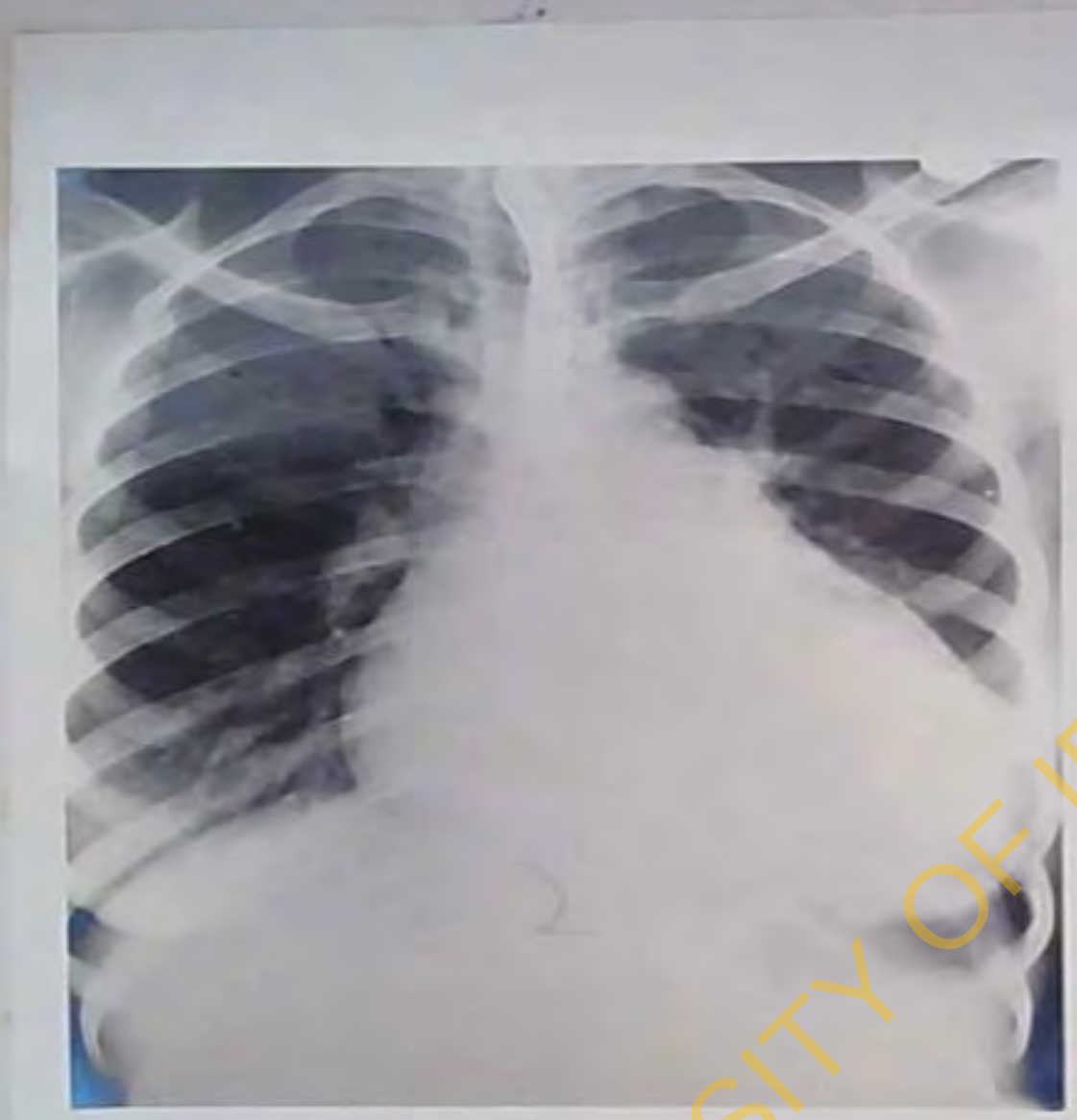


Fig. 5 Chest x-ray of a patient with organic mitral incompetence (Y.G. table 1) showing pancardiomegaly.



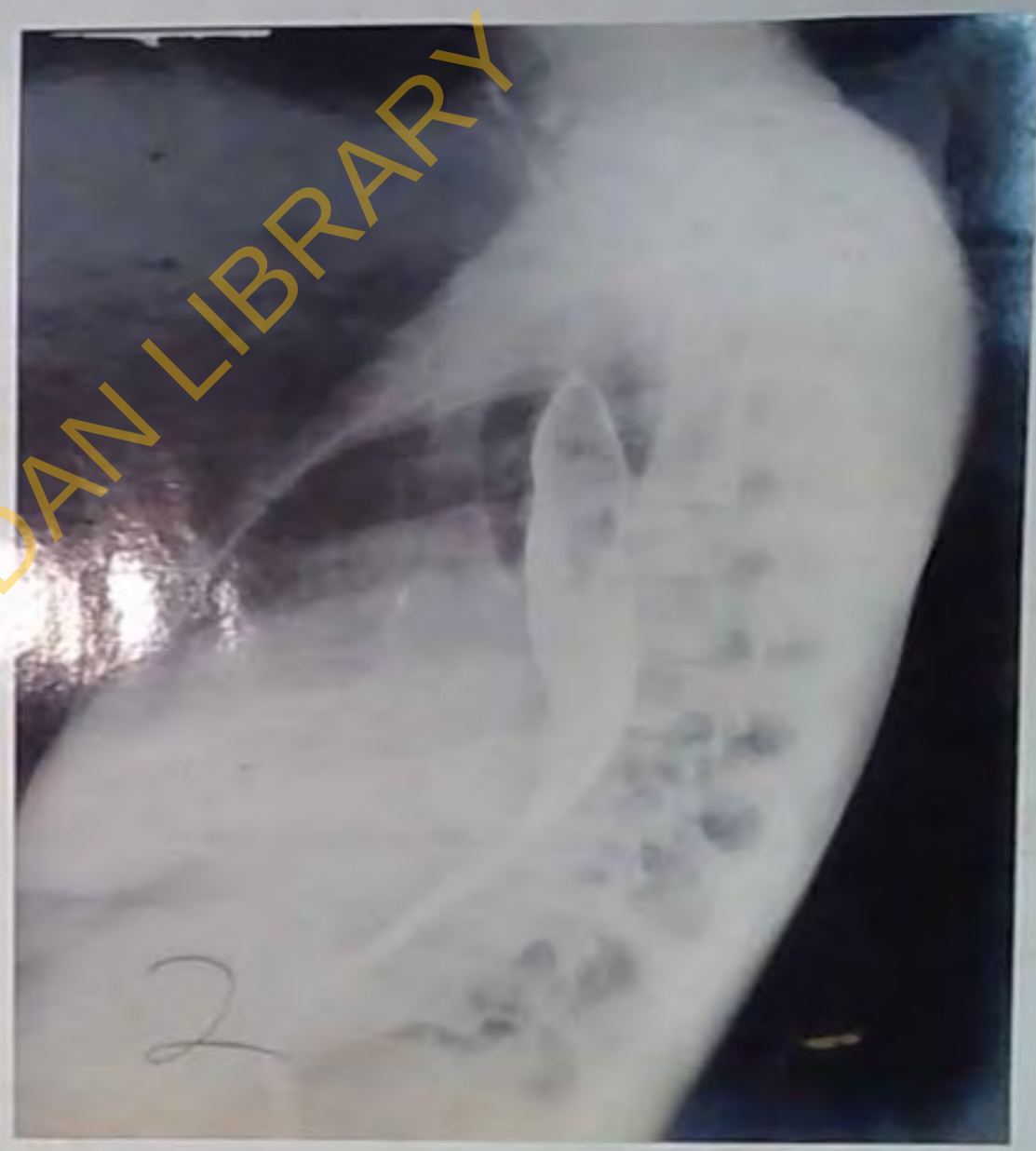
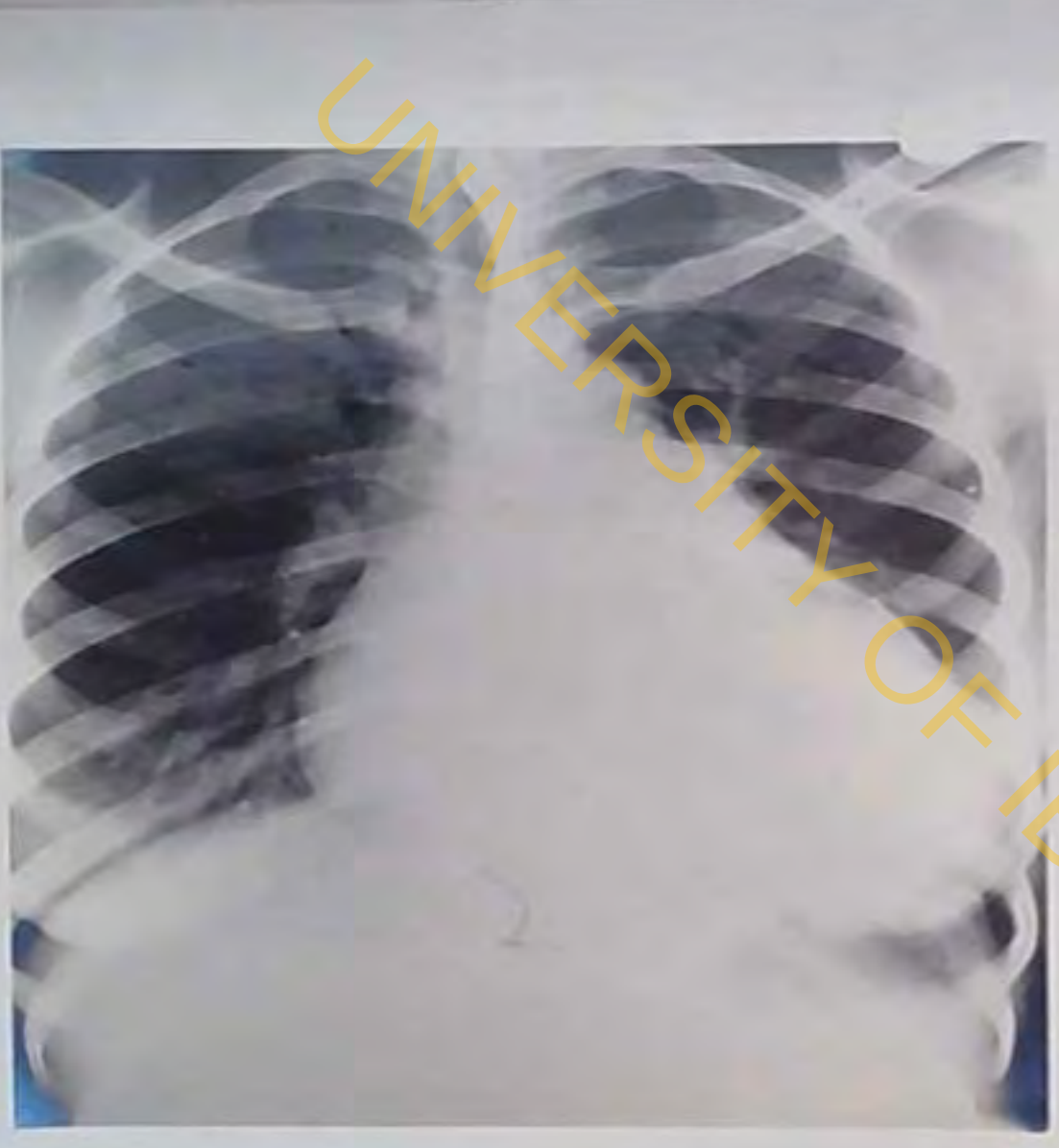


Fig. 6 Chest x-ray of a patient with heart muscle disease with cardiomegaly especially of the left ventricle.



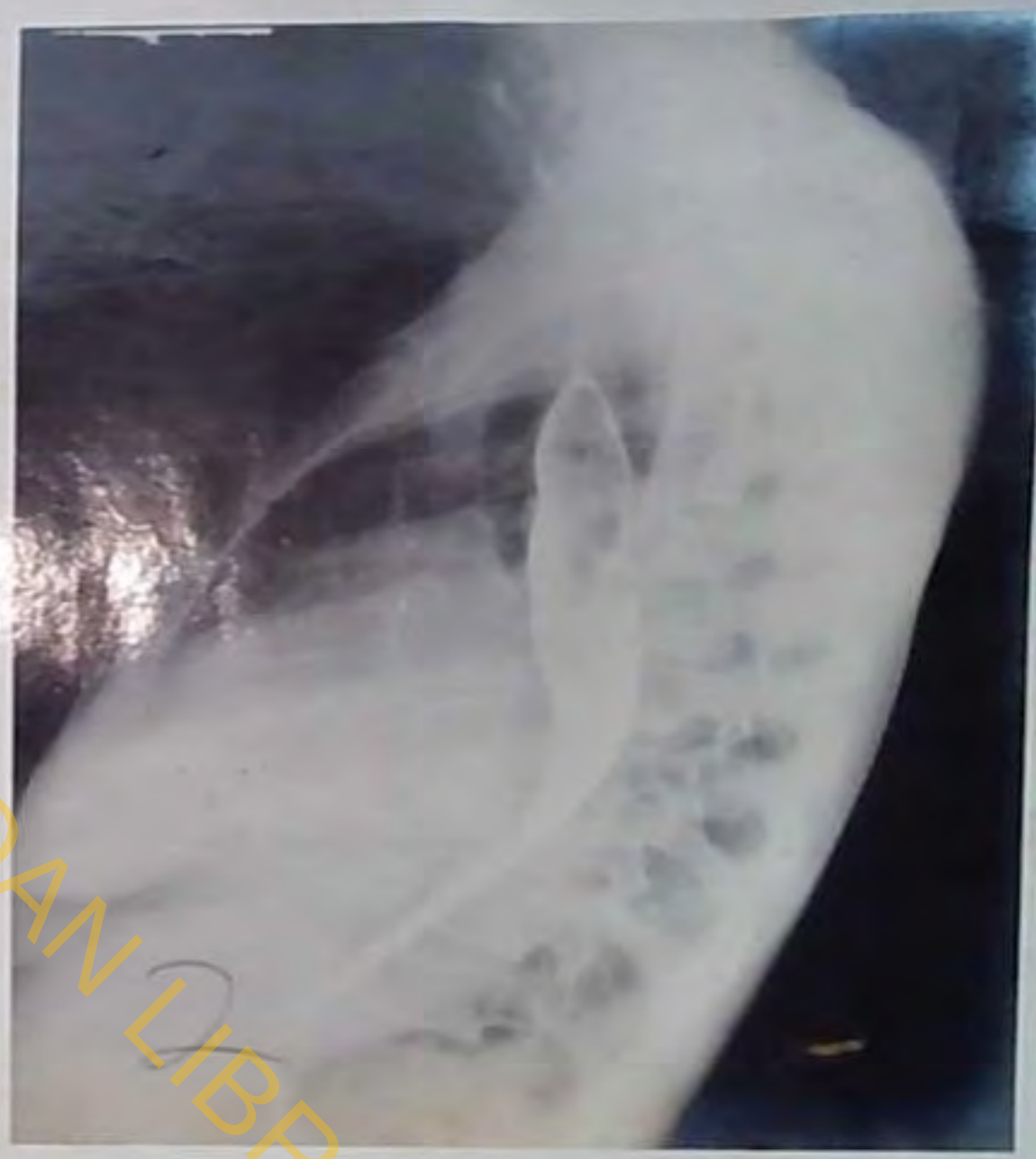


Fig. 6 Chest x-ray of a Patient with heart muscle disease with cardiomegaly especially of the left ventricle.

of patients in each group was not always comparable. Patients with organic MR were younger (mean age in years = 26.5 ± 7.6 (standard deviation)) than patients with HMD (mean age = 51.6 ± 13.1 years). The duration of symptoms in those patients with organic MR ranged between a month and six months (mean = 4 months) and was shorter than that of patients with HMD (range 2-84 months; mean 11 months).

An apical systolic thrill was not recorded in any of the patients with HMD and in the majority of them the first heart sound and murmurs were of soft quality. In a few patients, the murmurs were mid-systolic and localised to the apex. Conversely, the murmurs of patients with organic MR were louder and pansystolic with radiation to the axilla and occasionally to the back. 3 of them (50%) had apical systolic thrills.

9 patients with HMD who had normal heart sounds and loud murmurs had a mean systolic ejection fraction of 44.3 ± 21.6% (tables 4 and 5). This was significantly higher than the mean ejection fraction of those with soft heart sounds and murmurs (21.9 ± 15.3; $P < 0.01$). The systolic ejection fraction of patients with organic MR (62.4 ± 12.5) was not significantly higher than patients with HMD and normal heart sounds ($P > 0.05$) but was significantly higher than those with soft heart sounds and murmurs ($P < 0.01$).

TABLE 4

COMPARISON BETWEEN THE AUSCULTATORY FINDINGS IN PATIENTS WITH ORGANIC MITRAL INCOMPETENCE AND THEIR SYSTOLIC EJECTION FRACTION

PATIENT	Apical S_1	MR murmur	Character of murmur	Change with treatment	TI	EF
L. L.	Normal	+	Loud	None	-	67%
G. K.	Normal	+	Loud	None	-	77.2%
K. O.	Normal	+	Loud	None	-	58.2%
Y. G.	Normal	+	Loud	None	+	42%
M. O.	Normal	+	Loud	None	-	58%
A. O.	Normal	+	Loud	None	-	72%

MR = Mitral incompetence; TI = tricuspid incompetence

EF = Systolic ejection fraction

TABLE 5

Comparison Between the Auscultatory Findings in Patients With Heart Muscle Disease and their Systolic Ejection Fraction

	Aspical S_1	MI murmur	Character of murmur	Change with treatment	TI	EF
E. A.	Soft	+	Soft	None	-	20%
A. O.	Soft	+	Soft	Yes	+	27%
Y. M.	Soft	+	Soft	None	-	1.5%
H. T.	Normal	-	-	-	-	27.4%
M. A.	Soft	+	Soft	Yes	-	6.6%
S. L.	Soft	-	-	-	-	22.2%
D. O.	Soft	-	-	-	-	10.4%
A. A.	Normal	+	Loud	Yes	+	36%
S. M.	Normal	+	Loud	Yes	-	44.8%
L. A.	Soft	-	-	-	-	40.5%
J. O.	Normal	+	Loud	Yes	-	45.4%
S. O.	Normal	+	Loud	Yes	-	66.4%
J. U.	Soft	-	-	-	-	12.9%
R. E.	Soft	+	Soft	Yes	+	34.8%
A. Y.	Normal	+	Loud	Yes	-	51.4%
S. A.	Soft	+	Soft	Yes	-	14.7%
B. T.	Soft	+	Soft	None	-	16%
J. F.	Soft	+	Soft	None	-	15.8%
T. O.	Soft	-	-	-	-	12.2%
C. O.	Soft	+	Soft	None	+	34.7%
W. E.	Soft	-	-	-	-	41.4%
O. A.	Normal	+	Loud	None	-	9.7%
S. R.	Normal	+	Loud	Yes	-	83.7%
O. O.	Normal	-	-	-	-	34.4%
T. L.	Soft	+	Soft	None	+	57.0%
A. I.	Soft	+	Soft	None	-	3.8%

MI = Mitral incompetence TI = Tricuspid incompetence

EF = Systolic ejection fraction

One of the criteria for distinguishing between organic MR and HMD is the disappearance of the murmurs with improvement of heart failure (Parry, 1968; Fowler, 1972). The murmurs of patients with HMD diminish and disappear with treatment while those of patients with organic MR persist. In this study, the murmurs of all the patients with organic MR persisted but only those of 17 out of 27 patients with HMD disappeared. The mean systolic ejection fraction of those patients with HMD whose murmurs disappeared (41.08 $\pm$ 22.96) was significantly higher than that of patients whose murmurs persisted (19.8 $\pm$ 18.2; $P<0.05$) implying that murmurs of patients with very poor myocardial function may not disappear even with improvement clinically in their heart failure.

One patient (W.E., table 2) with no murmurs had mitral incompetence on left ventricular angiography while three patients (S.R., S.A. and S.O.; table 5) who had murmurs of mitral incompetence clinically had no incompetence on angiography. The latter were, however, investigated after their heart failure had improved by which time their murmurs had disappeared.

The left ventricular end-diastolic pressures of patients with HMD were higher than those with organic MR (tables 6 and 7). Patients with organic MR also did not have ECG

TABLE 6

AORTIC AND LEFT VENTRICULAR PRESSURES IN PATIENTS WITH ORGANIC MITRAL INCOMPETENCE

	Left Ventricle		Aorta	
	Systolic	End diastolic pressure	Systolic	Diastolic
L. L.	120	16	120	80
G. K.	95	10	95	60
A. O.	100	10	110	80
K. O.	100	6	100	60
Y. G.	140	32	135	82
H. O.	110	10	115	80

TABLE 7

AORTIC AND LEFT VENTRICULAR PRESSURES (mmHg) IN PATIENTS WITH HMD WHO HAD ANGIOGRAPHIC STUDIES

	LEFT VENTRICLE		AORTA	
	SYSTOLIC	END-DIASTOLIC PRESSURE	SYSTOLIC	DIASTOLIC
E. A.	150	35	150	80
A. O.	120	20	125	60
Y. M.	110	24	115	80
H. T.	200	20	200	100
M. A.	120	20	120	80
S. L.	95	30	100	65
D. O.	160	30	160	96
A. A.	160	20	160	90
S. M.	140	18	140	80
L. A.	155	22	160	95
J. O.	130	25	140	80
S. O.	150	15	160	95
J. U.	150	20	162	98
R. E.	140	25	150	90
A. Y.	135	20	140	90
S. A.	110	23	110	60
B. T.	100	16	100	70
J. F.	95	20	95	60
T. O.	95	25	100	60
C. O.	160	56	160	85
W. E.	130	20	120	80
O. A.	150	20	120	60
S. R.	140	6	130	80
O. O.	100	20	100	60
T. L.	110	20	110	80
A. I.	90	40	95	60

evidence of severe myocardial damage such as intraventricular conduction defects, fascicular blocks and ventricular arrhythmias, compared with patients with HMD (tables 41-43).

HYPERTENSION:

The blood pressures of all the 50 patients were analysed for comparison since they received similar treatment during their admission and subsequent follow-up.

Presenting blood pressure: 24 of the 50 patients (Group A) presented with diastolic blood pressures below 90 mmHg. The remaining 26 patients (Group B) presented with diastolic blood pressures between 90 mmHg and 100 mmHg. Their presenting systolic pressures are shown in table 8.

Clinical Course:-

Group A: 17 of 18 of these patients (Groups A1 and A2; tables 9 and 10) remained normotensive and out of heart failure on digoxin and frusemide both as in-patients and out-patients. One died in hospital. The six patients with organic mitral incompetence made up the patients in group A1 while patients in group A2 had HMD.

The remaining 6 patients in group A (group A3; table 11) responded similarly on admission to digitalisation and frusemide but relapsed on these drugs into congestive cardiac failure with elevated blood pressures as out-patients. They subsequently improved when their diuretics

TABLE 8

PRESENTING SYSTOLIC PRESSURES IN THE 50 PATIENTS

SYSTOLIC BLOOD PRESSURE (mmHg)	NUMBER OF PATIENTS
100 mmHg (13.2 kPa) and below	4
101 - 110 mmHg (13.5-14.5 kPa)	11
111 - 120 mmHg (14.7-16 kPa)	8
121 - 130 mmHg (16.2-17.3 kPa)	16
131 - 140 mmHg (17.6-18.9 kPa)	7
141 - 150 mmHg (19.1-20 kPa)	1
151 - 160 mmHg (20.2-21.5 kPa)	3

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101 - 110 mmHg (13.5-14.5 kPa)	11
111 - 120 mmHg (14.7-16 kPa)	8
121 - 130 mmHg (16.2-17.3 kPa)	16
131 - 140 mmHg (17.6-18.9 kPa)	7
141 - 150 mmHg (19.1-20 kPa)	1
151 - 160 mmHg (20.2-21.5 kPa)	3

TABLE 9

SUMMARY OF THE CLINICAL COURSE OF PATIENTS IN GROUP A1. THEY WERE ON DIGOXIN AND FRUSEMIDE AS IN-PATIENTS AND AT THEIR FIRST VISIT AS OUT-PATIENTS

PATIENT	NO.	FINDINGS AT ADMISSION				IN-PATIENT FINDINGS JUST BEFORE DISCHARGE				FIRST VISIT AS OUT-PATIENT				REMARKS
		CCF	Apical PSM	3rd Sound	B.P. (mmHg)	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	
Y. G.	1	+	+	+	120/80	-	+	+	110/70	-	+	+	120/80	Hhd tricuspid incompetence also
L. L.	2	+	+	+	130/80	-	+	+	120/75	-	+	+	120/70	
O. K.	3	+	+	+	125/85	-	+	+	110/70	-	+	+	120/70	
A. O.	4	+	+	+	90/70	-	+	+	100/75	-	+	+	100/60	
K. O.	5	+	+	+	110/85	-	+	+	120/80	-	+	+	120/80	
M. O.	6	+	+	+	95/60	-	+	+	100/60	-	+	+	100/60	

CCF = Congestive Cardiac Failure. PSM = Pansystolic murmur. B.P. = Blood Pressure

TABLE 10

Summary of the olinical course of the patients in group A2. They were on digoxin and frusenide as in-patients and at their first visit as out-patients

Patient	No.	FINDINGS AT ADMISSION				IN-PATIENT FINDINGS JUST BEFORE DISCHARGE				FIRST VISIT AS OUT-PATIENT				REMARKS
		Apical 3rd				Apical 3rd				Apical 3rd				
		CCF	PSM	Sound	B.P. (mm Hg)	CCF	PSM	Sound	B.P. (mm Hg)	CCF	PSM	Sound	B.P. (mm Hg)	
O. O.	7	+	-	+	120/80	-	-	+	120/80	-	-	+	100/60	Subsequently developed tricuspid incompetence
W. E.	8	+	-	+	110/70	-	-	-	110/70	-	-	-	120/75	
J. F.	9	+	+	+	90/55	-	-	+	100/60	-	+	+	100/60	
T. L.	10	+	+	+	130/80	-	+	+	125/85	-	+	+	120/80	Had tricuspid incompetence also
Y. A.	11	+	-	+	110/70	DIED IN HOSPITAL								
T. O.	12	+	-	+	120/80	-	-	-	100/60	-	-	-	110/70	
F. O.	13	+	-	+	110/80	-	-	-	130/85	-	-	-	120/80	
O. A.	14	+	+	+	120/85	-	+	+	120/80	-	+	+	110/70	
S. R.	15	+	+	+	110/70	-	-	+	110/80	-	-	+	120/75	
A. I.	16	+	+	+	100/70	-	+	+	110/75	-	+	+	110/70	Later developed tricuspid incompetence
C. O.	17	+	+	+	110/65	-	+	+	110/60	-	+	+	110/75	Had tricuspid incompetence also
E. L.	18	+	+	+	130/70	-	+	+	110/70	-	+	+	120/80	Had tricuspid incompetence also

CCF = Congestive Cardiac Failure PSM = Pansystolic Murmur B.P. = Blood Pressure

TABLE 11

Summary of the Clinical Course of the Patients in Group A3. They Were on Digoxin and Frusemide as In-Patients and at Their First Visit as Out-Patients

PATIENT	No.	FINDINGS AT ADMISSION				IN-PATIENT FINDINGS JUST BEFORE DISCHARGE				FIRST VISIT AS OUT-PATIENT				REMARKS
		Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	
A. O.	19	+	+	+	105/70	-	-	-	110/80	+	+	+	130/100	Improved on thiazides
J. A.	20	+	+	+	110/70	-	-	-	100/80	+	-	+	140/105	Improved on thiazides
E. A.	21	+	+	+	140/80	-	-	-	130/80	+	-	+	160/100	Improved on thiazides
A. O.	22	+	+	+	120/85	-	-	-	120/75	+	-	+	150/110	Improved on alpha methyl dopa and thiazides
B. T.	23	+	+	+	120/80	-	-	-	120/80	+	+	+	130/115	Improved on thiazides
A. O.	24	+	+	+	110/80	-	-	+	100/80	+	+	+	130/100	Improved on thiazides Had tricuspid incompetence also

CCF = Congestive Cardiac Failure. PSM = Pansystolic Murmur. B.P. = Blood Pressure

were changed to thiazides. One of them (case 22) required in addition alpha methyl dopa to keep him out of heart failure.

Group B: 20 (Group B1; table 12) of the patients in this group improved on digitalisation and frusemide as inpatients. Their diastolic blood pressures returned to normal within a week. However, on discharge from hospital and on the same dose of drugs as at discharge, they relapsed into heart failure with elevated blood pressures. 14 of the 20 patients subsequently improved when their diuretics were changed to thiazides. The remaining six patients required in addition to thiazides alpha methyl dopa to improve their heart failure. These six patients subsequently remained well on these drugs without added digoxin. The following are three illustrative case reports.

CASE 32: (Fig. 7). A 45 year old woman was admitted in congestive cardiac failure with a blood pressure of 145/100 mmHg. She had no murmurs but had a loud third sound and a loud pulmonary closure sound. Her ECG showed sinus tachycardia, left atrial enlargement and left anterior hemiblock. Her chest x-ray showed marked cardiomegaly with engorgement of the pulmonary vessels.
She was initially treated with digoxin, frusemide 80mg daily, bed rest and low salt diet. She improved considerably

TABLE 12

Summary of the clinical course of the patients in group B1. They were on the same dose of digoxin and Frusemide as in-patients and as out-patients.

PATIENT	No.	FINDINGS AT ADMISSION				IN-PATIENT FINDINGS JUST BEFORE DISCHARGE				FIRST VISIT AS OUT-PATIENT				REMARKS
		Apical 3rd			B.P. (mm Hg)	Apical 3rd			B.P. (mm Hg)	Apical 3rd			B.P. (mm Hg)	
		CCF	PSM	Sound		CCF	PSM	Sound		CCF	PSM	Sound		
T.M.	25	+	+	+	135/90	-	+	+	110/80	+	+	+	120/100	Improved on thiazides
M.A.	26	+	+	+	130/90	-	-	-	110/70	+	+	+	150/105	Improved on thiazides
O.O.	27	+	-	+	130/95	-	-	-	120/80	+	-	+	140/100	Improved on thiazides
B.F.	28	+	+	+	160/90	-	-	-	120/80	+	+	+	170/100	Improved on thiazides
S.L.	29	+	-	+	110/90	-	-	-	100/70	+	-	+	130/100	Improved on thiazides
M.A.	30	+	+	+	130/90	-	-	-	115/75	+	-	+	170/100	Improved on thiazides
K.B.	31	+	+	+	130/90	-	-	-	110/80	+	+	+	150/95	Improved on thiazides Had tricuspid incompetence also
B.S.	32	+	-	+	145/100	-	-	-	120/80	+	+	+	140/105	Improved on alpha methyl dopa and thiazide
S.M.	33	+	+	+	125/100	-	+	+	120/80	+	+	+	140/105	Improved on alpha methyl dopa and thiazides
L.A.	34	+	-	+	140/100	-	-	-	120/70	+	-	+	140/105	Improved on thiazides
J.O.	35	+	+	+	110/100	-	-	-	130/90	+	+	+	140/100	Improved on thiazides and alpha methyl dopa
B.O.	36	+	+	+	135/100	-	-	-	120/70	+	-	+	210/110	Improved on alpha methyl dopa and thiazides
J.B.	37	+	-	+	140/100	-	-	+	120/80	+	-	+	150/110	Improved on alpha methyl dopa and thiazides
B.O.	38	+	-	+	120/100	-	-	-	105/85	+	+	+	120/100	Improved on thiazides
O.O.	39	+	-	+	120/100	-	-	-	105/80	-	-	+	135/105	Improved on alpha methyl dopa and thiazides
J.U.	40	+	-	+	160/100	-	-	-	150/80	+	-	+	170/100	Improved on thiazides
B.E.	41	+	-	+	140/100	-	-	-	120/70	+	-	+	170/105	Improved on thiazides
E.E.	42	+	+	+	130/100	-	-	+	100/60	+	+	+	170/95	Improved on thiazides Had tricuspid incompetence in addition
L.O.	43	+	+	+	130/90	-	-	+	120/80	+	+	+	140/100	Improved on thiazides Had tricuspid incompetence also
S.A.	44	+	+	+	170/100	-	-	+	130/80	+	+	+	140/110	Improved on thiazides

CCF = Congestive cardiac failure. PSM = Pansystolic murmur. B.P. = Blood pressure.

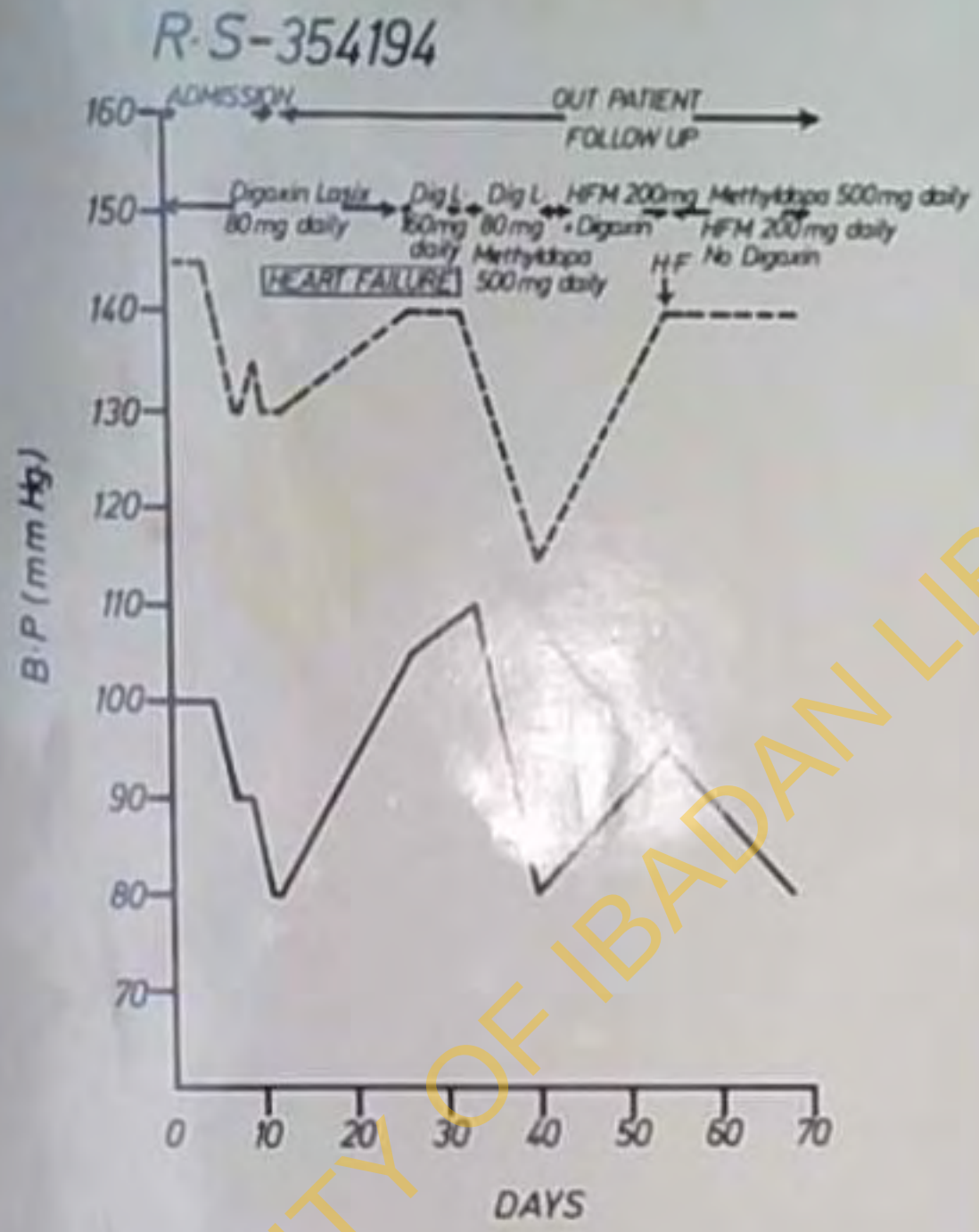


Fig. 7 Clinical course of case 32.

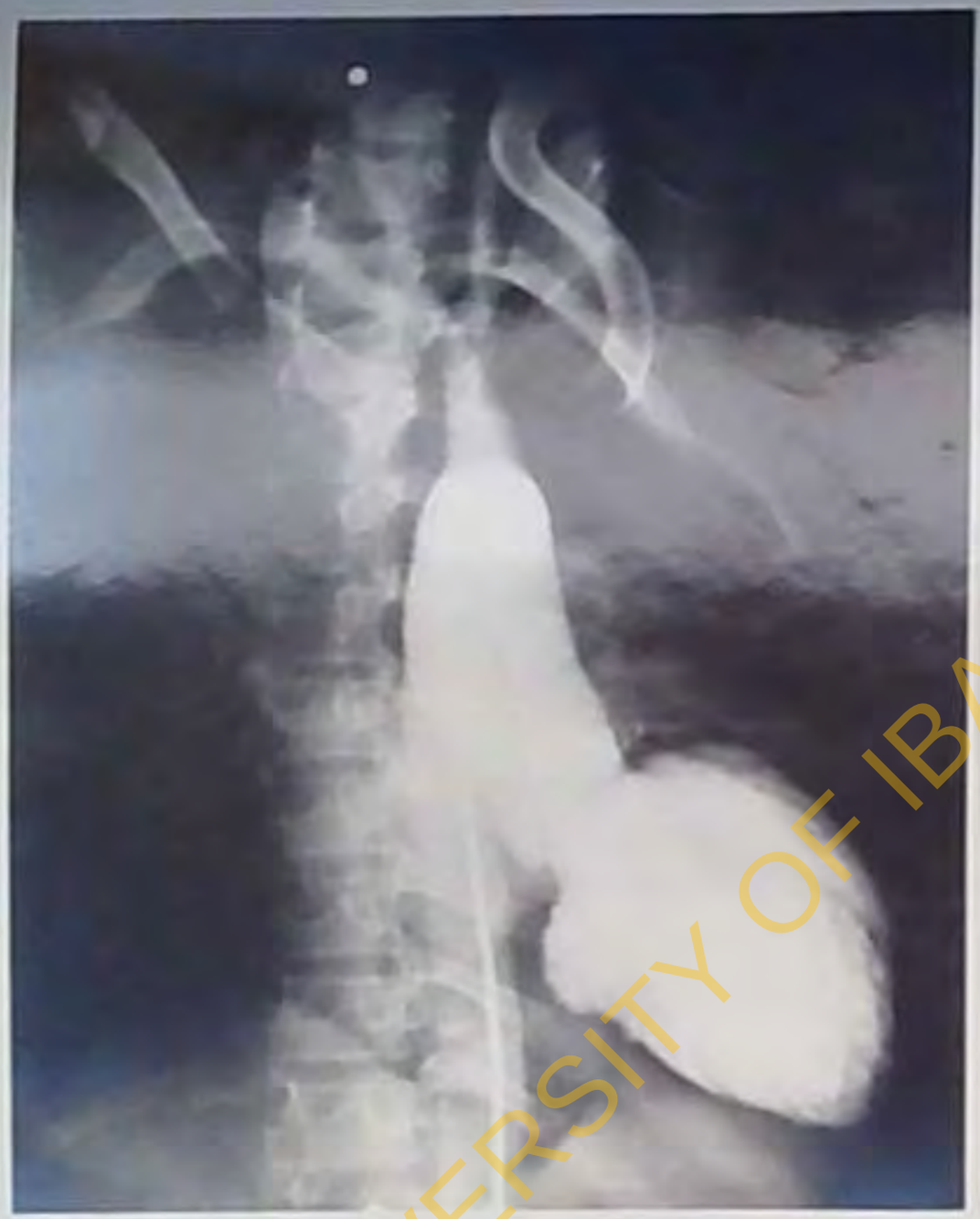
on these and at the time of discharge 10 days afterwards she was completely out of failure and nc third sound was audible. Her blood pressure showed a slow fall, over a period of one week, to a value of 130/80 mmHg.

She was seen at the out-patient clinic two weeks later. Although she claimed to be taking her drugs as at discharge, she was back in congestive cardiac failure. Her jugular venous pressure (JVP) was raised 6cm and had a prominent 'a' wave. Her blood pressure was 140/105 mmHg. A soft mid-systolic murmur thought to be due to mitral incompetence was heard at the apex and she had a loud third sound. Her frusemide was then increased to 160mg daily and she was seen one week afterwards. She was still in heart failure and her blood pressure had risen to 140/110 mmHg. Alpha methyl-dopa 500mg daily was then added to her drugs and the dose of her frusemide dropped to 80mg daily. When she was seen a week after, she had improved considerably. She was not in heart failure, her blood pressure was 110/80 mmHg. She had no murmurs and no third sound. She has since been kept well on alpha methyl-dopa 500mg daily and hydroflumethiazide (HFM) 200mg daily with no added digoxin. She has been followed up for a period of three years with no symptoms. At a stage during her follow-up, however, she ran out of drugs

for two weeks before her out-patient appointment was due and came back in congestive cardiac failure and a blood pressure of 170/110 mmHg. She responded promptly to methyl-dopa and thiazides.

CASE 33: A 40 year old woman admitted in severe congestive cardiac failure with a blood pressure of 125/100 mmHg and a murmur of mitral incompetence. A loud third heart sound was also audible at the apex. Her chest x-ray showed gross cardiomegaly and pulmonary venous congestion (fig. 6). Her ECG showed sinus tachycardia and left ventricular hypertrophy. Her left ventricular angiogram showed an enlarged poorly contractile left ventricle (fig. 8). She improved on digoxin and frusemide 80mg daily. Her blood pressure dropped to 120/80 mmHg within a week. At the time of discharge two weeks after, she was out of heart failure although a faint mid-systolic murmur together with a soft third sound, could be heard at the apex.

When seen two weeks later at the out-patient clinic, her congestive cardiac failure had recurred. Her blood pressure was 140/105 mmHg; her pulse was 90 per minute. Hydroflumethiazide 200mg daily was substituted for her frusemide, but she remained in congestive cardiac failure for a week by which time her blood pressure was 140/110 mmHg. Alpha methyl-dopa 500mg daily was then added to her



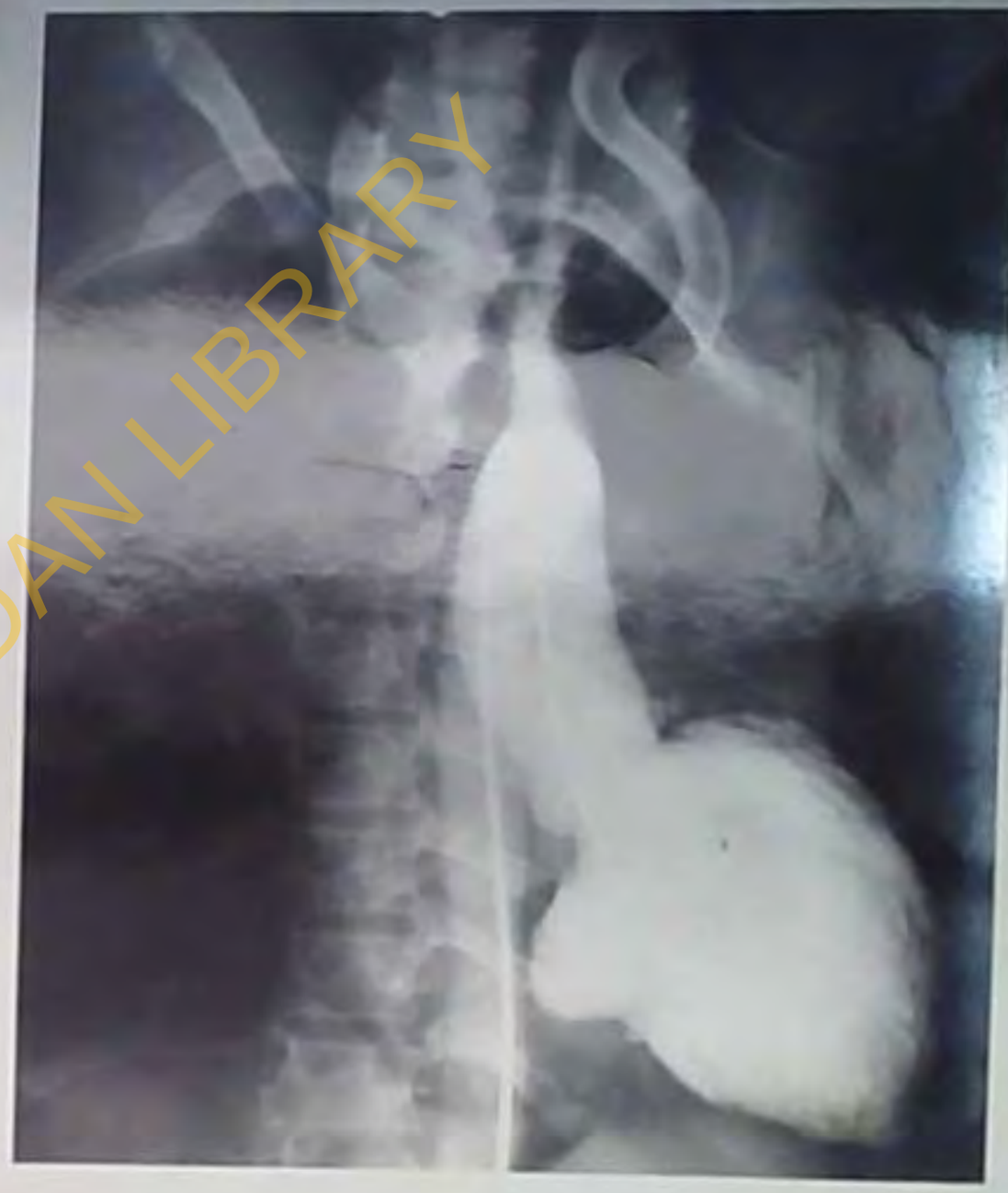
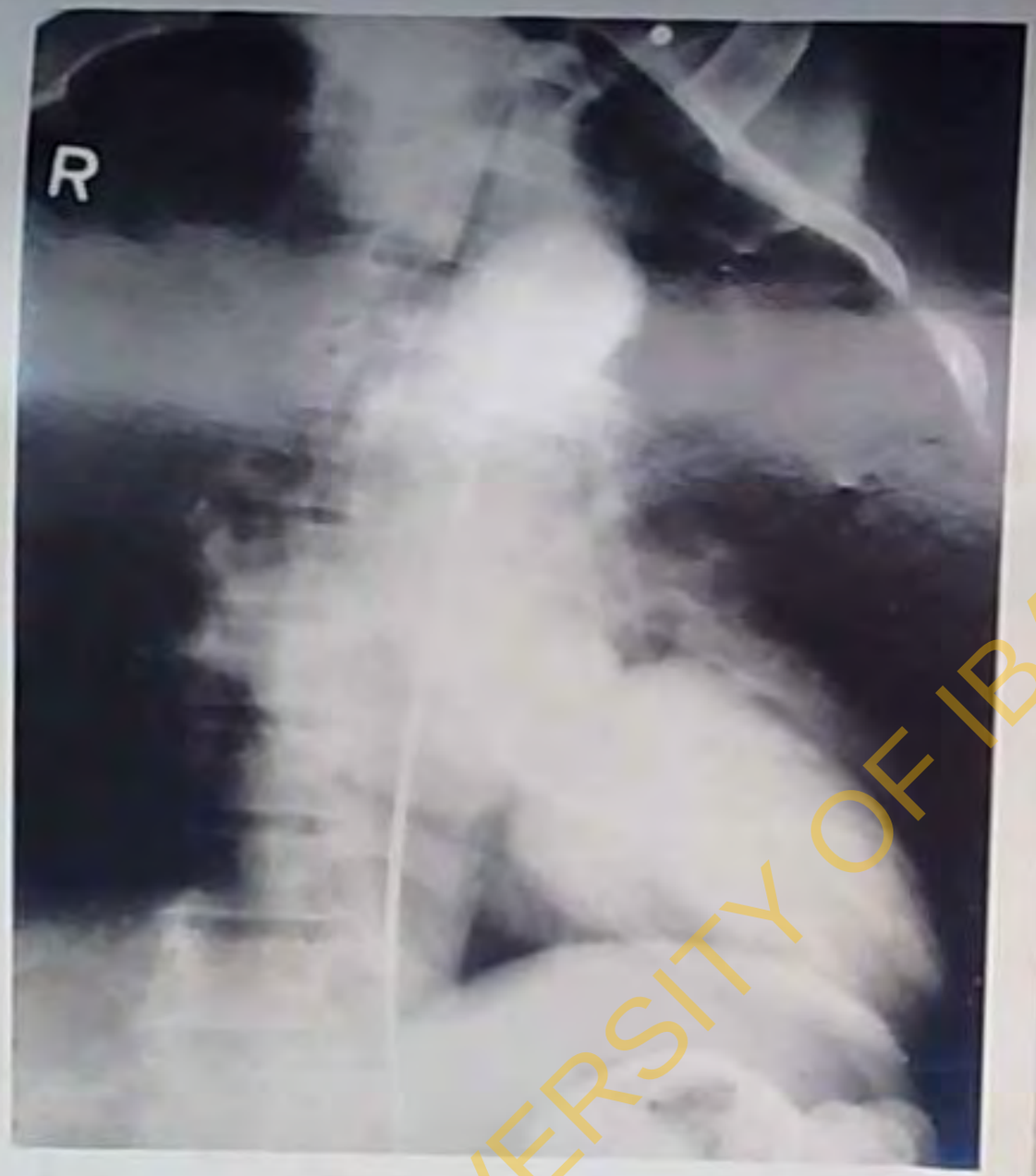


Fig. 8 Case 33. Left ventricular angiogram during systole (A) and diastole (B) showing a dilated, poorly contractile left ventricle. There is a submitral ventricular aneurysm.

therapy; a week later she was out of heart failure. Her blood pressure was 120/90 mmHg lying and 120/85 mmHg standing, she had no murmurs but a third sound could be heard. Her digoxin was discontinued but she was kept on methyl-dopa and HFM. She is well 2 years after her first presentation with a blood pressure of 140/90 mmHg.

A fourth sound could still be heard, her aortic closure sound was loud but no third sound could be heard. There is at present also no clinical evidence of mitral incompetence.

CASE 35: Was a 60 year old man who was admitted in severe congestive cardiac failure with a blood pressure of 110/100 mmHg. He was very ill with a small volume pulse and cold extremeties. At the apex could be heard a loud third heart sound and a pansystolic murmur which radiated to the axilla. His chest x-ray showed an enlarged heart; subsequent angiography showed dilated, poorly-contractile left ventricle (fig. 9). He improved within 5 days of admission and on digoxin, frusemide 80mg daily, low salt diet and bed rest. His third sound disappeared and the pansystolic murmur was no more audible. Six days after admission, he had a cerebrovascular accident which was thought to be embolic. His blood pressure was 100/65 mmHg. His frusemide was stopped and he was left on digoxin alone.



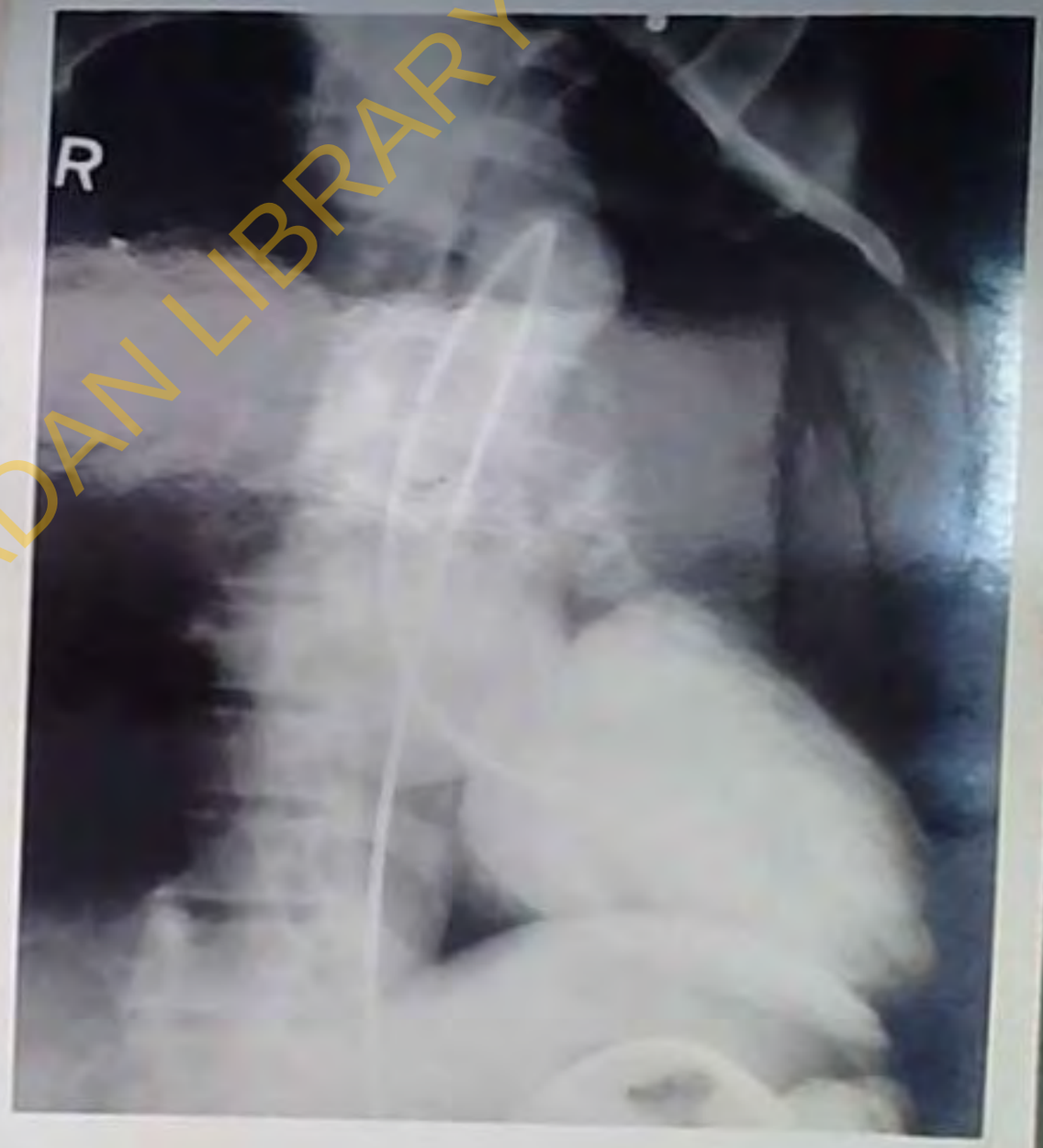


Fig. 9: Case 35. Left ventricular angiogram during systole (A) and diastole (B) showing a dilated, poorly contractile left ventricle. There is also mitral incompetence.

He recovered but within two weeks his blood pressure rose to a value of 140/100 mmHg. At this stage, a fourth sound was audible and a pansystolic murmur was heard at the apex. His aortic closure sound was also loud. He improved on HFM 200mg daily; his blood pressure came down to 130/90mmHg. At the time of discharge no murmur could be heard. A fourth sound was however still audible.

He remained well as an out-patient with a normal blood pressure for three months, following which his diuretic was changed to frusemide 80mg daily due to inavailability of HFM in the hospital. When he was seen three weeks after, he complained of exertional dyspnoea. On examination he was in mild congestive cardiac failure with a blood pressure of 140/100 mmHg.

He had an apical fourth sound and loud A2 and P2. He subsequently improved on hydrochlorothiazide 200mg daily. His blood pressure came down to 140/70 mmHg, he had no murmurs and no third sound was audible. He has since been followed up for almost 2 years.

The remaining six patients (Group B2; table 13) in group B showed no response to digoxin and frusemide as in-patients. Their diastolic blood pressures remained persistently elevated throughout the period they were in heart failure. One of them improved when his diuretic was

TABLE 13

SUMMARY OF THE CLINICAL COURSE OF THE PATIENTS IN GROUP B2

PATIENT AND NUMBER	FINDINGS AT ADMISSION				IN-PATIENT TREATMENT 1				IN-PATIENT TREATMENT 2				OUT-PATIENT 3			
	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)	Apical 3rd CCF	PSM	Sound	B.P. (mm Hg)
A. Y. (45)	+	+	+	130/100	+	+	+	130/105	-	-	+	120/85	-	-	+	120/100
D. O. (46)	+	-	+	160/90	+	-	+	150/105	-	-	-	170/75	-	-	-	150/70
H. T. (47)	+	-	+	130/95	+	+	+	170/100	-	+	+	140/85	-	-	+	150/95
*A. A. (48)	+	+	+	140/100	+	-	-	140/110	-	-	-	110/75	-	-	-	150/80
A. G. (49)	+	+	+	130/100	+	+	+	130/115	-	-	-	110/80	-	-	-	120/80
A. B. (50)	+	-	+	130/100	+	-	-	140/105	-	-	-	110/80	-	-	-	130/85

1 = Response to digoxin and frusemide

2 = Response to thiazides (patient 45) or alpha methyl dopa and thiazides (remaining patients)

3 = Subsequent response as out-patients. Patients were on the same drugs as in 2.

CCF = Congestive cardiac failure.

PSM = Pansystolic murmur

B.P. = Blood pressure.

* Had tricuspid incompetence also.

changed to hydrochlorothiazide. The other five patients required alpha methyl dopa in addition to thiazide diuretics to improve their heart failure. The following is an illustrative case.

CASE 49. A 50 year old cattle dealer was admitted in severe congestive cardiac failure with mitral incompetence murmur and a loud third heart sound. His blood pressure was 130/100 mmHg. He had never had any chest pain. He was cyanosed and blood gases showed severe arterial desaturation. He had for the preceeding week been on digoxin and diuretics from his general practitioner. His ECG showed sinus rhythm, frequent ventricular ectopics and pathological q waves in leads II, III and aVF (fig. 10). His chest x-ray showed gross cardiomegaly with bilateral pleural effusion (fig. 11).

On admission, he was treated with digoxin, frusemide 80mg daily, bed rest and low salt diet with no improvement. Two days afterwards, his dyspnoea increased and his blood pressure was 125/95 mmHg. The dose of frusemide was increased to 240mg daily over the next two weeks. He became more dyspnoeic, confused and restless and had severe arterial desaturation despite continuous administration of oxygen by polymask. 20 days after admission, he had not improved, his blood pressure was by now 130/115 mmHg. Methyl-dopa 500mg daily was added and the dose of his frusemide dropped to

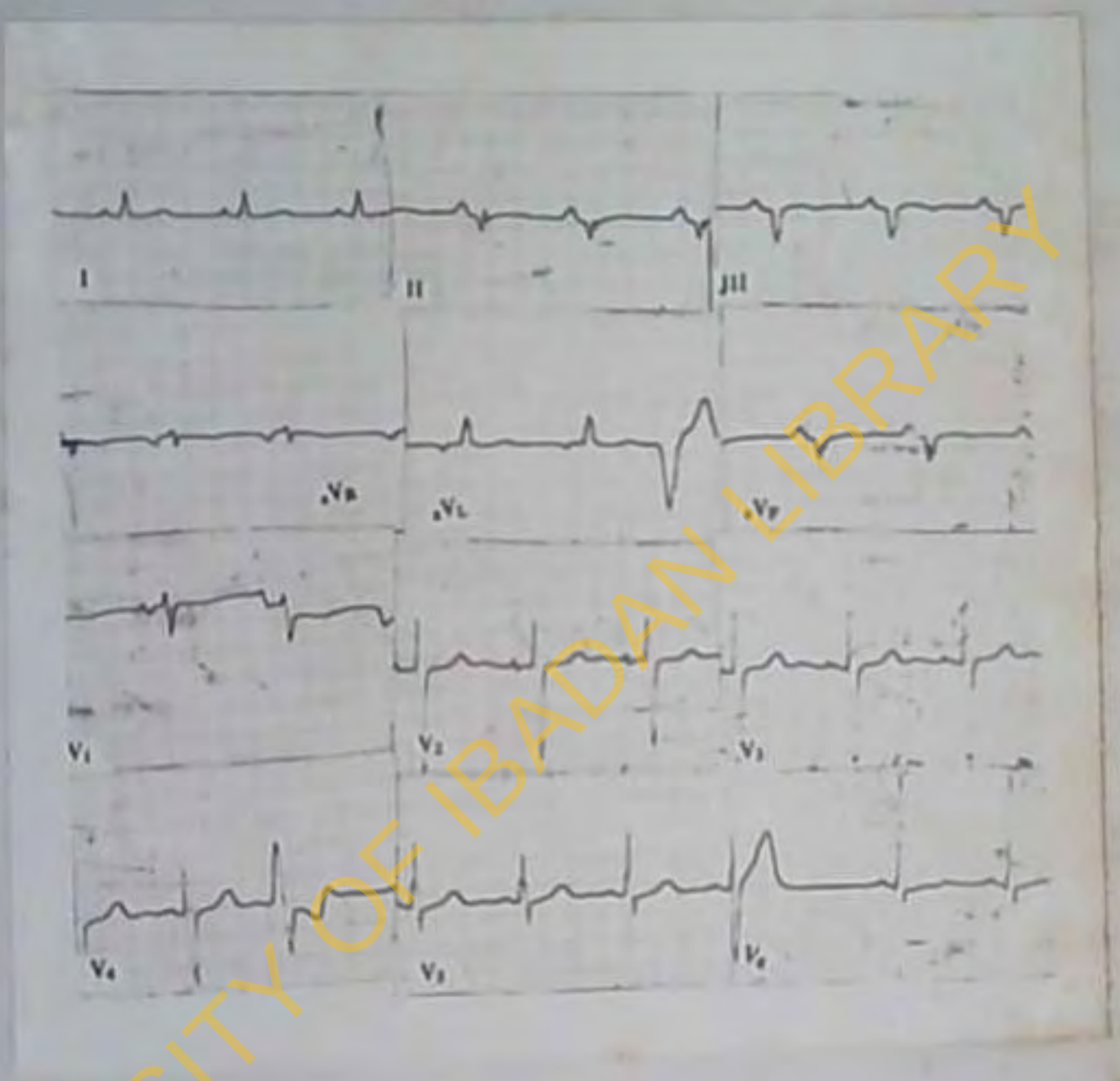


Fig. 10 The electrocardiogram of case 49 showing ventricular ectopics and pathological q waves in leads II, III and aVF.

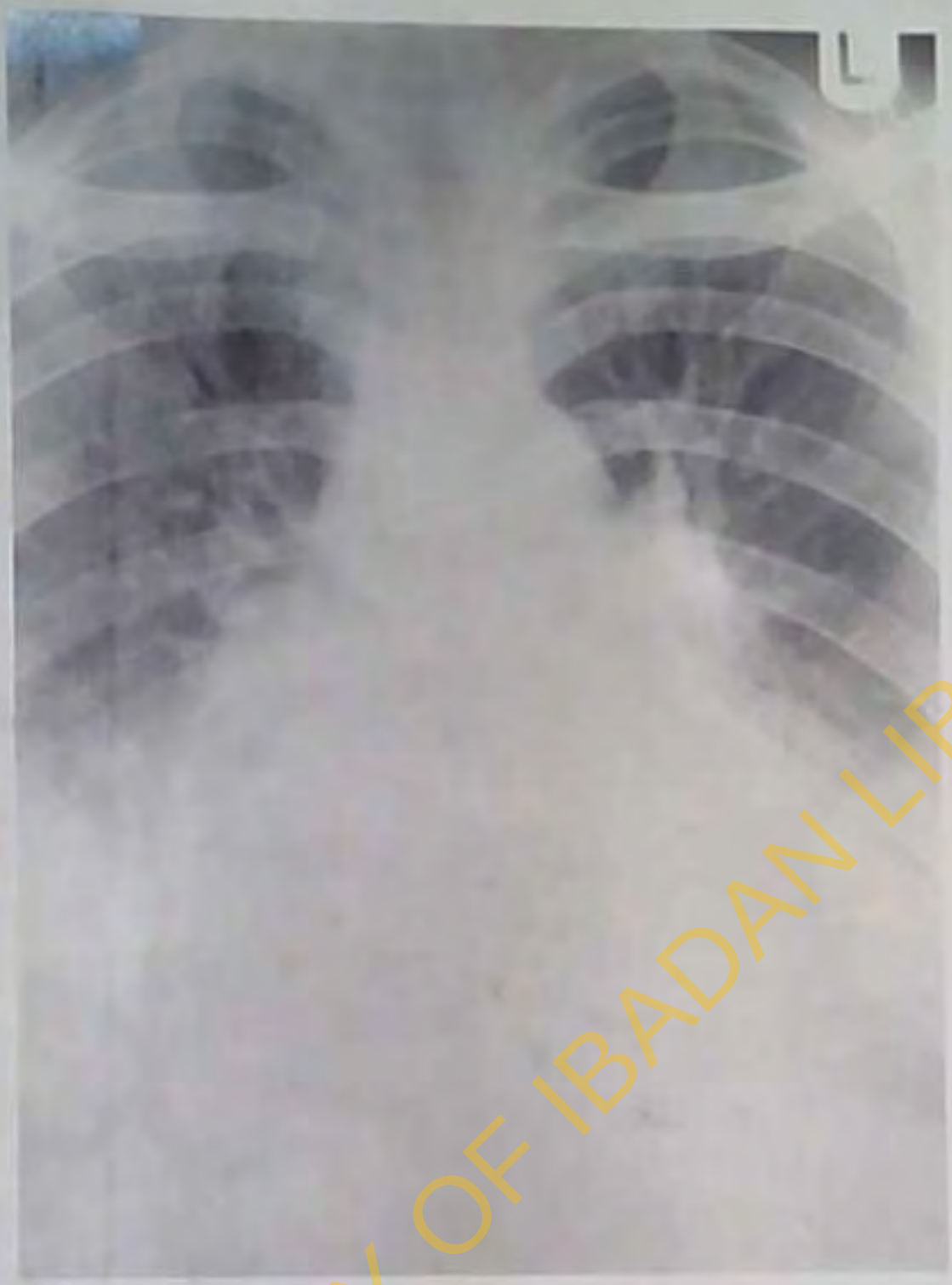


Fig. 11: The chest x-ray of case 49 showing cardiomegaly, bilateral basal congestions and pleural effusions.

80mg daily. Following this, he had a massive diuresis lasting one week. His blood pressure dropped to 110/80 mmHg. and his third heart sound subsequently disappeared. He has now been followed up for about 2 years. He remains out of heart failure on hydrochlorothiazide 100mg daily and alpha methyl-dopa 500mg daily without added digoxin.

PATIENTS OBSERVED ON DIGOXIN WITHOUT DIURETICS

Figures 12 and 13 show the behaviour of the blood pressures of 20 patients, who, after recovery, were readmitted to hospital and observed on digoxin alone with no salt restriction. 3 of them were from group A1 5 from group A2, 2 from group A3, 8 from group B1 and 2 from group B2. They had all previously been observed as in-patients, then discharged and observed for varying periods as out-patients before their readmission.

All the 20 patients had symptoms of heart failure between the fourth and the seventh day of readmission. The 8 patients in Groups A1 and A2 however had no prior rise in blood pressure before they had symptoms of heart failure (fig. 12). The remaining 12 patients on the other hand had an initial rise in blood pressure (fig. 13). The following is on illustrative case report.

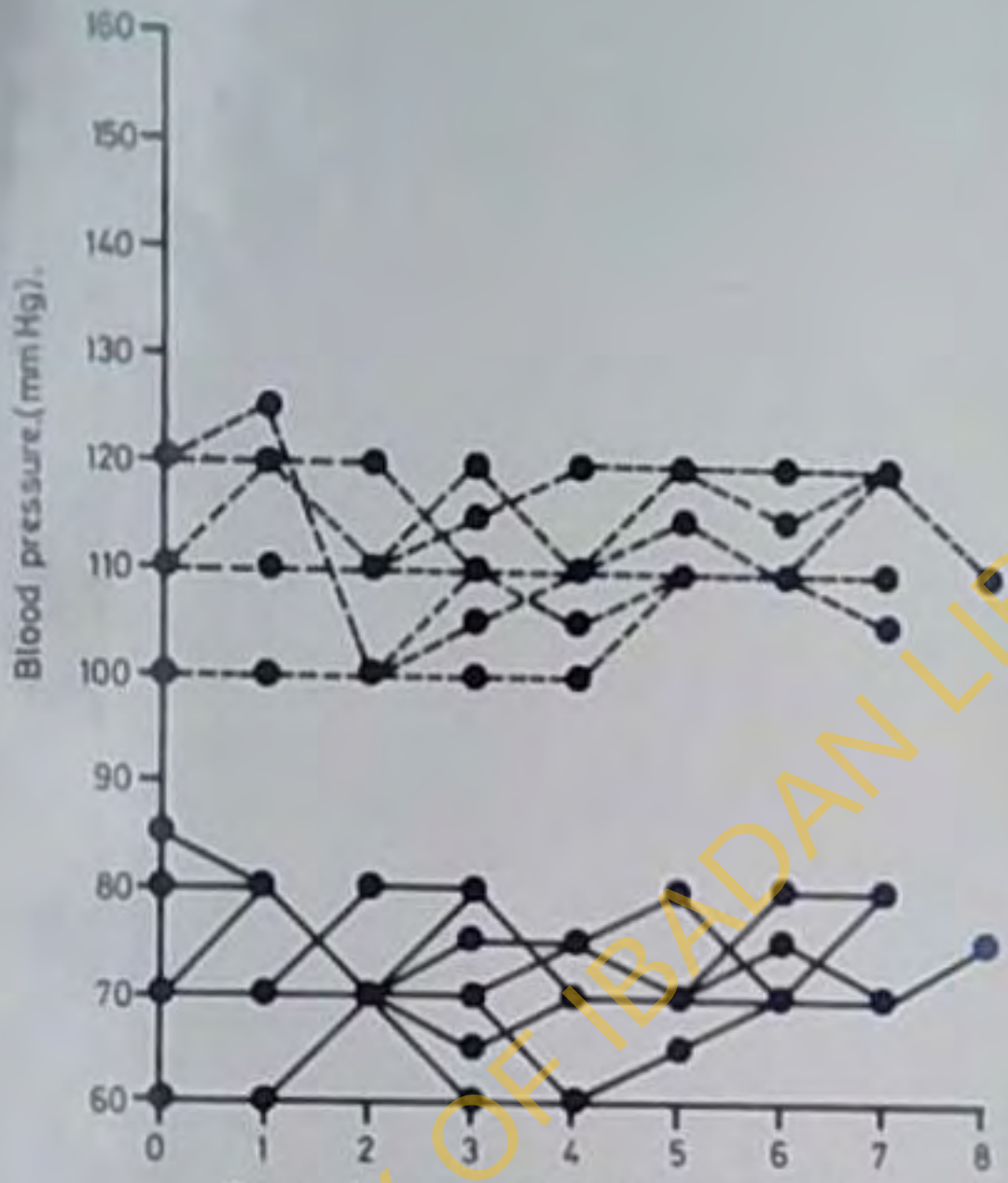


Fig. 12: The behaviour on admission of the blood pressures of the 8 patients in groups A1 and A2 to digoxin alone without diuretics or restricted salt intake.

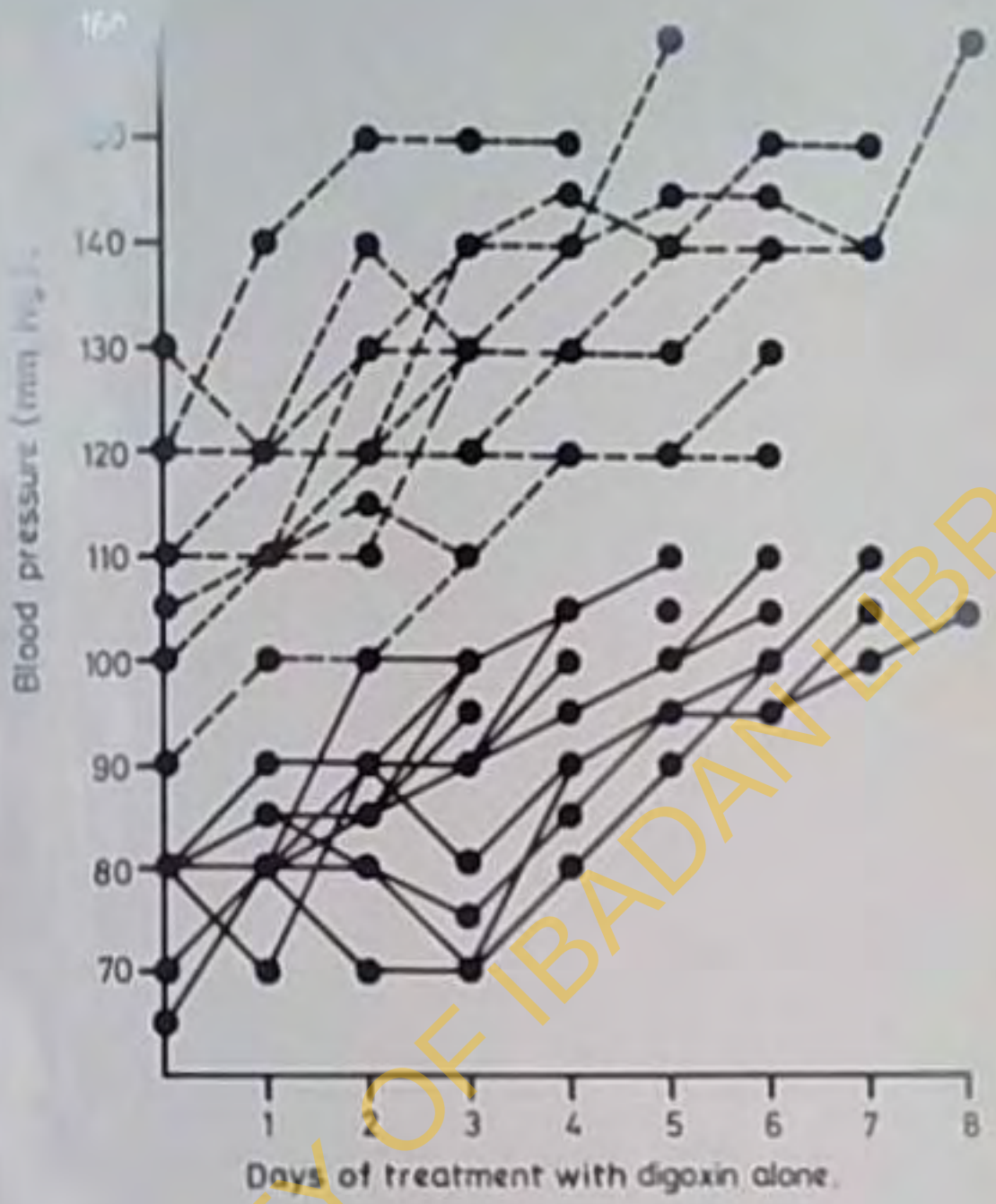


Fig. 13: The behaviour on admission of the blood pressures of the 12 patients in groups A3, B1 and B2 to digoxin alone without diuretics or restricted salt intake.

A woman of 50 years was admitted three months previousl in congestive cardiac failure with mitral incompetence and a loud third sound. Her blood pressure then was 140/100 mmH She subsequently improved on digoxin and hydrochlorothiazide (100 mg daily). At the time of her second admission, she was free of heart failure, her blood pressure was 120/80mmHg, she had no third heart sound and no apical systolic murmur (fig. 14). Her hydrochlorothiazide was then stopped and she was allowed liberal use of salt.

Three days later, her blood pressure was 120/95 mmHg, a fourth sound was heard at the apex together with a soft mid-systolic murmur. Two days after this, her blood pressure was 140/100 mmHg, her systolic murmur was louder and both third and fourth sounds were audible. 7 days after her diuretics were stopped, she complained of dyspnoea. Her blood pressure was 150/110 mmHg her JVP was raised and a loud third heart sound together with a mid-systolic murmur were heard at the apex. Her pulmonary closure sound was louder but she had no crepitations in the chest. She subsequently improved when hydrochlorothiazide (100 mg daily) was again commenced.

PREVIOUS TREATMENT BEFORE PRESENTATION

3 of the patients in group A1, 3 in group A2 and all the patients in group A3 had been put on digoxin and frusemide before they were seen in the clinic.

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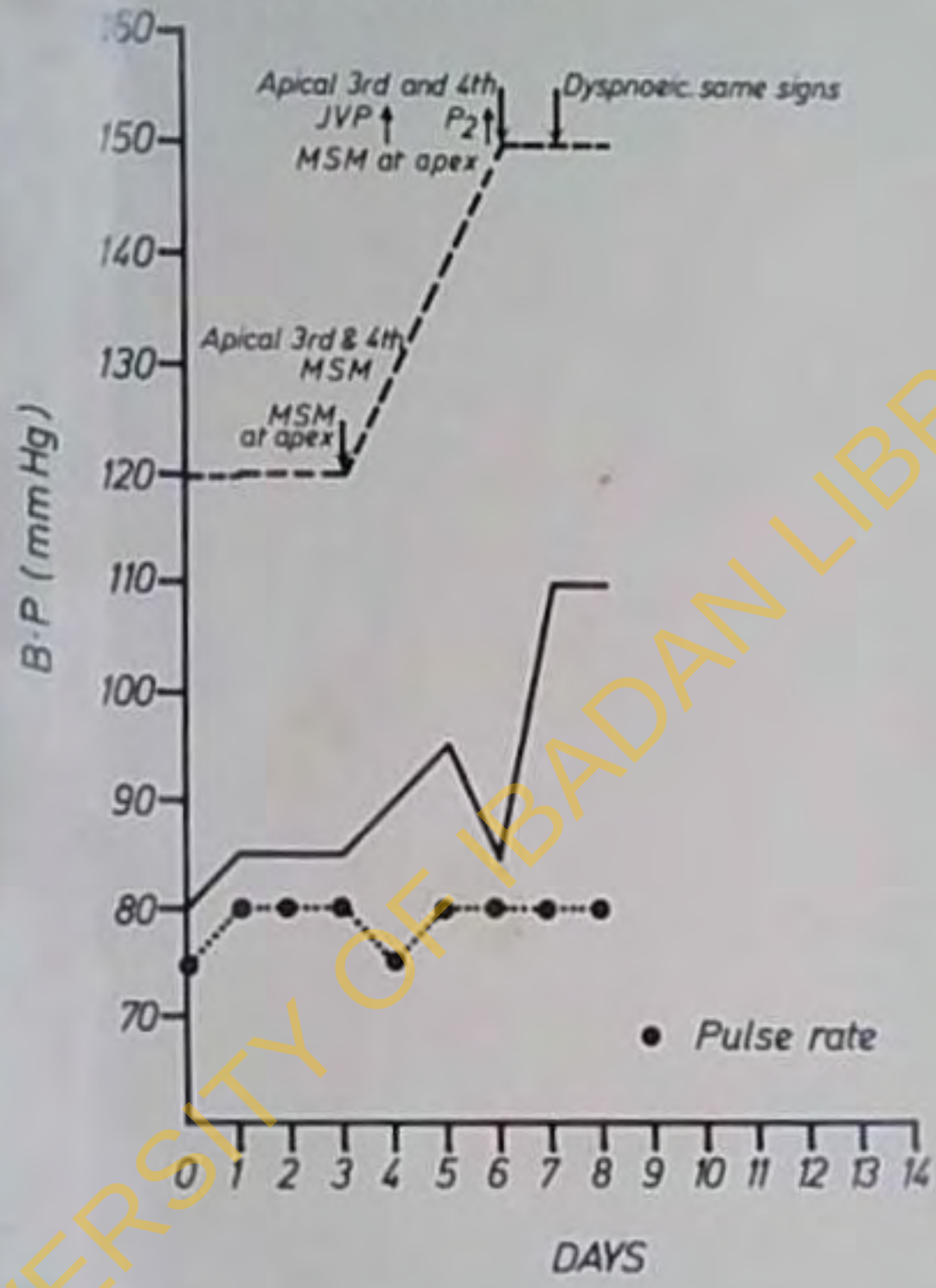

Fig. 14: The clinical course of case 22 on second admission to hospital. She was observed on digoxin alone without diuretics or restricted salt intake.

8 of the patients in group B1 similarly received treatment before they were seen in the clinic. 5 of these eight patients received frusemide while one patient had a combination of frusemide and HFM. The diuretics given to the remaining two patients were not specified.

LONG-TERM FOLLOW UP:

Group A1 (table 14). These patients remained out of heart failure and normotensive on digitalis and frusemide. Two follow ups were incomplete. One could not be traced while the other died at home.

Group A2 (table 15). These patients similarly remained normotensive and out of heart failure on digitalis and frusemide. Some of them, (cases 7, 12, 17, 18) however required increasingly larger doses of frusemide to keep them out of heart failure. In 4 patients, follow up was incomplete because 2 had died at home while the remaining 2 patients could not be traced.

3 other patients ran out of drugs before their clinic appointment. All the 3 patients relapsed into heart failure but remained normotensive (table 16).

One patient (A.I. case 16) died in hospital after she was readmitted in severe heart failure. A limited post-mortem examination showed a large, flabby heart with left ventricular endomural thrombosis. There were scattered

TABLE 14

Summary of the Medium Term/Long-term Follow-up of Patients in Group A1

		3 Months					6 Months					9 Months					12 Months					18 Months					24 Months					36 Months				
PATIENT	No.	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx
T.O.	1	-	+	+	110/70	1,4	-	+	+	115/70	1,4	-	+	+	110/70	1,4	+	+	+	115/75	-	+	+	+	110/80	-	-	+	+	115/65	1,4	-	+	+	120/70	1,4
L.L.	2	-	+	+	110/60	1,4	-	+	+	110/65	1,4	-	+	+	105/60	1,4	-	+	+	100/75	1,4	-	+	+	130/75	1,4	-	+	+	100/70	1,4	-	+	+	100/70	1,4
S.E.	3	-	+	+	140/85	1,4	-	+	+	125/80	1,4	-	+	+	120/80	1,4	-	+	+	100/80	1,4	-	+	+	140/90	1,4	-	+	+	130/70	1,4	-	+	+	130/80	1,4
A.O.	4	-	+	+	95/60	1,4	-	+	+	100/60	1,4	DIED	AT	HOME	NOT	TRACED																			
E.O.	5	-	+	+	120/80	1,4	-	+	+	120/80	1,4	-	+	+	120/85	1,4	-	+	+	115/70	1,4	-	+	+	120/80	1,4	-	+	+	120/80	1,4	DIED	AT	HOME		
E.O.	6	-	+	+	100/80	1,4	-	+	+	105/60	1,4	-	+	+	100/65	1,4	-	+	+	105/60	1,4	-	+	+	120/80	1,4	-	+	+	100/65	1,4					

1 = Digoxin
2 = Thiazide
3 = Methyl dopa
4 = Frusemide

CCF = Congestive Cardiac Failure.
PSM = Pansystolic Murmur.
B.P. = Blood Pressure.

TABLE 15

Summary of the Medium Term/Long-term Follow-up of Patients in Group A2

		3 Months					6 Months					9 Months					12 Months					18 Months					24 Months					36 Months				
PATIENT	No.	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx
O.O.	7	-	-	+	120/80	1,4	-	-	+	100/70	1,4	-	-	+	110/85	1,4	-	-	+	100/80	1,4	-	-	+	130/70	1,4										
K.A.	8	-	-	-	120/80	1,4	DEFAULTED.			DOES	NOT	BE	TRACED.																							
J.T.	9	-	+	+	140/80	1,4	-	+	+	150/70	1,4	-	+	+	130/80	1,4	-	+	-	140/70	1,4	-	+	-	140/80	1,4										
T.I.	10	-	+	+	120/80	1,4	-	+	+	120/80	1,4	-	+	+	120/75	1,4	-	+	+	120/80	1,4														
T.A.	11	DIED	IN	HOSPITAL																		-	-	+	120/70	1,4									
S.O.	12	+	-	+	120/70	1,4	-	-	+	120/75	1,4	-	+	+	110/80	1,4	-	-	+	120/70	1,4	-	-	+	120/80	1,4									
F.O.	13	-	-	-	120/80	1,4		DEFAULTED.					OCCD	NOT	BE	TRACED																			
O.A.	14	-	+	+	120/70	1,4		DIED	AT	HOME												-	-	-	130/80	1,4	-	-	+	120/80	1,4	-	-	-	120/70	1,4
A.A.	15	-	-	-	130/80	1,4	-	-	-	120/70	1,4	-	-	-	120/70	1,4	-	-	-	120/70	1,4	-	-	-	130/70	1,4	-	+	+	120/80	1,4					
A.I.	16	+	+	+	95/60	1,4	DEFAULTED.			DIED	IN	HOSPITAL										-	+	+	130/80	1,4	DIED	AT	HOME							
S.O.	17	-	+	+	110/70	1,4	-	+	+	115/70	1,4	-	+	+	110/70	1,4	+	+	+	120/80	1,4	-	+	+	130/80	1,4										
E.I.	18	+	+	+	130/80	1,4	-	+	+	130/80	1,4	-	+	+	140/80	1,4	-	+	+	130/80	1,4	-													

1 = Digoxin
2 = Thiazide Diuretics
3 = Methyl dopa
4 = Frusemide

CCF = Congestive Cardiac Failure.
B.P. = Blood Pressure.
PSM = Pansystolic Murmur.

TABLE 16 - (Group A2)

CLINICAL FINDINGS IN 3 PATIENTS WHO RAN OUT OF DRUGS BEFORE THEIR CLINIC APPOINTMENT WAS DUE

PATIENT AND NO.	TREATMENT	CLINICAL STATE				DURATION IN WHICH DRUGS WERE NOT USED	CLINICAL STATE			
		CCF	Apical PSM	3rd Sound	B.P. (mm Hg)		CCF	Apical PSM	3rd Sound	B.P. (mm Hg)
T. L. (10)	Digoxin. Frusemide 80 mg daily. HFM 50 mg daily K^+	-	+	+	110/70	1/52	+	+	+	120/80
O. A. (14)	Digoxin. Frusemide 80 mg daily K^+	-	+	+	110/70	2/52	+	+	+	120/80
A. I. (16)	Digoxin. Frusemide 160 mg daily HFM K^+	-	+	+	110/70	2/52	+	+	+	95/70

CCF = Congestive cardiac failure. PSM = Pansystolic murmur.

K^+ + Potassium supplements. B.P. = Blood Pressure.

embolic renal infarcts and liver congestion. One other patient (Y.A. case 11) died in hospital during his first admission. He had hypothyroidism and is presented in more detail later.

Groups A3, B1 and B2 (table 17). These patients were grouped together since their behaviour was similar. They continued to require thiazides or alpha methyl dopa and thiazides to keep them out of heart failure.

At a stage during their follow-up, the hospital ran out of thiazide diuretics. 8 who had improved on thiazides were therefore given frusemide. All of them relapsed into heart failure at their next visit (table 18). 2 were then given alpha methyl dopa in addition to the frusemide they were already receiving. These 2 patients improved within two weeks. The remaining 6 patients were given hydrochlorothiazide from a small stock of samples I possessed. They too, improved by the time they were seen two weeks afterwards.

11 patients ran out of drugs for one to four weeks before their clinic appointment was due and came back in heart failure with elevated blood pressures (table 19).

The blood pressures of 5 other patients who initially were stabilised on either thiazide diuretics alone or in combination with small doses of methyl dopa subsequently continued to rise despite the fact that the patients were

TABLE 17

Summary of the findings during long-term follow-up of patients in Groups A, B, and Bp

PATIENT	No.	3 Months					6 Months					9 Months					12 Months					18 Months					24 Months					36 Months				
		CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	Rx
A. O.	19	-	-	-	100/70	1,2	-	-	-	120/80	1,2	DEFAULTED					WOULD NOT HAVE DIED AT HOME																	
J. A.	20	-	-	-	130/80	1,2	-	-	-	130/90	1,2	-	-	-	120/80	1,2	-	-	-	120/80	1,2													
E. A.	21	-	-	+	140/80	1,2	-	-	+	140/80	1,2	-	-	+	160/80	1,2	-	-	+	160/80	1,2													
A. O.	22	-	-	-	120/80	2,3	-	-	-	110/80	2,3	-	-	-	120/70	2,3	-	-	-	120/80	2,3													
B. T.	23	-	+	+	120/80	1,2	-	+	+	120/90		-	+	+	110/80	1,2	-	+	+	110/75	1,2	-	+	+	110/70	1,2									
A. O.	24	-	-	-	120/70	1,2	-	-	-	120/75	1,2	-	-	-	130/80	1,2	-	-	-	130/80	1,2													
T. E.	25	+	+	+	120/80	1,2	-	+	+	110/80	1,2	-	+	+	120/80	1,2	-	+	+	100/70	1,2													
E. A.	26	-	+	+	130/80	1,2	+	+	+	140/110		+	+	+	140/115		DEFAULTED																	
A. O.	27	-	-	-	130/80	1,2	DEFAULTED		WOULD	NOT BE	TRACED																							
B. T.	28	-	+	+	140/80	1,2	-	+	+	130/80	1,2	-	+	+	130/70	1,2	-	+	+	110/70	1,2	-	+	-	110/80	1,2	-	+	+	150/80	1,2	-	+	+	140/85	1,2
A. A.	29	-	+	+	120/80	1, 2	DEFAULTED																												
E. A.	30	-	-	-	160/80	1,2	DEFAULTED		WOULD	NOT BE	TRACED																								
T. A.	31	-	+	+	130/85	1,2	-	-	+	130/80	1,2	-	-	+	120/85	1,2	-	-	+	120/85	1,2	-	-	+	130/85	1,2									
E. A.	32	-	-	-	140/80	2,3	+	-	-	160/110	2,3	-	-	-	150/85	2,3	+	-	-	170/110	2	+	-	-	170/80		-	-	-	150/80	2,3	-	-	-	140/85	2,3
E. M.	33	-	-	-	140/100	1,2,3	-	-	-	150/100	2,3	+	+	+	180/115		-	+	-	180/110	2,3	-	-	-	150/80	2,3	-	-	-	140/90	2,3					
E. A.	34	-	-	-	160/80	1,2	-	-	-	140/75	1,2	DEFAULTED																							
J. O.	35	+	-	+	140/95		-	-	-	140/70	1,2	-	-	-	150/80	1,2	-	-	-	100/100		+	+	+	150/80	1,2,3	-	-	-	140/70	1,2,3					
O. O.	36	+	-	-	200/100	1,2,3,	-	-	-	150/80	2,3	-	-	-	130/80	2,3	+	-	+	170/110	1,2,3	+	-	+	150/80	1,2,3	-	-	-	140/80	1,2,3					
J. E.	37	+	-	+	130/90	1,2,3	-	-	+	130/70	1,2,3	+	-	+	130/70	1,2,3	+	-	+	130/70	1,2,3	DIED AT HOME													
O. O.	38	-	-	-	120/70	1,2	-	-	+	140/90	1,2	+	+	+	150/115	-	-	-	-	120/80	1,2	-	-	-	120/70	1,2	+	+	+	130/100	1,2					
O. O.	39																													- DIED					
J. T.	40	-	-	+	105/80	1,2,3	-	-	+	110/80	1,2,3	DEFAULTED																							
J. A.	41	-	-	-	170/80	1,2	-	-	-	150/90	1,2	-	-	-	150/80	1,2	-	-	-	160/75	1,2	-	-	-											
J. A.	42	+	+	+	100/120	1,2,3	DIED AT HOME																												
A. O.	43	-	-	-	160/80	1,2	+	+	+	150/100	-	-	-	-	150/80	1,2	-	-	-	150/80	1,2													
A. A.	44	-	-	-	130/85	1,2	-	-	-	130/80	1,2	-	-	-	130/80	1,2	-	-	-	140/85	1,2													
A. T.	45	-	+	+	110/80	1,2	-	-	-	110/70	1,2	-	-	-	110/85	1,2	-	-	-	110/85	1,2	-	-	-										
O. O.	46	-	-	-	150/80	1,2	-	-	-	170/110	-	-	-	-	160/95	1,2	-	-	-	150/90	1,2	-	-	-										
E. T.	47	-	-	-	150/85	2,3	-	-	-	160/90	2,3	-	-	-	160/70	2,3	-	-	-	170/90	2,3	-	-	-										
A. A.	48	-	+	+	120/105	1,2	-	-	-	150/95	1,2,3	-	-	-	150/95	1,2,3	-	-	-	130/80	1,2,3	-	-	+										
A. O.	49	-	-	-	120/100	1,2,3	+	-	+	120/100	1,2,3	-	-	-	120/80	1,2,3	+	-	+	150/110	-	-	-	-											
A. E.	50	+	+	+	140/105	-	-	-	-	110/80	2,3	+	+	+	110/70	2,3	ABSCONDED																	

Diuretic = 1
Digoxin = 2
Digoxin = 3

CCF = Congestive Cardiac Failure. PSM = Pansystolic Murmur. B.P. = Blood Pressure

TABLE 10

(GROUPS A3, B1 AND B2). CLINICAL COURSE OF PATIENTS WHOSE DIURETICS WERE CHANGED TO FRUSEMIDE WHEN THIAZIDES WERE NOT AVAILABLE

Patient	No.	MAINTENANCE TREATMENT					STATE WHEN THIAZIDES NOT AVAILABLE					STATE ON ADDITION OF KETHYL-DOPA OR RESUMPTION OF THIAZIDE DIURETICS				
		TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE			
			CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)
E. L.	21	Dig. HTN 200 mg daily, K+	-	-	-	150/70	Dig. Frusemide 80mg daily K+	+	+	+	160/100	Dig. Frusemide 80mg daily K+ MD 500mg daily	-	-	-	120/75
E. T.	23	Dig. HTN 200mg daily, K+	-	-	-	120/80	Dig. Frusemide 80mg daily K+	+	+	+	120/100	Dig. HCT 100mg daily, K+	-	-	+	110/70
E. B.	25	Dig. HTN 200mg daily, K+	-	+	+	110/85	Dig. Frusemide 80mg daily K+	+	+	+	120/100	Dig. HCT 100mg daily K+	-	+	+	120/80
E. F.	28	Dig. HTN 200mg daily, K+	-	+	-	160/95	Dig. Frusemide 80mg daily, K+	+	+	+	170/95	Dig. HCT 100mg daily K+	-	+	+	140/80
E. E.	31	HCT 200mg daily, K+	-	-	-	130/80	Dig. Frusemide 80mg daily, K+	+	-	+	160/105	Dig. Frusemide 80mg daily. MD 500mg daily K+	-	-	-	140/75
J. E.	35	HTN 200mg daily, K+	-	-	-	130/80	Dig. Frusemide 80mg daily K+	+	+	+	140/100	Dig. HCT 100mg daily, K+	-	-	-	140/70
L. E.	43	Dig. HCT 100mg daily K+	-	-	-	130/80	Dig. Frusemide 80mg daily K+	-	-	+	130/100	Dig. HCT 100mg daily, K+	-	-	-	125/80
E. A.	44	Dig. HCT 100mg daily K+	-	+	+	130/70	Dig. Frusemide 80mg daily K+	+	+	+	140/110	Dig. HCT 100mg daily, K+	-	+	+	140/80

CCF = Congestive Cardiac Failure. PSM = Pansystolic murmur B.P. = Blood Pressure

Dig = Digoxin HCT = Hydrochlorothiazide HTN = Hydroflumethiazide K+ = Potassium supplements

TABLE 10

(GROUPS A3, B1 AND B2). CLINICAL COURSE OF PATIENTS WHOSE DIURETICS WERE CHANGED TO FRUSEMIDE WHEN THIAZIDES WERE NOT AVAILABLE

Patient	No.	MAINTENANCE TREATMENT	CLINICAL STATE				STATE WHEN THIAZIDES NOT AVAILABLE	CLINICAL STATE				[illegible]	[illegible]			
		TREATMENT	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	TREATMENT	CCF	Apical PSM	3rd Sound	B.P. (mmHg)	TREATMENT	CCF	Apical PSM	3rd Sound	B.P. (mmHg)
E. A.	21	Dig. HYH 200 mg daily, K+	-	-	-	150/70	Dig. Frusemide 80mg daily K+	+	+	+	160/100	Dig. Frusemide 80mg daily K+ BD 500mg daily	-	-	-	[illegible]
E. T.	23	Dig. HYH 200mg daily, K+	-	-	-	120/80	Dig. Frusemide 80mg daily K+	+	+	+	180/100	Dig. HCT 100mg daily, K+	-	-	-	[illegible]
I. E.	25	Dig. HYH 200mg daily, K+	-	+	+	110/85	Dig. Frusemide 80mg daily K+	+	+	+	120/100	Dig. HCT 100mg daily K+	-	-	-	[illegible]
I. F.	28	Dig. HYH 200mg daily, K+	-	+	-	160/85	Dig. Frusemide 80mg daily, K+	+	+	+	170/95	Dig. HCT 100mg daily K+	-	-	-	[illegible]
E. I.	31	HCT 200mg daily, K+	-	-	-	150/80	Dig. Frusemide 80mg daily, K+	+	-	+	160/105	Dig. Frusemide 80mg daily, BD 500mg daily K+	-	-	-	[illegible]
I. E.	35	HYH 200mg daily, K+	-	-	-	150/80	Dig. Frusemide 80mg daily K+	+	+	+	140/100	Dig. HCT 100mg daily, K+	-	-	-	[illegible]
L. E.	43	Dig. HCT 100mg daily K+	-	-	-	150/80	Dig. Frusemide 80mg daily K+	+	-	+	130/100	Dig. HCT 100mg daily, K+	-	-	-	[illegible]
E. A.	44	Dig. HCT 100mg daily K+	-	+	+	150/70	Dig. Frusemide 80mg daily K+	+	+	+	140/110	Dig. HCT 100mg daily, K+	-	+	+	[illegible]

CCF = Congestive Cardiac Failure. PSM = Pansystolic murmur B.P. = Blood Pressure

Dig = Digoxin HCT = Hydrochlorothiazide HYH = Hydroflumethiazide K+ = Potassium supplements

TABLE 19

(GROUP A3, B1 AND B2). CLINICAL FINDINGS IN 11 PATIENTS WHO RAN OUT OF DRUGS BEFORE THEIR CLINICAL APPOINTMENT WAS DUE

PATIENT AND NO.	MAINTENANCE TREATMENT	CLINICAL STATE ON MAINTENANCE TREATMENT				DURATION FOR WHICH NO DRUG WAS USED	CLINICAL STATE AFTERWARDS			
		CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P (mmHg)
A.O. (19)	Dig. HFM K^+	-	-	-	130/85	2/52	+	+	+	160/95
F.N. (25)	Dig. HFM, K^+	-	+	+	105/75	3/52	+	+	+	140/110
M.A. (26)	Dig. HCT K^+	-	-	-	120/70	2/52	+	+	+	140/110
R.S. (32)	MD. HFM K^+	-	-	-	120/80	1/52	mild	-	-	170/110
S.M. (33)	MD. HFM K^+	-	+	-	150/100	4/52	+	+	+	180/115
J.C. (35)	Dig. HFM K^+	-	-	-	110/85	2/52	+	-	+	140/100
B.O. (38)	Dig. HFM, K^+	-	-	-	110/70	3/52	+	+	+	130/100
R.B. (42)	Dig. HCT, K^+	-	-	-	150/80	1/52	+	+	+	150/100
L.O. (43)	Dig. HCT K^+	-	-	-	130/85	1/52	+ (mild)	-	-	170/110
A.A. (48)	Dig. Ald. HFM K^+	-	-	-	120/80	2/52	+	-	+	150/110
A.B. (50)	Dig. MD. HFM. K^+	-	-	-	120/80	1/52	+	+	+	140/105

CCF = Congestive cardiac failure. PSM = Pansystolic murmur. B.P. = Blood pressure
Dig = Digoxin K^+ = Potassium supplements HFM = hydroflumethiazide MD = Methyl dopa
HCT = hydrochlorothiazide

taking their drugs regularly. They, therefore, required increasing doses of methyl dopa to keep the blood pressures normal (table 20). 2 of them did not relapse into heart failure despite these increases in blood pressures.

9 had incomplete follow up - 3 died at home while 6 could not be traced.

2 patients died in hospital. One of them (A.B, case 50) had terminally hepatic and renal failure and had to be dialysed. At necropsy, he had biventricular cardiac dilatation with mural thrombi, septic infarcts in both kidneys and chronic venous congestion of the liver, lungs, spleen and the kidneys. The other patient had bilaterally contracted kidneys. His case-history is therefore briefly presented:

Case 38: He was a 67 year old petrol dealer who presented in congestive cardiac failure with a blood pressure of 120/100 mmHg. His first heart sound was soft. He had a loud third sound but no murmurs. His heart was enlarged on chest x-ray. An ECG showed left bundle branch block with ST-T changes in the infero-lateral leads. His blood urea was 35mg%. This patient improved on digitalisation and frusemide and before discharge, he was out of heart failure, no third sound was audible and his blood pressure

TABLE XO

(GROUPS A3, B1 AND B2) CLINICAL COURSE OF PATIENTS WHOSE BLOOD PRESSURES CONTINUED TO RISE DESPITE ANTI-HYPERTENSIVE AGENTS

PATIENT	NO.	TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE				TREATMENT	CLINICAL STATE			
			CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)		CCF	Apical PSM	3rd Sound	B.P. (mmHg)
L. S.	32	MD 500mg daily, HTH & K+	-	-	-	150/80	MD 500mg daily HTH, K+	-	-	-	100/110	MD 750mg daily, HTH K+	+	-	+	170/110	MD, 1Gm daily, HTH K+	-	-	-	140/95					
L. K.	33	MD 500mg daily HTH, K+	-	+	-	160/110	MD 500mg daily HTH, K+	-	+	-	140/110	MD 500mg daily, HTH K+	+	+	+	100/115	MD 750mg daily, HTH, K+	-	-	-	170/100	MD 1Gm daily HTH, K+	-	-	-	150/80
I. O.	35	Dig. HTH K+	-	+	-	120/90	Dig. HTH, K+	-	+	-	140/100	Dig. HTH, K+	+	+	+	140/100	Dig. HCT K+	-	-	+	140/70	Dig. HCT K+	-	-	+	170/110
A. O.	36	Dig. HCT K+	-	-	-	150/110	Dig. MD 250mg daily HCT, K+	+	-	+	210/110	Dig. HCT, MD 500mg daily K+	+	-	-	200/100	Dig. HCT MD 750mg daily K+	-	-	+	160/110	MD 1Gm daily HCT, K+	-	-	-	140/90
B. O.	46	Dig. HTH, K+	+	-	+	150/90	Dig. MD 250mg daily HCT, K+	-	-	-	170/75	Dig. MD 250mg daily HCT, K+	-	-	-	150/90	MD, 250mg daily HCT, K+	-	-	-	170/105	MD 500mg daily HCT, K+	-	-	-	160/85

CCF = Congestive Cardiac Failure, PSM = Pansystolic Murmur B.P. = Blood Pressure

MD = Methyl Dopa HTH = hydroflumethiazide HCT = hydrochlorothiazide, Dig = Digoxin K+ = Potassium supplements

* He subsequently relapsed into heart failure with a blood pressure of 190/120 and required the addition of methyl dopa 500mg daily to improve his condition.

was 105/85 mmHg.

When he was seen three weeks afterwards in the out-patient clinic, he had relapsed into congestive cardiac failure with a blood pressure of 120/100 mmHg. A mid-systolic murmur and a third heart sound were also audible at the apex. He improved on thiazides, his blood pressure came down to 120/70 mmHg his third sound and systolic murmur also disappeared. He was then followed up for over 3 years. At a stage during his follow-up he defaulted from the clinic for two months and came back in heart failure with a blood pressure of 150/115 mmHg. He again improved on digoxin and thiazide diuretics. Before his last admission, he had run out of drugs for three weeks. He was in heart failure with a blood pressure of 130/100 mmHg. He had an apical soft mid-systolic murmur and a loud third heart sound.

Terminally, his serum urea rose to 137mg per 100ml. His serum creatinine also rose to 6mg per 100ml. Despite all measures he died eight days after admission. At autopsy, his heart was enlarged weighing 655Gm. All the chambers were dilated, there was an old healed mitral valvulitis and both kidneys were contracted and granular (fig. 15). The renal changes were in keeping with those of arteriolonephrosclerosis.

Fig. 15: The heart and the kidneys of case 38 at post-mortem. The heart was dilated and the kidneys were bilaterally contracted and granular.

Optic Fundi: 5 patients from groups A3, B1 and B2 had grade I changes according to Wagener and Keith classification (1939). None of the other patients had arteriolar changes.

Intravenous Pyelography (IVP): The renal measurements of 18 patients (16 in groups A3, B1 and B2; 2 in group A2) in whom the kidneys were visualised on IVP are shown in table 21. The renal shadows were not seen in 8 other patients (4 in groups A3, B1 and B2; 2 in group A2 and 2 in group A1). There is little knowledge on the normal renal sizes in Nigerians. Akinkugbe and Abiose (1970) measured the surface area of the kidneys of 56 females with carcinoma of the cervix and 16 males with carcinoma of the prostate. They found in males that the mean area for the left kidney was 109.70 sq. cm (± 14.28) and for the right 108.63 (± 8.71) sq. cm. In the females the corresponding figures for left and right were 111.70 sq.cm (± 20.82) and 106.98 sq. cm (± 19.40). These figures are higher than those quoted in Caucasians by Moell (1961). He found that the right kidney measured 12.9 cm (± 0.80) x 6.2 cm. (± 0.45) the left kidney 13.2 cm (± 0.79) x 6.3 (± 0.49) cm in the males. Corresponding figures for surface area were 79.6 (± 8.75) and 82.7 (± 8.34) sq. cm. respectively. In the females, the figures for the right kidney were 12.3 cm (± 0.79) x 5.7

TABLE 21

RENAL SIZES OF THE PATIENTS WHO HAD INTRA-VENOUS PYELOGRAPHY

PATIENT	SEX	NUMBER	GROUP	RIGHT KIDNEY			LEFT KIDNEY		
				Length (cm)	Width (cm)	Surface area (sq.cm)	Length (cm.)	Width (cm)	Surface area (sq. cm)
L. G.	M	45	B_2	10.5	5.5	45.4	10.3	6.9	55.8
E. A.	F	21	A_3	10.3	4.5	36.4	9.5	5.6	41.8
A. O.	F	22	A_3	10.9	4.8	41.1	10.7	4.8	40.4
A. O.	F	24	A_3	12.1	5.3	50.38	12.5	6	58.9
J. A.	M	20	A_3	11.8	5.9	54.70	11.3	6.3	55.9
E. T.	F	47	B_2	10.8	5.5	46.7	12	5.7	53.7
S. F.	M	28	B_1	11.3	5	44.4	11	5.9	51.0
D. O.	F	46	B_2	11.5	6	54.2	11.6	5.6	51.0
L. O.	M	43	B_1	13	7	71.5	12.7	6.5	64.9
L. L.	F	48	B_2	10.2	4.5	36.1	10.1	6.7	53.2
S. M.	F	33	B_1	10.5	5.7	47.0	10.6	5.8	48.3
F. O.	M	35	B_1	10.7	5.4	45.4	13.4	6.5	68.4
I. U.	F	40	B_1	9.2	4.7	34.0	10.3	5.1	41.3
L. T.	F	45	B_2	12.5	5.5	54.0	12.7	6.6	65.9
B. T.	M	23	A_3	11.3	5.4	47.9	11	6.8	58.8
I. L.	M	44	B_1	10.2	5.5	44.1	10.2	5.7	45.7
T. O.	M	12	A_2	11.4	5.5	49.3	11.5	6	54.2
O. O.	F	7	A_2	14.2	6.9	76.9	13.7	6.9	74.3

(± 0.46) cm and for the left 12.6 cm (± 0.77) x 5.9 (± 0.42) cm. The areas were 70.1 (± 8.00) and 74.1 (± 7.31) sq. cm. respectively. As Akinkugbe and Abiose (1970) pointed out in their paper, the assumption that their figures were not affected by the conditions the patients had was difficult to justify. Hodson (1962) produced a figure of between 12 cm and 15 cm in males and 11 cm to 14 cm in females.

The figures obtained in this study in comparison with the above therefore show that many of the patients in groups A3, B1 and B2 had small kidneys. Figures 16 and 17 are two illustrative cases. Only 3 of the 50 patients however had blood ureas greater than 40mg per 100ml on admission. These 3 patients had received diuretics before admission and their blood ureas subsequently came down on follow-up.

Large flabby hearts in established hypertension: A study was then undertaken to determine whether large flabby hearts could occur in established cases of hypertension. The hearts of 79 patients (38 males and 41 females) who died of hypertension were examined by Dr. Ed. Attah and the author. These 79 hearts were separated into three types - the classical concentric or selective left ventricular hypertrophy, large flabby hearts and hearts with intermediate

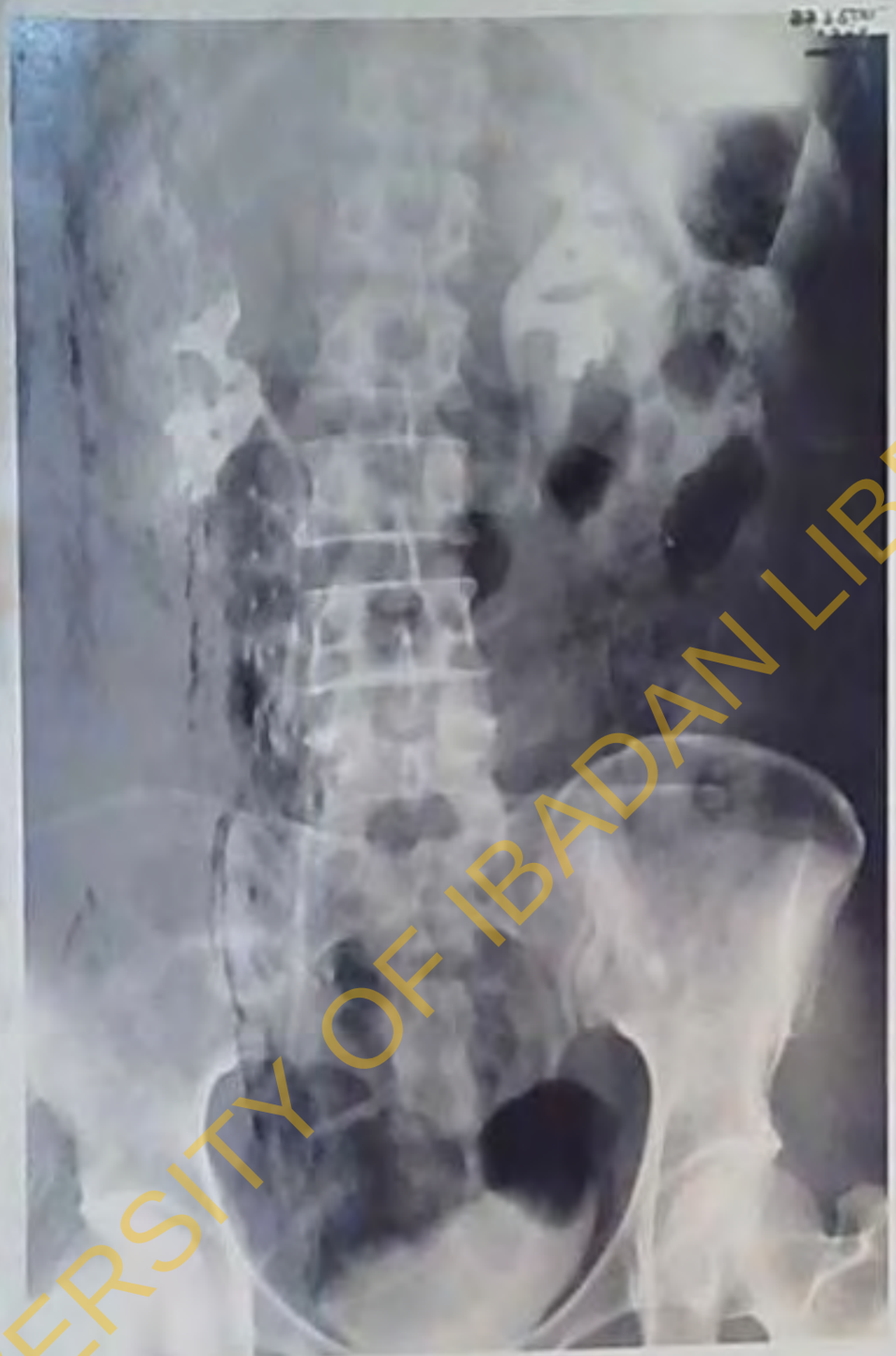

Fig. 16: The 30 min. full length IVP film of case 48 showing bilateral small kidneys with smooth outlines. The collecting systems appear normal.

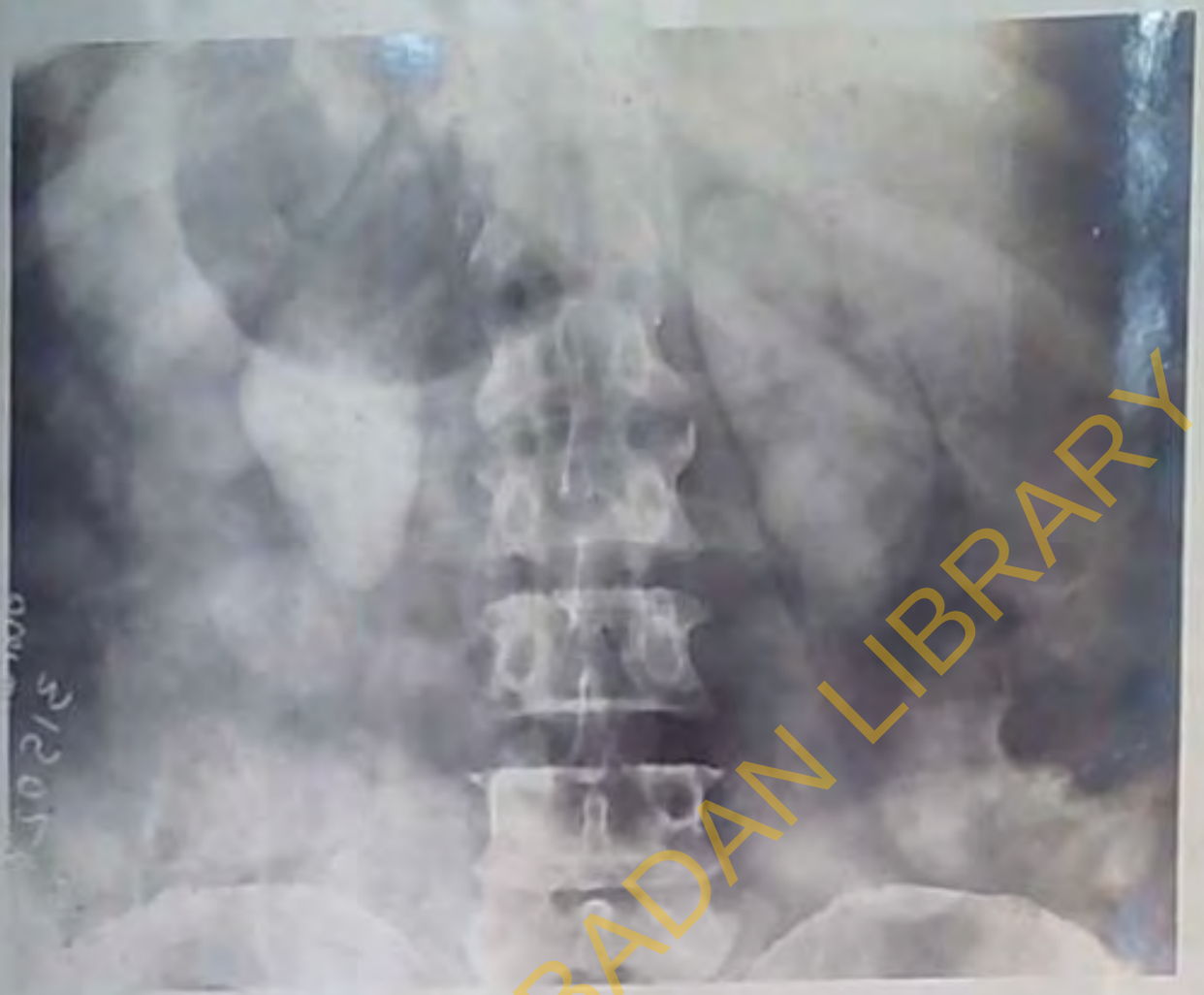

Fig. 17: The nephrogram phase on the IVP of case 22 demonstrating bilaterally small kidneys.

configuration. All hearts with other identifiable disease e.g. rheumatic heart disease or EMF were excluded. The large flabby hearts were also examined histologically. Of the 79 patients, 65 had contracted granular kidneys, 7 had enlarged kidneys of cystic disease, hydronephrosis and compensatory hypertrophy following previous nephrectomy. The remaining 7 kidneys with weights within the normal range were histologically abnormal with features ranging from rapidly progressive glomerulonephritis to infarcts and chronic pyelonephritis. Not a single kidney was found to be normal.

The patterns recognisable macroscopically were as shown in table 22. 36 had large flabby hearts while 33 had concentric left ventricular hypertrophy. Table 23 shows the haematocrit of 39 patients (23 males and 16 females) whose reports were available. Among the 23 males only 3 had haematocrit of 40% or above. In 10 patients the haematocrit was less than 25%. Among the 16 females only 3 had haematocrit of 35% or above. In 9 cases the haematocrit was less than 25%.

Among the males with flabby hearts, the haematocrit was known in 13 cases (table 24). In 9 of these it was below 30%. In all the 8 females with flabby hearts whose haematocrit was known, it was below 30%.

TABLE 22

APPEARANCE OF HEARTS AT AUTOPSY: HYPERTENSIVE PATIENTS

	LARGE FLABBY HEARTS	SELECTIVE L.V HYPERTROPHY	INTERMEDIATE NON-FIGURATION	TOTAL
MALE	18	15	5	38
FEMALE	18	18	5	41

TABLE 23

HEMATOCRIT OF 39 PATIENTS WHOSE REPORTS WERE AVAILABLE

MALE		FEMALE		
Hematocrit: 40% or above	3	Hematocrit: 35% or above	3	
25% to 39%	10	25% to 34%	4	
Less than 25%	10	Less than 25%	9	
TOTAL	23		16	39

TABLE 24

HEMATOCRIT OF 21 PATIENTS WITH LARGE FLABBY HEARTS

	Male	Female
Hematocrit: 30% or above	4	0
Below 30%	9	8
TOTAL	13	8 = 21

Histological examination of the 36 dilated hearts showed left ventricular myocardial hypertrophy in 13, patchy fibrosis in 3 and myocytolysis in 2. The myocardial fibres were disposed in an orderly arrangement and in 10 hearts, there were zones of irregularity of shape and size of myocardial nuclei, this feature showing no particular association. It was present in the 2 hearts which manifested myocytolysis but was not more prominent in these than in some of the other hearts. Other degenerative alterations (e.g. myocardial basophilic degeneration) were not a feature. In no case was there evidence of myocarditis, vasculitis or myocardial infarction.

Left ventricular mural thrombosis with organisation was demonstrated in several hearts including one with myocytolysis. In these cases there was subjacent endothelial lymphocytic reaction. Foci of interstitial oedema was present in 6 hearts. The coronary arteries were free of atheroma except for minor inconspicuous lesions in a few elderly patients and diabetics.

NUTRITION (Tables 25-27)

Alcohol: 20 (40%) patients (16 males and 4 females) gave a history of excessive and prolonged intake of alcohol. Six of them belonged to group A2 (table 26) while the rest were in groups A3, B1 and B2 (table 27). Two of the four female

TABLE 25

THE NUTRITIONAL DATA OF PATIENTS IN GROUP A1

Patient	No.	Sex	Age	Socio-economic status	Alcohol	Thiamine Status (in % hexose)	Cardiac Index litres/min/m^2	Fasting Pyruvic acid (mg%)	Fasting lactic acid (mg%)	Serum Albumin (Gm %)	Serum Globulins (Gm %)	Serum Potassium (mEq/litre)	PCV
I. G.	1	M	17	L	-	5.8%	2.4	1.50 mg%	10.6 mg%	2.6	3.9	3.6	40%
L. L.	2	F	30	L	-	12%	2.5	-	-	2.4	5.1	3.8	33%
O. K.	3	F	30	L	-	5%	3.1	1.0 mg%	10.6 mg%	3.5	3.4	4.8	42%
A. O.	4	F	30	L	-	11%	3.1	0.8 mg%	12 mg%	1.8	4.4	3.2	32%
K. O.	5	M	35	L	-	8%	2.9	1.0 mg%	-	2.5	4.4	3.7	42%
M. O.	6	F	17	L	-	0.5%	-	0.8 mg%	9.7 mg%	3.2	4.0	4.1	38%

L = Low socio-economic group.

H = High socio-economic group.

PCV = Packed cell volume

TABLE XI

THE NUTRITIONAL STATUS OF PATIENTS WITH [illegible]

PATIENT	IN+	SEX	AGE	SOCIO-ECONOMIC STATUS	ALCOHOL	SERUM IRON	CARDIAC INDEX	PLASMA PYRUVIC ACID	PLASMA LACTIC ACID	SERUM ALBUMIN	SERUM GLOBULINS	SERUM POTASSIUM	PCV
A. O.	19	F	56	L	+	6.8/	2	-	-	3.6	4.7	4.4	4
J. A.	20	M	52	L	+	16.6/	-	0.57	10.2	3.0	3.5	4.4	4
E. A.	21	F	60	L	-	67.2/	1.76	1.2	12.5	3.4	3.6	4.1	40
A. O.	22	F	61	L	-	9.6/	-	0.5	9.6	3.7	3.5	3.4	38
B. T.	23	M	62	L	-	3.4/	-	0.54	3.9	3.5	3.2	4.0	42
A. O.	24	F	49	L	-	13.9/	2	0.7	5.8	3.0	4.1	3.8	38
T. E.	25	F	60	L	-	8.7/	1.65	-	-	3.2	3.4	4.1	45
E. -	26	F	49	L	-	81.5/	-	1.9	21.3	3.0	3.5	4.7	41
S. S.	27	F	50	L	-	11.3/	3.2	-	-	3.5	3.9	3.6	34
S. F.	28	M	75	H	+	26/	1.6	-	-	3.8	3.5	3.9	45
S. S.	29	F	60	L	-	26/	2.6	1.01	11.2	3.5	4.3	3.8	40
E. A.	30	F	43	L	+	29.7/	-	1.10	9.1	3.7	3.7	3.8	43
E. B.	31	M	40	H	+	50/	1.63	0.93	10.5	3.0	3.0	3.4	45
S. S.	32	F	43	L	-	5.2	2.2	-	-	3.3	4.1	4.0	40
S. E.	33	F	40	L	-	2.8/	2.6	0.9	10.0	3.6	4.6	4.6	45
L. A.	34	M	60	L	+	20/	2.93	1.0	10.5	2.6	5.2	4.2	48
F. O.	35	M	50	L	+	6.6/	2.7	0.45	9.7	3.0	3.7	4.6	50
S. O.	36	M	45	H	-	10/	-	1.37	27.4	3.7	3.5	4.1	40
F. S.	37	M	41	H	+	0/	-	1.23	7.5	3.5	3.0	4.5	45
S. O.	38	M	67	H	+	12.7/	-	2.0	22	3.5	3.6	3.8	43
O. O.	39	M	53	H	+	26.6/	-	1.2	20	2.8	3.9	4.4	45
J. O.	40	F	61	L	+	12.2/	-	0.5	8.4	3.7	6.8	4.0	34
S. E.	41	F	65	L	-	10.6/	-	0.83	12.5	2.4	2.8	5.2	34
E. O.	42	F	65	L	-	9.2/	-	0.60	8.4	3.2	5.2	4.0	43
L. O.	43	M	74	H	+	8.3/	-	0.34	5.8	2.3	3.8	3.2	52
S. A.	44	M	60	L	-	17.2/	-	2.9	11	2.4	2.1	5.2	43
A. T.	45	F	35	L	-	10.8/	-	0.85	6.8	3.2	2.8	3.7	40
D. O.	46	F	63	L	-	5.6/	2.2	0.90	8.0	3.3	4.7	3.3	40
E. T.	47	F	50	L	-	3.6/	-	0.76	2.9	3.6	4.6	3.1	41
A. A.	48	F	40	L	-	3.4	2.6	2.3	13.9	1.8	4.7	3.8	34
A. O.	49	M	50	H	+	40/	3.1	1.76	24.5	2.8	4.7	4.7	40
A. A.	50	M	26	H	+	28.7/	-	0.88	9.3	3.6	3.4	4.3	43

L = Low socio-economic group. PCV = Packed cell volume

H = High socio-economic group.

TABLE XI

THE NUTRITIONAL STATUS OF PATIENTS ON HAEMODIALYSIS AT UCH IBADAN

PATIENT	IN.	SEX	AGE	SOCIO-ECONOMIC STATUS	EDEMA	BLOOD UREA NITROGEN	SERUM CHLORIDE	PLASMA PYRUVIC ACID	PLASMA LACTIC ACID	SERUM SODIUM	SERUM CHLORIDE	SERUM POTASSIUM	PCV
A. O.	19	F	56	L	+	6.8	2	-	-	3.6	4.7	4.4	42
J. A.	20	M	52	H	+	14.6	-	0.57	10.2	3.0	3.5	4.4	42
M. A.	21	F	60	L	-	67.2	1.75	1.2	12.5	3.4	3.6	4.1	30
A. O.	22	F	61	L	-	9.4	-	0.5	9.6	3.7	3.5	3.4	38
B. I.	23	M	62	L	-	3.44	-	0.54	3.9	3.5	3.2	4.0	40
A. O.	24	F	40	L	-	13.9	2	0.7	8.8	3.0	4.1	3.8	30
T. M.	25	F	60	L	-	8.7	1.65	-	-	3.2	3.4	4.1	43
M. ...	26	F	40	L	-	81.2	-	1.9	21.8	3.0	3.5	4.7	41
O. I.	27	F	50	L	-	11.8	3.2	-	-	3.5	3.9	3.6	54
B. F.	28	M	75	H	+	26	1.6	-	-	3.8	3.5	3.9	45
E. I.	29	F	60	L	-	26	2.4	1.03	11.2	2.9	4.3	3.8	40
T. A.	30	F	43	L	+	29.7	-	1.10	9.1	3.7	3.7	3.8	43
E. B.	31	M	40	H	+	50	1.63	0.93	10.5	3.0	3.0	3.4	46
I. E.	32	F	45	L	-	5.2	2.2	-	-	3.3	4.1	4.0	40
A. O.	33	F	40	L	-	2.8	2.6	0.9	10.0	2.8	4.6	4.6	45
I. A.	34	M	60	L	+	20	2.93	1.0	10.5	2.6	3.2	4.2	46
J. O.	35	M	60	L	+	6.6	2.7	0.45	9.3	3.0	3.7	4.6	50
B. O.	36	M	48	H	-	10	-	1.37	27.4	3.7	3.5	4.1	42
J. I.	37	M	41	H	+	0	-	1.23	7.5	3.5	3.0	4.5	45
B. O.	38	M	67	H	+	13.7	-	2.0	22	3.5	3.6	3.6	42
O. O.	39	M	53	H	+	26.6	-	1.2	30	2.8	3.9	4.4	42
J. O.	40	F	41	L	+	12.2	-	0.5	8.4	3.7	4.8	4.0	34
A. I.	41	F	65	L	-	10.6	-	0.83	12.9	2.4	2.8	5.2	34
M. A.	42	F	65	L	-	9.2	-	0.65	8.4	3.2	3.2	4.0	42
A. O.	43	M	74	H	+	8.3	-	0.34	5.8	2.3	3.8	3.8	50
B. A.	44	M	60	L	-	17.2	-	2.9	11	2.4	2.1	5.2	42
A. T.	45	F	39	L	-	10.8	-	0.8	6.3	3.2	2.8	3.7	40
B. O.	46	F	63	L	-	5.6	2.2	0.90	8.0	3.3	4.7	3.3	40
S. ...	47	F	50	L	-	3.8	-	0.7	2.9	3.8	4.6	3.1	41
A. ...	48	F	60	L	-	3.4	2.6	2.2	13.9	1.3	4.7	3.4	34
A. O.	49	M	50	H	+	40	2.1	1.3	28.5	3.2	4.7	4.7	46
A. O.	50	M	35	H	+	28.7	-	0.8	9.3	3.8	3.4	4.2	42

L = Low socio-economic group. PCV = Packed cell volume

H = High socio-economic group.

patients were engaged in the manufacture and sale of the alcoholic beverages, one of them with her husband up till the time of his death five years previously.

Twelve of the 20 patients belonged to the high socio-economic class. The 12 included 2 civil engineers, 1 customs officer, 1 petrol dealer, 1 civil servant, 2 secondary school teachers, 1 Hausa cattle dealer with taxi-cabs and houses in Ibadan and 4 business executives each with a good deal of landed property. It is significant to note that only one patient in the high socio-economic class did not consume alcohol excessively in this study. He was a draughtsman.

The types of alcoholic beverages they consumed are shown in table 28. Only those in the high socio-economic class consumed beer, spirits and imported wine. Those in the low socio-economic class consumed mainly locally-brewed alcoholic beverages (palm-wine, ogogoro and burukutu) which were cheaper, easily-obtainable although non-standardised. In a control group of 52 patients with no heart disease (appendix 2), only 3 (6%) were identified as alcoholics.

Tables 29-31 show respectively the alcohol, carbohydrate, mineral and electrolyte contents of 60cl. bottles of 5 brands of locally brewed beer, 18 brands of imported lager beers and palm-wine from four species of Elaeis. Table 32 shows the mean values of the nutrients. Nigerian

TABLE 28

TYPES OF ALCOHOLIC BEVERAGES TAKEN IN EXCESS BY THE 20 PATIENTS

PATIENT	NO.	SEX	SOCIAL STATUS	BEER	SPIRITS	IMPORTED WINE	PALM-WINE	OGOGORO	BURUKUTU
V. E.	8	M	H	+					
J. F.	9	M	L				+		
T. O.	12	M	H	+			+		
F. O.	13	M	L				+		
C. O.	17	F	L				+	+	+
E. L.	18	M	H	+	+	+			
L. O.	19	F	L				+	+	+
J. A.	20	M	H	+			+	+	
S. F.	28	M	H	+	+				
M. L.	26	F	L				+	+	
E. E.	31	M	H	+	+		+	+	
L. A.	34	M	L				+		
J. O.	35	M	L				+		
J. S.	37	M	H	+			+		
B. O.	38	M	H	+	+		+	+	
O. O.	39	M	H	+	+		+	+	
J. U.	40	F	L				+	+	
L. O.	43	M	H	+	+		+		
A. G.	49	M	H	+				+	
A. B.	50	M	H	+					

H = High socio-economic class

L = Low socio-economic class

TABLE 29

Amounts of Nutrients present in 60 cl Bottle of Nigerian Lager Beer

Beer Type	Alcohol (g)	Carbohydrates (g)	Electrolytes (m.eq)		Minerals			
			Na	K	Ca	Mg	Fe	P
B_1	27.4	17.4	4.6	47.1	1.8	78.0	Nil	158.7
B_2	22.6	15.3	14.1	38.6	6.3	64.0	Nil	131.3
B_3	31.2	16.7	19.1	46.4	6.0	76.9	Nil	167.7
B_4	28.8	23.6	10.2	55.7	3.6	82.9	Nil	149.7
B_5	29.8	25.0	6.9	68.9	1.8	99.9	Nil	223.9

TABLE 30

AMOUNTS OF NUTRIENTS PRESENT IN 60 cl BOTTLE OF BEER IMPORTED INTO NIGERIA

Beer Type	Alcohol (g)	Carbohydrates (g)	Protein (g)	Electrolytes (m.eq)		Mineral (mg)			
				Na	K	Ca	Mg	Fe	P
1	28.8	20.4	3.2	1.0	3.7	6.0	45.6	2.4	480
2	35.5	19.7	1.9	1.1	3.7	5.4	43.2	3.6	570
3	32.6	24.0	2.7	0.8	5.1	4.8	44.4	2.4	660
4	32.2	19.7	2.2	1.9	4.0	3.0	45.6	1.2	600
5	26.0	22.1	4.4	0.5	3.4	5.4	45.6	3.6	426
6	42.6	22.8	1.8	0.6	3.7	7.2	51.6	4.8	420
7	29.5	23.8	1.4	1.1	3.7	7.2	51.6	1.2	330
8	30.2	17.9	3.1	1.5	5.5	3.6	52.8	2.4	300
9	33.9	18.9	2.9	1.7	6.9	12.6	75.6	1.2	570
10	32.6	26.4	2.6	2.6	6.3	3.6	52.8	1.2	1050
11	25.4	5.4	1.3	0.5	2.6	6.6	32.4	2.4	330
12	31.2	26.9	1.9	0.7	4.7	3.0	38.4	Nil	690
13	32.9	19.1	2.0	0.7	3.5	12.6	48.0	1.2	480
14	29.8	23.1	1.7	0.7	4.4	4.8	55.2	1.2	750
15	28.8	22.5	2.3	1.9	4.3	9.0	46.8	2.4	570
16	28.4	23.8	1.9	0.5	4.6	6.0	45.6	1.2	810
17	26.7	23.7	2.0	0.8	2.7	4.2	4.8	2.4	450
18	29.8	23.1	1.8	2.3	3.8	5.4	51.6	2.4	660

TABLE 31

NUTRIENT CONTENT OF 60 cl. BOTTLE OF PALM WINE

Source	Alcohol (gm)	Carbohydrates (g)	Electrolytes m.eq		Mineral mg		
			Na	K	Ca	P	Fe
1. Elaeis Macrocarya	13.76	32.3	4.7	1.8	84.0	39.0	1.50
2. E. dura	14.48	29.4	4.7	1.8	81.6	38.4	1.38
3. E. tenera	12.80	28.7	4.8	1.8	82.8	40.8	1.44
4. E. pisifera	14.16	31.5	4.8	1.8	85.8	39.0	1.50

*Modified from Faparusi, S. I. (1966)

TABLE 32

MEAN VALUES OF THE NUTRIENT CONTENTS OF 60 cl. BOTTLES OF THE THREE ALCOHOLIC BEVERAGES

Beverages	Alcohol g.	Carbohydrates g.	$^{1}Na^{+}$ (MEg)	$^{1}K^{+}$ (MEg)	Ca^{++} (mg)	Mg^{++} (mg)	Fe (mg)	P (mg.)
Locally-brewed Beer	27.96	19.60	10.98	51.34	3.9	80.34	Nil	166.26
Imported Beer	30.94	21.79	1.16	4.25	6.13	46.2	4.13	563.67
Palm-wine	13.80	30.48	4.75	1.8	83.55	NE	1.46	39.3

NE = Not estimated

brewed lager beer is normally sold in bottles of minimum content of 60cl. Some of the imported beer are marketed in cans (about 30cl.) or in 60cl. bottles. A beer-drinking adult normally consumes at least 60cl. (a bottle) at a sitting.

Palm wine is sold in a number of ways. Some hawkers use 60cl. bottles, others use up to one litre bottles. For purposes of comparison with other alcoholic beverages, tho nutrient content of 60cl. of palmwine was calculated.

There was very little difference in the alcohol content between imported and locally brewed beers. However, these lager beers contained twice as much of alcohol as palmwine. Palmwine on the other hand contained more carbohydrate than does beer. Locally brewed beer appeared to have higher amounts of sodium and potassium compared with palm-wine or imported beer. Palmwine contains nutritionally significant amounts of calcium and drinkers may obtain up to 17% of their daily calcium allowance from palmwine. Imported beers are generally high in their phosphorous content and will normally meet up to 33% of the daily iron needs of an adult Nigerian (Idusogie, 1972). Locally brewed beer contains no detectable amount of iron.

Ogogoro contains 87.6% alcohol by weight and 91% by volume. The proof spirit is 160 and minerals are present in negligible quantities (Ketiku, personal communication).

Thiamine Status:- The mean TPP effect (% hexose) in patients with HMD was (18.1 ± 17). This was significantly higher than the controls (10.2 ± 10.9; $0.01 > P < 0.001$). 17 (39%) of the patients with HMD had TPP effect greater than 15% (normal value in Nigerians = 0 - 15%, Basile et al 1973) compared with 10 (19.6%) of controls. 5 of the 17 belonged to group A2 while the rest belonged to groups A3, B1 and B2. 11 consumed alcohol excessively (mean TPP effect = 29.17 ± 11.2); 8 of these 11 belonged to the high socio-economic class. 9 other alcoholics had normal thiamine status (mean TPP effect = 7.24 ± 4.1) while 6 patients had thiamine deficiency although they did not consume alcohol excessively. Their mean TPP effect was 40.2 ± 3.7.

All the 3 alcoholics in the control group had normal thiamine status (appendix 2). The mean TPP effect of the 10 patients with thiamine deficiency was 27.19 while the mean TPP effect of the remaining 42 patients was 6.5.

Only one of the patients with thiamine deficiency in the study group responded to thiamine administration alone. Her case will be presented in more detail later on.

Fasting pyruvic and lactic acids:- Fasting pyruvic acid levels were measured in 46 patients. 18 (39%) of these had levels greater than 1mg% (the upper limit of normal).

One of these 18 patients was in group A1, 6 were in group A2 while the remaining 11 patients belonged to groups A3, B1 and B2.

10 of the 18 patients had thiamine deficiency; 6 patients who had normal fasting pyruvic acid levels had thiamine deficiency.

11 patients (26%) had fasting lactic acid levels greater than 18mg% (the highest limit of normal). 6 of them had thiamine deficiency while 5 had normal thiamine status. 10 patients had thiamine deficiency although their lactic acid levels were normal.

Cardiac Output:- The resting cardiac output was measured in only 28 patients as the machine developed a fault which could not be put right immediately. The mean cardiac index of the 23 patients with HMD was 2.4 ± 1.1. This was not different from the mean cardiac index of 5 patients with organic MR (2.8 ± 0.3; $P > 0.05$). The mean values in alcoholics with thiamine deficiency (2.2 ± 0.6), alcoholics without thiamine deficiency (2.2 ± 0.4), non-alcoholics with thiamine deficiency (3.4 ± 2.4) and patients without alcoholism or thiamine deficiency (2.4 ± 0.5) were also not significantly different ($P > 0.05$).

One patient, however, had a high output heart failure and responded to parenteral thiamine hydrochloride. She was a 40 year old woman who lived (S.R. case 15) in purdah and

presented in heart failure with an apical systolic murmur, a third sound and a blood pressure of 110/70. Her chest x-ray showed an enlarged heart (cardio-thoracic ratio = 0.62). She had right atrial and right ventricular hypertrophy on the ECG. Her cardiac index was 6.9 litres/min/m^2 of body surface area. Her TPP effect was raised at 29.4%, her fasting serum pyruvic acid was 2.29mg% while her fasting lactic acid was 21.17mg%.

Following treatment with parenteral thiamine hydrochloride 200mg daily for two weeks, her TPP effect, serum pyruvic and lactic acid levels returned to normal values (5.6%, 0.6mg% and 10mg% respectively). Her cardiac index also became normal at 3.6 litres/min/m^2. Her ECG, however still showed right ventricular hypertrophy.

Serum Albumin: The mean serum albumin of the patients with HMD who are not alcoholics (3.09 $\pm$ 0.6) was significantly lower than the mean serum albumin in controls (3.8 $\pm$ 0.4; $P < 0.001$).

The mean serum albumin of the patients with alcoholism (3.15 $\pm$ 0.5) was also significantly lower compared with the controls ($P < 0.001$). Similarly the mean serum albumin levels of patients in the high (3.04 $\pm$ 0.5) and low (3.2 $\pm$ 0.4) socio-economic classes were significantly lower than controls ($P < 0.001$).

TABLE 33

THE SERUM POTASSIUM LEVELS OF THE 50 PATIENTS STUDIED

SERUM POTASSIUM (mEq/litre)	NUMBER OF PATIENTS
3.0 and below	2
3.1 - 3.5	11
3.6 - 4.0	16
4.1 - 4.5	14
4.6 - 5.0	5
5.1 - 5.5	2

The mean serum albumin of the alcoholics was however, not significantly different from that of non-alcoholics ($P > 0.05$). There was also no significant difference between the mean serum albunin of patients in the high and the low socio-economic groups ($P > 0.05$).

Serum Potassium: The distribution of the serum potassium levels of the patients is shown in table 33. 8 of the 13 patients with serum potassium below 3.5mEq/litre had received diuretics before admission. There was no significant difference between the mean levels of patients with HMD (3.95 ± 0.58) and controls (3.86 ± 0.54; $P > 0.05$).

Packed cell volume (PCV): As shown in tables 25-27, none of the patients had PCV below 30%.

INFECTIONS (tables 34-36)

TOXOPLASMA: 9 (20.45%) of the 44 patients with HMD and 18 (32.29%) of 51 controls (appendix 2) had fourfold antibody rise or fall to toxoplasma gondii. The result was not statistically significant ($x^2 = 2.56$; $0.2 > P > 0.1$).

There was also no significant difference between the number of patients with HMD who had positive antibody titres (59.09%) and controls (56.86%; $x^2 = 0.05$; $P > 0.5$).

The frequency of antibody distribution in the sera of the patients with HMD and controls is shown in table 37. 55.68% of the sera in the study group and 44.12% in the

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TABLE 34

DATA ON INFECTIONS AMONG THE PATIENTS IN GROUP A1

NAME	NO.	Parasites in stool	Micro-filariae	Trypano-somes	Asotitre	WBC	Eosino-phil Count	VDRL	TOXO-PLASMA INITIAL	SECOND	COXSACKIE B VIRUSES											
											B_1		B_2		B_3		B_4		B_5		B_6	
T. O.	1	1	-	-	200	7,500	-	-	-	-												
L. L.	2	4	-	-	125	6,250	2%	-	1/1024	1/512	-	-	-	-	-	-	-	-	-	-	-	-
O. K.	3	NONE	-	-	333	5,000	-	-	-	-	1/8	1/8	1/4	1/4	1/4	1/4	1/4	1/4	1/8	-	1/8	1/32
A. O.	4	NONE	-	-	200	5,800	-	-	-	-	-	-	1/32	1/32	-	-	-	1/4	1/8	-	-	-
K. O.	5	1, 2	-	-	125	5,400	12%	-	1/512	1/256	-	1/4	1/16	-	1/32	1/32	-	-	-	-	-	1/4
M. O.	6	1, 2	-	-	333	4,500	21%	-	1/16	1/16	-	-	1/4	1/4	1/16	1/32	-	-	-	-	-	-

1 = Ascaris ova
2 = Hookworm ova
3 = Trichuris ova
(4) = Entamoeba histolytica
ASO titre = Anti-streptolysin O titre
WBC = White blood cells

TABLE 35

DATA ON INFECTIONS AMONG THE PATIENTS IN GROUP A2

NAME	NO.	Parasites in stool	Micro-filariae	Trypano-somes	Asotitre	WBC	Eosino-phil Count	VDRL	TOXO-PLASMA INITIAL	SECOND	COXSACKIE B VIRUSES											
											B_1		B_2		B_3		B_4		B_5		B_6	
O. O.	7	1	-	-	166	6,500	2%	-	1/1024	1/256	-	-	-	-	-	-	1/16	1/32	-	-	1/4	1/4
V. I.	8	NONE	-	-	125	3,000	2%	+	-	-	-		1/8		-		1/4		-		-	
J. F.	9	NONE	-	-	166	6,900	20%	-	-	-	-	-	1/32	1/32	-	-	-	-	-	-	-	1/4
T. L.	10	NONE	-	-	333	5,700	10%	-	1/512	1/128	-	-	-	-	-	-	1/4	1/4	1/4	-	1/16	1/32
T. A.	11	NONE	-	-	125	9,900	17%	-	-	-	-		1/8		-		1/16		-		-	
T. O.	12	NONE	-	-	125	6,100	8%	-	-	-	-	-	-	-	1/4	1/16	-	-	-	-	-	-
F. O.	13	NONE	-	-	125	5,200	4%	-	-	-	-		1/16		-		-		-		-	
O. A.	14	1, 2, 3	-	-	125	4,300	17%	-	1/4	1/4	1/32	1/4	1/32	1/4	1/4	1/4	-	1/4	1/4	1/4	-	1/4
S. K.	15	1	-	-	200	9,650	8%	-	-	-	-	-	-	-	1/16	1/16	1/4	1/8	-	-	-	-
A. I.	16	1, 2, 3	-	-	333	9,200	-		-	1/4	1/32	1/32	1/32	1/16	-	-	1/32	1/8	-	1/32	-	-
C. O.	17	1, 2	-	-	333	6,550	19%	-	1/512	1/64	-	-	1/16	-	-	-	-	1/4	-	1/4	1/4	-
E. L.	18	NONE	-	-	250	6,200	2%	-	1/8	1/4	-	-	1/4	-	1/32	1/32	-	-	-	-	-	-

1 = Ascaris ova
2 = Hookworm ova
3 = Trichuris ova
(4) = Entamoeba histolytica
ASO titre = Anti-streptolysin O titre
WBC = White blood cells

TABLE 36

Data on Infections among the Patients in Groups A3, B1 and B2

Ward	No.	Parasites in stool	M	T	Ano titre	WBC	Eosinophil Count	VDRL	Toxoplasma Initial	Toxoplasma Second	COXSACKIE B VIRUSES											
											B_1		B_2		B_3		B_4		B_5		B_6	
A Ex.	19	None	-	-	125	10,750	2%	-	-	-	1:4	-	1:16	1:32	-	-	-	-	-	-	-	-
A. L.	20	None	-	-	125	3,750	4%	-	1:16	1:8	1:4	-	1:16	1:32	-	1:4	-	-	-	-	1:4	-
A. L.	21	1	-	-	166	6,800	1%	-	-	-	-	-	1:32	-	1:4	-	-	1:32	-	-	-	-
A. L.	22	None	-	-	250	3,900	2%	-	1:2	-	-	-	-	-	-	-	-	-	1:32	1:32	1:4	-
A. L.	23	1	-	-	125	5,200	4%	+	-	-	1:32	1:16	1:4	1:4	-	-	-	-	-	-	1:4	1:4
A. M.	24	1,2,3	-	-	125	4,500	-	-	1:8	1:4	-	-	-	-	-	-	-	-	1:32	1:32	1:4	-
A. L.	25	None	-	-	200	6,000	-	-	-	-	-	-	1:16	1:32	-	-	-	-	-	-	1:4	-
A. L.	27	1,2	-	-	125	9,200	2%	-	1:4	1:8	-	-	-	-	1:32	1:16	-	-	-	-	-	-
A. M.	28	1	-	-	200	5,200	1%	-	-	-	-	-	1:8	-	-	-	-	-	-	-	1:32	
A. L.	29	1	-	-	200	7,600	3%	-	-	-	-	-	-	1:32	-	-	-	-	-	-	-	-
A. L.	30	1	-	-	125	5,950	7%	-	1:32	1:8	1:4	1:32	1:32	1:32	1:8	1:4	-	1:4	-	1:16	-	1:32
A. L.	31	None	-	-	125	4,100	15%	-	1:8	1:8	-	-	1:4	1:32	-	-	-	-	1:4	1:4	-	-
A. L.	32	1,3	-	-	125	5,100	4%	+	-	-	1:4	-	-	-	1:4	1:4	1:16	1:32	-	-	-	-
A. M.	33	None	-	-	200	4,500	-	-	-	-	-	-	-	-	1:8	1:32	-	-	-	-	1:16	1:8
A. L.	34	1	-	-	125	4,900	-	-	1:8	1:8	-	-	-	-	-	-	1:4	-	1:16	1:32	-	-
A. L.	35	1	-	-	166	5,700	26%	-	1:32	1:16	-	-	-	1:4	-	-	1:8	1:32	-	-	-	-
A. L.	36	None	+L	-	125	4,300	32%	-	-	-	-	-	-	-	1:16	1:32	1:4	-	1:16	1:32	-	-
A. L.	37	None	-	-	125	6,500	11%	-	-	-	1:4	1:4	-	-	-	-	1:4	-	-	-	1:32	1:16
A. L.	38	None	-	-	250	6,700	9%	-	-	-	-	-	-	-	-	-	1:16	1:32	1:8	1:4	-	-
A. L.	39	None	-	-	333	6,200	-	-	1:2	1:2	-	-	1:4	1:4	1:32	1:4	-	-	1:8	1:4	-	-
A. L.	40	1,2	-	-	166	2,700	-	-	1:4	1:2	-	-	-	-	-	-	-	1:4	1:8	1:16	1:4	-
A. L.	41	None	-	-	125	7,400	16%	-	1:8	1:4	1:8	1:8	1:4	1:8	1:32	1:32	1:4	1:4	1:8	1:8	1:16	1:32
A. L.	42	None	-	-	166	4,700	-	-	1:32	1:16	1:4	1:8	-	1:32	-	1:4	-	1:4	-	1:4	1:32	1:4
A. L.	43	None	-	-	166	7,600	32%	+	1:32	1:16	-	-	-	-	-	-	1:16	1:32	-	-	1:4	-
A. L.	44	1	-	-	125	4,500	6%	-	1:4	1:8	1:32	1:16	1:32	1:32	1:8	-	-	-	1:16	1:32	1:4	-
A. L.	45	1,2	-	-	125	4,100	-	-	1:16	1:4	1:4	1:4	1:8	1:4	1:8	1:4	1:4	1:4	1:4	1:8	1:16	1:8
A. L.	46	None	-	-	125	5,200	10%	-	-	1:8	-	-	1:32	1:16	-	-	1:16	1:32	-	-	1:8	-
A. L.	47	None	-	-	166	5,500	3%	-	1:8	1:16	-	-	1:16	1:32	1:4	1:4	-	-	-	-	-	-
A. L.	48	None	-	-	125	4,100	-	-	1:8	1:32	1:4	-	1:32	1:32	1:8	1:4	-	-	-	-	-	-
A. L.	49	None	-	-	333	5,900	2%	-	1:8	1:8	1:16	-	1:4	1:8	-	1:32	-	-	-	-	1:8	-
A. L.	50	None	-	-	125	5,900	-	-	1:16	1:64	-	-	1:16	1:4	-	-	1:32	1:32	-	-	-	1:4
			+	-	333	7,600	12%	-	-	-	-	-	-	-	-	-	-	-	1:16	1:32	1:8	-

1 = Ascaris ova
2 = Trichuris ova
3 = Entamoeba histolytica
Ano titre = Anti-streptolysin O titre
WBC = White blood cells
M = Microfilariae
T = Trypanosomes
L = Leishm.

TABLE 37

FREQUENCY OF ANTIBODY DISTRIBUTION IN THE SERA OF PATIENTS WITH HEART MUSCLE DISEASE (HMD) AND CONTROLS

Titre	HMD		CONTROLS	
	Number	%	Number	%
< 2	39	44	57	56
2	5	6	1	1
4	10	11	23	23
8	16	18	10	10
16	8	9	8	8
32	5	6	3	3
64	3	3	-	-
128	-	-	-	-
256	-	-	-	-
512	1	1	-	-
1024	1	1	-	-

control group had antibodies against Toxoplasma. This result was also not statistically significant (x^2 = 2.53; 0.2 > P > 0.1).

46.15% of the patients in the high socio-economic group in the study group had positive antibody titres against 64.52% of the patients in the low socio-economic group. Statistically, this was not significant (x^2 = 0.63; P > 0.5).

Although the above showed no significant difference in the rate and frequency of infection between patients with HMD and controls, two patients probably had toxoplasma cardiomyopathy. One of them (O.O, case 7, table 35) was a 23 year old trader (para 3 + 0) who three months after her last delivery had a febrile illness associated with headache which lasted for one month. This was followed by exertional dyspnoea, orthopnoea and subsequent swelling of both ankles and abdomen. She was seen 5 months after her symptoms started and was found to be in congestive cardiac failure. She had no murmurs but a loud, early third sound was audible at the apex. Her chest x-ray showed an enlarged heart with bilateral pleural effusion (fig. 18).

Her ECG showed sinus tachycardia and T wave inversions in leads II, III, aVF and V_6. Left heart cardiac catheterisation showed a left ventricular pressure of 100/20 mmHg and

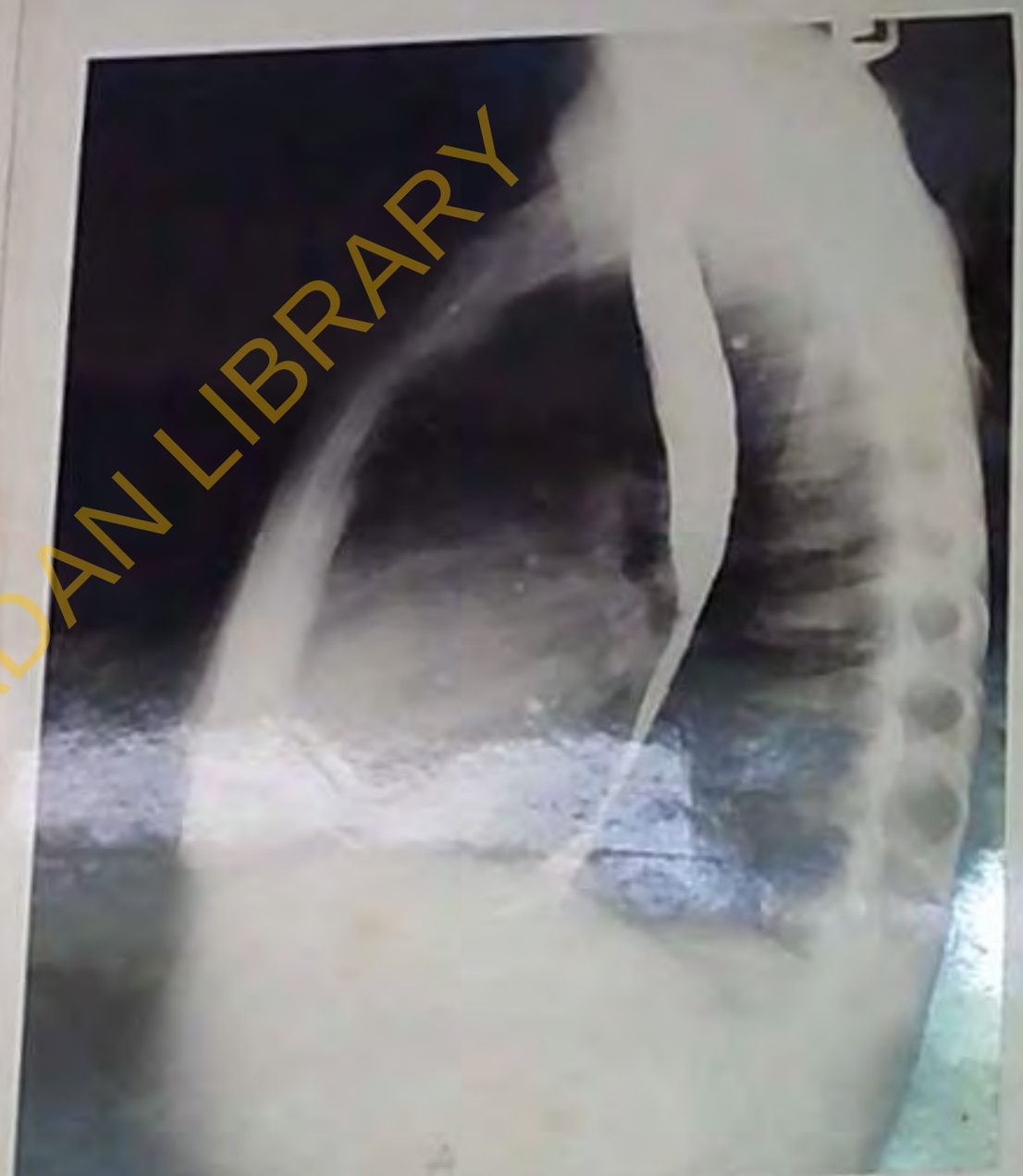

Fig. 18: The chest x-ray of case 7 showing an enlarged heart with bilateral pleural effusion.

aortic pressure of 100/60 mmHg. Left ventricular angiography (figure 19) showed mild mitral incompetence with a systolic ejection/fraction of 34.4%. An IVP showed good excretion with normal sized kidneys.

Her antibody titres against toxoplasma gondii were very high. The first titre was 1:1024 and the second titre, taken six weeks after, was 1:512. A third titre taken 4 months after the first was 1:256 (titre of 1:8 using the agglutination method is equivalent to 1:4000 dye test (Beverley et al, 1973).

She had no significant eosinophilia although ascaris ova were found in her stools. Her ASO titre was 166 Todd units.

She also had positive antibody titres to Coxsackie B_4 (initial titre 1:16, second titre 1:32) and Coxsackie B6 (initial titre 1:4, second titre 1:4).

While in the ward she had low-grade pyrexia which lasted two weeks and which did not respond to antimalarials. She also had persistent tachycardia despite adequate digitalisation. She subsequently developed tricuspid incompetence on follow-up.

The other patient (T.L case 10, table 35) presented in severe congestive cardiac failure with mitral and tricuspid incompetence. Her illness started with fever and headache

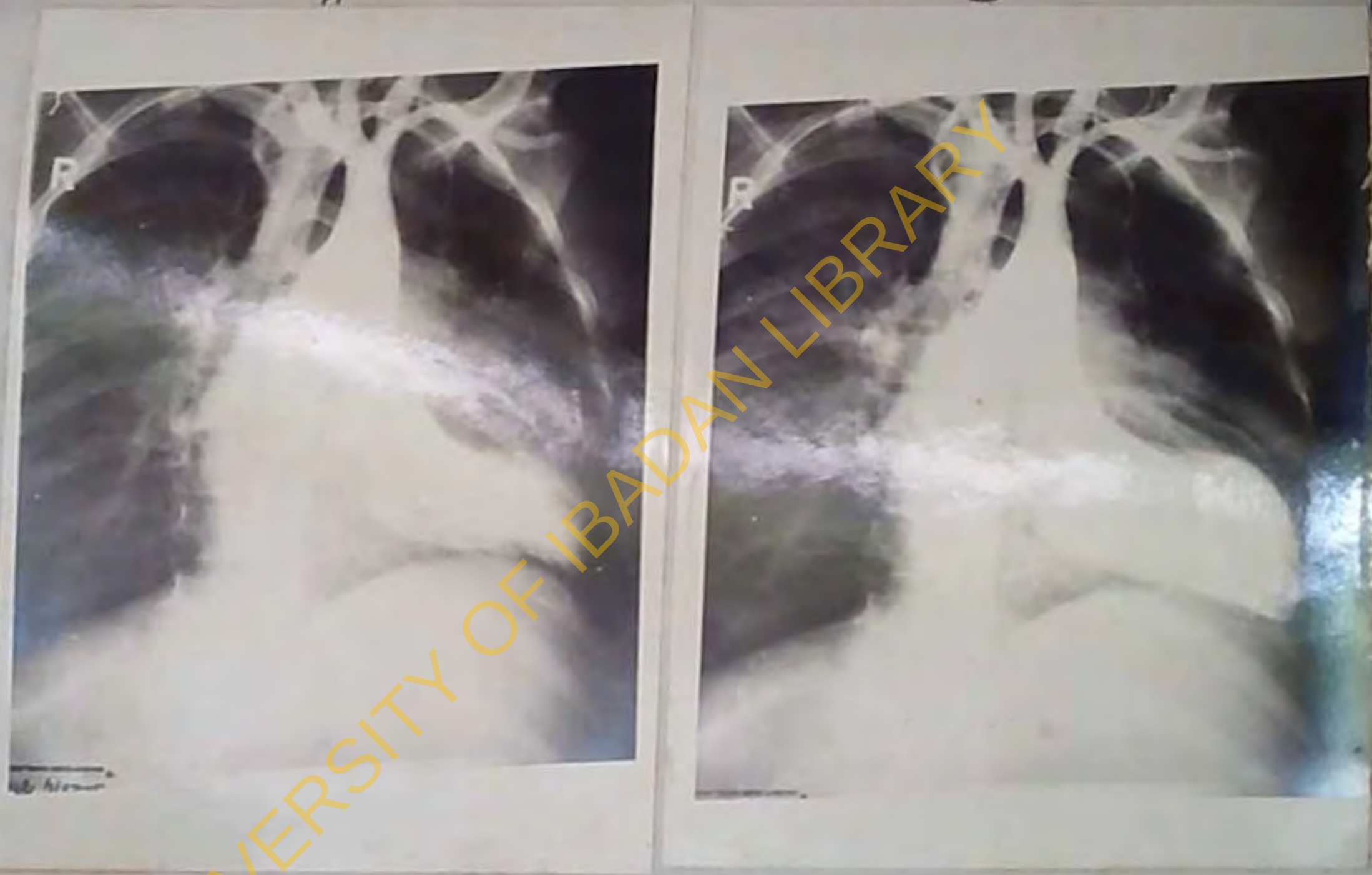

Fig. 19: The left ventricular angiogram of case 7 showing a slightly dilated left ventricle in diastole (B) and fairly good contraction in systole (A). There was mild mitral incompetence.

two months following the delivery of her 4th child. Her blood pressure was not raised; her ECG showed right bundle branch block and incomplete left anterior hemiblock. Her thiamine status was normal (TPP effect was 10.6%); her serum albumin was 3.8Gm. She had significant fourfold antibody fall (1:512 to 1:128) to Toxoplasma gondii but no significant rise or fall to the Coxsackie B viruses.

Trypanosoma cruzi: As the supply of Trypanosoma cruzi antigen was small, 108 sera chosen randomly from those with HMD and controls were tested. 36 were negative when the sera were tested undiluted; 72 showed anticomplementary reactions. On dilution to 1:4, 46 were negative while the remaining 62 showed anticomplementary reaction. 54 were negative on further dilution to 1:16.

Coxsackie B viruses: The number of pairs of specimen which had fourfold rise or fall to the viruses are shown in table 38. There was no significant difference between the study group and the controls. Similarly there was no significant difference between the study and the control groups of patients when the number of pairs of specimen showing fourfold rise or fall but excluding low titres i.e. 1:8 and below were compared (table 39).

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TABLE 38

PAIRS OF SPECIMEN OF PATIENTS WITH HEART MUSCLE DISEASE (HMD) AND CONTROLS THAT HAD FOURFOLD RISE OR FALL TO THE COXSACKIE B VIRUSES

COXSACKIE B VIRUS	HMD	CONTROLS
B_1	7	8
B_2	10	12
B_3	8	8
B_4	11	14
B_5	5	10
B_6	14	13
TOTAL	55 out of 240 pairs (20.45%)	65 out of 264 pairs (32.29%)

$X^2 = 0.20$ $P > 0.5$

TABLE 39

Those pairs showing fourfold rise or fall to Coxsackie B Viruses Excluding Titres

COXSACKE B VIRUS	HMD	CONTROLS
B_1	3	1
B_2	6	6
B_3	4	-
B_4	3	3
B_5	2	3
B_6	2	2
	20	15
	(8.33%)	(5.68%)

$\chi^2 = 1.37$ $\quad 0.2 > P > 0.3$

72.09% of the patients with HMD had a fourfold rise or fall to at least one of the Coxsackie B viruses. This was significantly different from the controls, 51.92% of whom had fourfold rise or fall to at least one of the viruses (x^2 = 4.03; 0.05 > P > 0.02).

13 out of 43 patients (30.23%) with HMD had at least a fourfold rise or fall to two or more of the Coxsackie B viruses. Compared with 19 out of 45 controls (42.22%), the result was not significant (x^2 = 1.37; 0.2 > P > 0.3).

58 out of 240 pairs (24.17%) of specimen of patients with HMD examined had at least a high titre (1.16 and above) compared with 21 of 264 pairs (7.95%) of specimen of controls. This result was statistically significant (x^2 = 25.00 P < 0.001).

There was no significant difference in the rate of infection between patients in the high and the low socio-economic groups (table 40).

Table 41 shows the frequency of antibody distribution in all the sera examined. Coxsackie viruses B_1, B_2, B_3 and B_6 were significantly present in the sera of patients with HMD compared with the controls.

One patient (S.F. case 28) had no serum reaction to any of the B virus group when he was first seen. During one of his clinic appointments, he complained of fever,

TABLE 40

COXSACKIE B VIRUSES - PATIENTS WITH FOURFOLD RISES OR FALL ACCORDING TO SOCIO-ECONOMIC GROUP

VIRUS	HIGH		LOW	
	No.	%	No.	%
B_1	2	12.5	5	12.82
B_2	4	25	6	15.38
B_3	4	25	4	10.26
B_4	2	12.5	9	23.08
B_5	-	-	5	12.82
B_6	4	25	10	25.64

$x^2 = 0.09$ $P > 0.5$

TABLE 40

COXSACKIE B VIRUSES - PATIENTS WITH FOURFOLD RISES OR FALL ACCORDING TO SOCIO-ECONOMIC GROUP

VIRUS	HIGH		LOW	
	No.	%	No.	%
B_1	2	12.5	5	12.82
B_2	4	25	6	15.38
B_3	4	25	4	10.26
B_4	2	12.5	9	23.08
B_5	-	-	5	12.82
B_6	4	25	10	25.64

$x^2 = 0.09$ $P > 0.5$

TABLE 41

COXSACKIE B VIRUSES - FREQUENCY OF ANTIBODY DISTRIBUTION IN THE SERA OF PATIENTS WITH HEART MUSCLE DISEASE (HMD) AND CONTROLS

TITRES	B1				B2				B3				B4				B5				B6			
	HMD		CONTROL		HMD		CONTROL		HMD		CONTROL		HMD		CONTROL		HMD		CONTROL		HMD		CONTROL	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
< 4	60	72	81	84	37	45	62	63	50	60	72	75	50	60	66	69	50	60	71	74	51	61	74	77
4	14	13	9	9	13	16	17	17	14	17	13	14	15	18	20	21	13	16	13	14	17	20	17	17
8	3	4	5	5	5	6	7	7	5	6	7	7	3	4	7	7	5	6	4	4	3	4	3	2
16	3	4	1	1	9	11	4	4	5	6	3	3	5	6	1	1	6	7	3	3	5	6	1	1
32 or greater	6	7	0	0	19	23	6	6	9	11	1	1	10	12	2	2	9	11	5	5	7	8	1	1

Levels of significance:

B1 $X^2 = 3.89$; $0.05 > P > 0.02$

B2 $X^2 = 7.21$; $0.01 > P > 0.001$

B3 $X^2 = 4.47$; $0.05 > P > 0.02$

B4 $X^2 = 1.41$; $0.3 > P > 0.2$

B5 $X^2 = 3.82$; $0.10 > P > 0.05$

B6 $X^2 = 5.17$; $0.05 > P > 0.02$

malaise and dizziness and was found to be in congestive cardiac failure. His ECG showed supraventricular tachycardia (fig. 20) and his serum was positive (1:32) to Coxsackie virus B_2. Subsequent titres were higher than 1:32. Unfortunately, no isolation from the stool was done. However, he was considered to have had a Coxsackie B2 virus myocarditis.

Fresh stools of 20 of the patients with HMD were examined for Coxsackie B viruses. No isolation of any of the viruses was made.

OTHER INFECTIONS: Ascaris ova were found in the stools of 21 patients with HMD; 9 also had hookworm ova. 4 had trichuris ova while 1 had entamoeba histolytica. 28 patients had no parasites in their stools. In a study of 50 consecutive patients without any heart disease, 31 had ascaris ova, 9 hookworm ova, 7 trichuris ova. None had entamoeba histolytica.

2 patients with HMD had microfilariae on blood film examination. ASO titre was greater than 333 Todd units in 6 patients with HMD and 2 patients with organic mitral incompetence.

3 patients had positive VDRL although Reiter protein complement fixation test was negative.

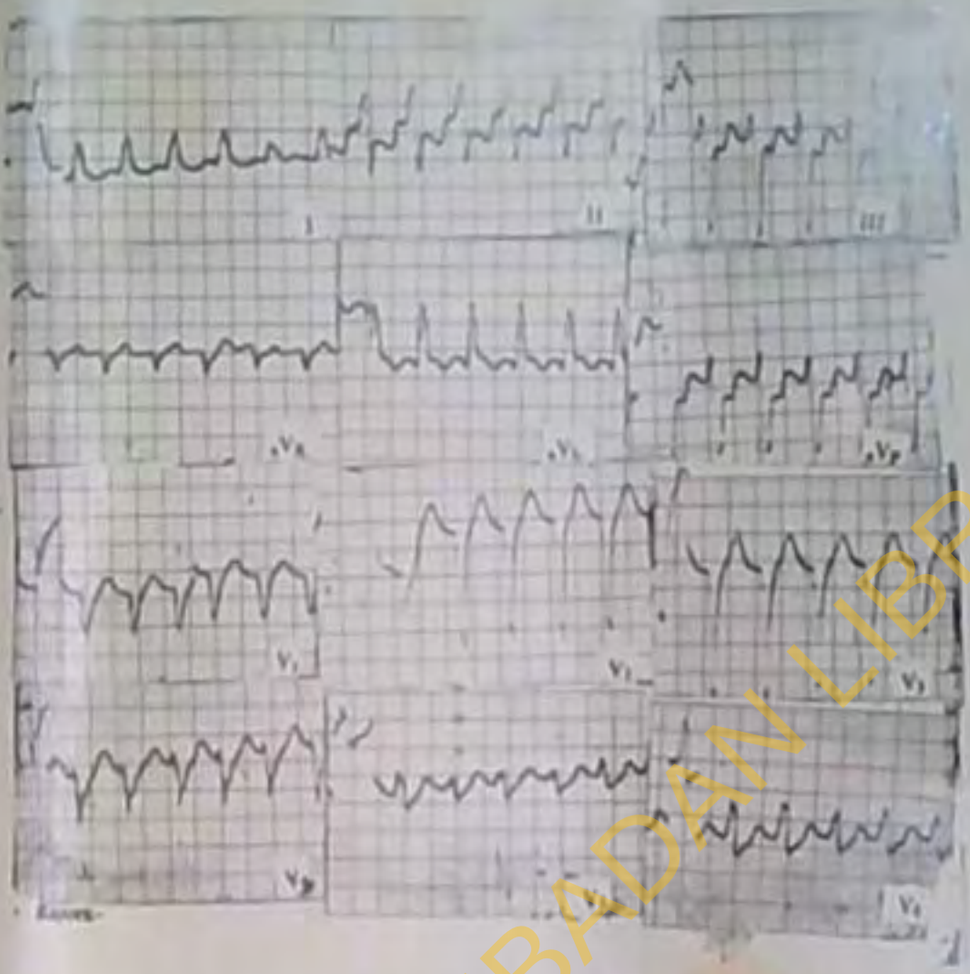


Fig. 20: The electrocardiogram of case 28. This was recorded during his second admission with what was considered to be an acute myocarditis from Coxsackie virus B2 infection.

17 (38.6%) patients with HMD had eosinophilia of 5% or more. 2 (33%) of the patients with organic mitral incompetence also had significant eosinophilia. In a study of 50 consecutive patients without any heart disease 35.2% of them had eosinophilia greater than 5%.

One patient had schistosoma mansoni ova on histological examination of her rectal biopsy. No ova were found in her stools.

None of the patients had ova of S. haematobium in their urine.

Amyloid: None of the patients had amyloid deposits in the rectal mucosa. No amyloid deposits were found in 7 cases who had liver biopsy.

Endocrine disorders: One patient (Y.A. case 11, table 43) was hypothyroid. He presented in congestive cardiac failure with a third sound but no murmurs. His chest x-ray showed an enlarged heart (fig. 21). His ECG showed low voltage complexes (fig. 22), q waves in the inferior leads, an extreme axis deviation and right ventricular hypertrophy. He, however, had no bradycardia.

His T_3-uptake was raised at 160 but he died before other thyroid function tests could be done. No consent was given for post-mortem examination.

TABLE 42

Results of other Investigations performed on Patients in Group A1

Patient	No.	Serum Iron (mg %)	TIBC (mg %)	% Sat.	^{59}Fe uptake	Rectal biopsy	Liver biopsy
T.O.	1	50	490	10.20	100	Negative	
L.L.	2	70	447	15.7	90	"	Granulomatous reaction
S.E.	3	35	410	9	110	"	
A.O.	4	-	-	-	112	"	
E.O.	5	134	459	29.19	104	"	Granulomatous reaction
E.O.	6	292	744	39.25	105	"	

TIBC = Total Iron binding capacity.

TABLE 43

Results of Other Investigations performed on Patients in Group A2

Patient	No.	Serum Iron (mg %)	TIBC (mg %)	% Sat.	^{59}Fe uptake	Rectal biopsy	Liver biopsy
O. O.	7	50	869	5.75	106	Negative	Granulomatous reaction
V. E.	8	150	520	29.6	100	"	
J. F.	9	149	519	28.6	102	"	Normal
T. I.	10	185	493	60.06	100	"	Non-specific reactive hepatitis with hepatofibrosis.
T. L.	11	8	446	1.79	160	"	
T. O.	12	104	3 73	27.9	110	"	Regeneration +. Fat globules + Congested liver.
T. O.	13	200	400	35	109	"	
O. L.	14	70	513	13.64	110	"	
E. E.	15	98	450	21.4	100	"	
L. I.	16	-	-	-	104	"	
O. O.	17	435	805	54.03	98	"	
E. I.	18	-	-	-	100	"	

TIBC = Total Iron Binding Capacity.

TABLE 44

Results of other investigations performed on patients in groups A1, B1 and B2

Patient	No.	Serum Iron (mg %)	TIBC (mg %)	% Sat.	ESR mm/hr	Rectal biopsy for amyloid	Liver biopsy
A. O.	19	-	-	-	100	Negative	
J. L.	20	-	-	-	101	"	
Z. A.	21	111	498	22.28	110	"	
A. O.	22	90	450	20.00	104	"	
B. T.	23	472	766	61.62	104.2	"	
A. O.	24	151	530	28.49	105	"	
I. K.	25	130	465	27.95	111	"	
M. A.	26	-	-	-	99	"	
O. S.	27	-	-	-	90.6	"	
S. F.	28	120	370	32.4	102	"	Small amount of iron in hepatic cells Regeneration +. No alcoholic hyaline
E. L.	29	-	-	-	104	"	
M.L.	30	-	-	-	103	Negative for amyloid Had schistosoma ova	
M. E.	31	-	-	-	103.2	Negative	
R. S.	32	65	397	16.4	105	"	
S. M.	33	243	340	71.26	104	"	
L. A.	34	-	-	-	102	"	
J. O.	35	58	110	52.72	101	"	
S. O.	36	100	530	18.59	100.6	"	
J. S.	37	120	400	30	99.8	"	
B. O.	38	71	439	16.17	100	"	
O. O.	39	139	560	24.3	101.1	"	
J. U.	40	-	-	-	101	"	
S. E.	41	99	450	22	108	"	
R. E.	42	63	333	18.9	108	"	
L. O.	43	132	527	25.05	109	"	
S. A.	44	110	510	21.57	110	"	
L. T.	45	33	451	7.32	107.7	"	
B. O.	46	73	397	18.86	106.2	"	
E. T.	47	88	472	18.64	104.6	"	
A. A.	48	89	350	25.42	105	"	
A. O.	49	251	601	36.05	106	"	
A. B.	50	223	668	33.38	103.2	"	

TIBC = Total iron binding capacity.

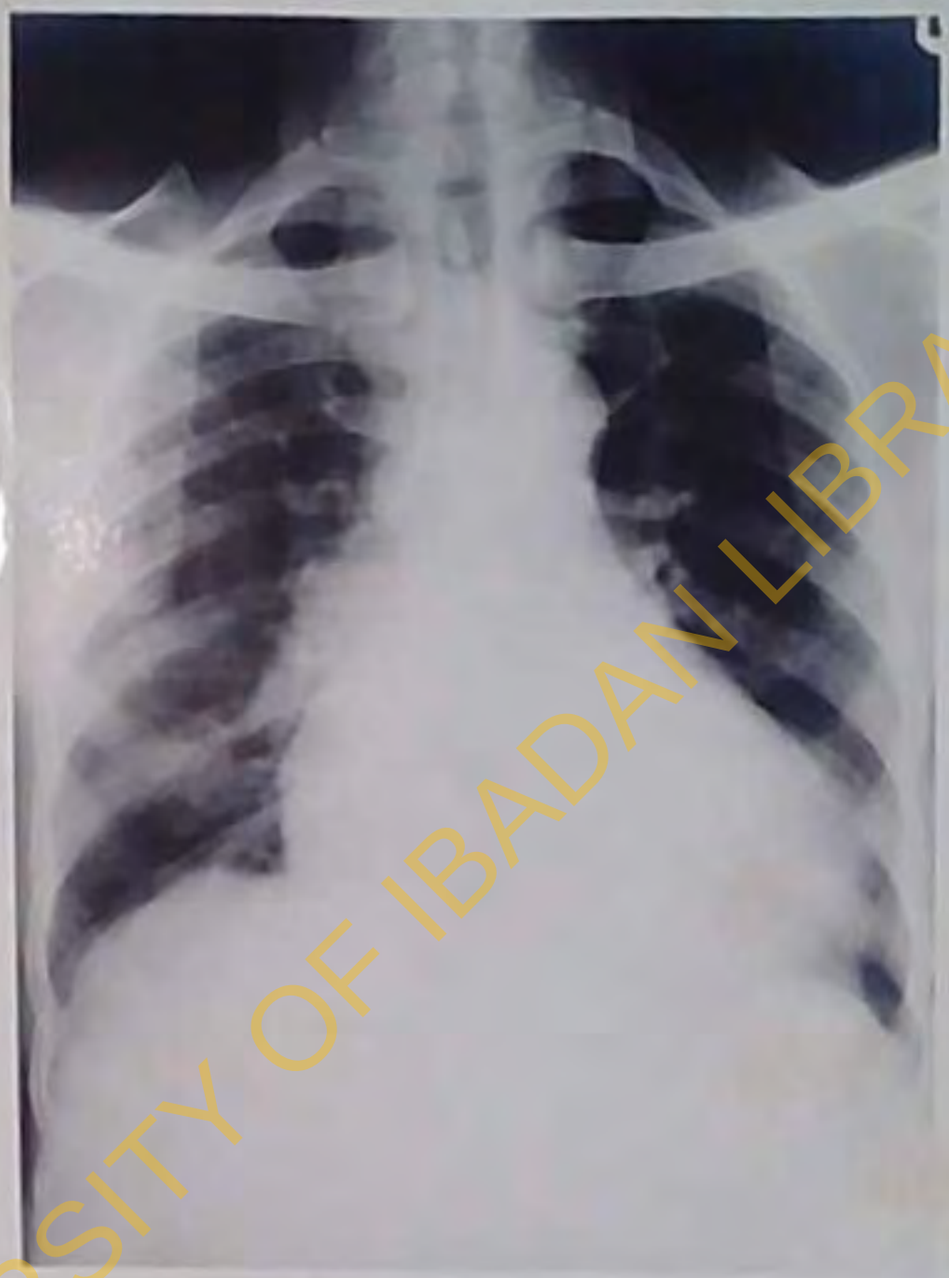


Fig. 21: Chest x-ray of case 11 with hypothyroidism with cardiomegaly.

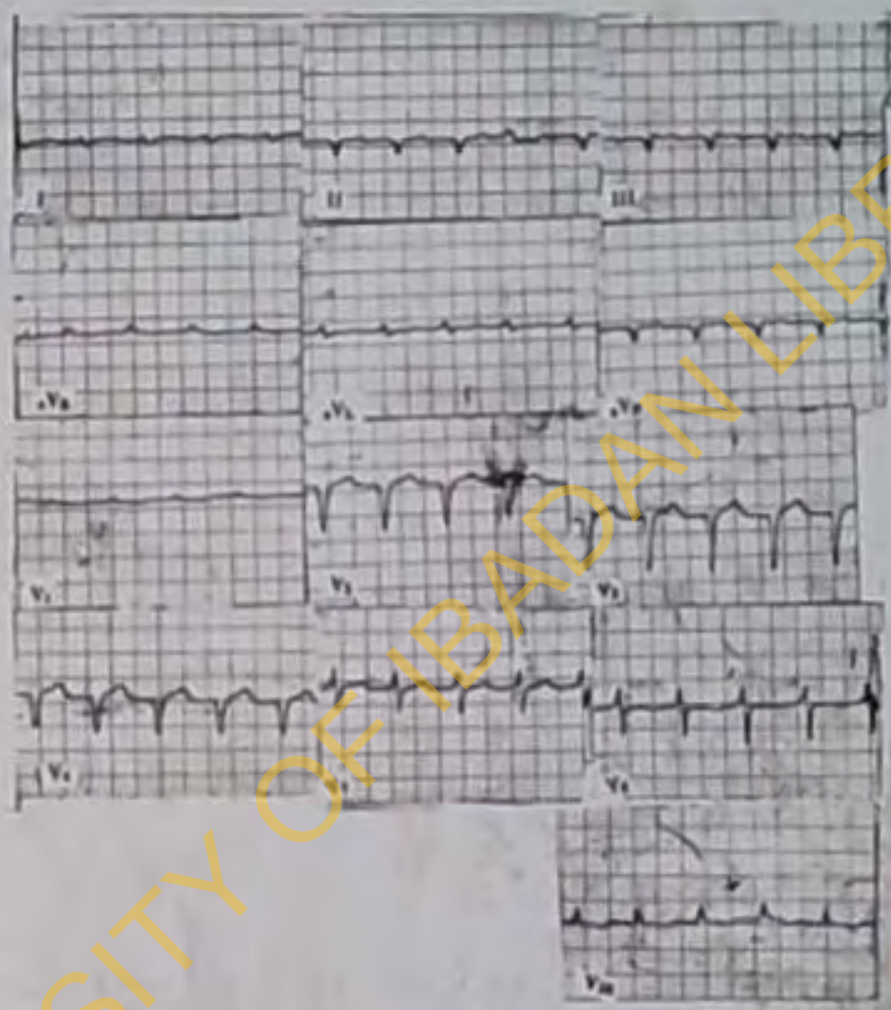


Fig. 22: The electrocardiogram of case 11 with hypothyroidism. It shows a low voltage QRS complexes, q waves in leads II, III and aVF and right ventricular hypertrophy.

Iron: 8 patients with HMD and 1 with organic mitral incompetence had raised serum iron levels (above 150ug%). The total iron-binding capacity was also higher than 450µg% in 19 patients with HMD and 3 patients with organic mitral incompetence. 3 patients with HMD had percentage saturation above 55%; none of the patients with organic mitral incompetence had high saturation. However, none of the patients had other signs suggestive of haemochromatosis.

Liver biopsy: Liver biopsy was performed in 7 patients, two of whom had organic mitral incompetence. 3 showed granulomatous reaction, one was normal while the findings in the remaining 3 were non-specific. All the 3 patients who showed granulomatous reaction had high titres against toxoplasma gondii.

OTHER CLINICAL FEATURES:

History:

Chest Pain: 22 (50%) patients with HMD and 5 patients (83%) with organic mitral incompetence gave a history of chest pain at the onset of their illness. In 13 patients with HMD and 3 patients with organic mitral incompetence, the chest pain was a vague discomfort and not typically anginal. The remaining patients had pleuritic type of chest pain.

Febrile illness before symptoms of heart failure:

17 patients (39%) with HMD and 3 patients (50%) with organic mitral incompetence volunteered a history of febrile illness prior to onset of the symptoms. The majority however, could not remember the interval between their febrile illness and the onset of their symptoms of heart failure.

Paraesthesiae: 17 patients (39%) with HMD gave a history of paraesthesiae of both hands and feet. None of them had objective signs of peripheral neuropathy. All the 17 patients were thiamine deficient.

Parity: 20 (83%) of the 24 female patients with HMD have had 5 pregnancies and above. One (R.S. case 32 table 44) had never been pregnant. Three patients had symptoms of heart failure within six months of delivery. Two of them had toxoplasma cardiomyopathy (O.O case 7, T.L. case 10, Table 43) and has previously been described.

Family History: Two patients with HMD belonging to group B1 had a strong family history of hypertension. One other female patient in group B1 had a husband who was hypertensive; both of them drank alcohol excessively.

Fever: Two patients were febrile on admission. One of them (O.O case 7, Table 43) a female, has been described previously as a possible case of toxoplasma cardiomyopathy.

The other (J.S. case 37, table 44) was found to have an acute exacerbation of chronic bronchitis. He had smoked cigarrettes excessively for over 10 years and also drank heavily.

Native Medication: 22 patients (50%) with HMD took native medicine (agbo) at the onset of their illness. 2 belonged to the high socio-economic group while 20 belonged to the low socio-economic group. 4 patients with organic mitral incompetence also took 'agbo' at the onset of their illness.

Hb. Genotype: 10 patients had Hb Genotype AS. One other patient had Hb Genotype AC; the rest were AA.

Cerebro-vascular accident: Two patients (both in group B_1) had cerebrovascular accidents thought to be embolic. Both of them partially recovered but left disabled from residual hemipareses.

ELECTROCARDIOGRAM (ECG): Tables 45-47

Group A1: 5 of the 6 patients in this group were in sinus rhythm on admission. The remaining patient had atrial fibrillation. None of them had ventricular arrhythmias. Four had left atrial enlargement; one had right atrial enlargement in addition. Their P-R intervals ranged between 0.12 and 0.20 seconds (mean = 0.15 seconds). Their QRS duration and axis were also normal (QRS axis ranged between + 54° and + 88°; mean = 76.2). 4 of them had left ventricular hypertrophy using the criteria of Sokolow and Lyon (1949). ST-T changes were present in 5 patients; 3 had Q-Tc higher than 0.44 secs.

TABLE 45

The Electrocardiographic Changes in Group A1 Patients

Name	Rate	Rhythm	VES	ASE	LAE	RAE	P-R	QRS dur.	QRS axis	LVH	RVH	LBBB	RBBB	R/S V_5	R/S V_6	ST-T	Low T	Q-To	Remarks
L. L.	120	Sinus	-	-	-	-	0.14	0.06	+85°	+	-	-	-	18/0	17/0	II,III,aVF, V4-V6	I, aVL	0.53	
G. E.	105	Sinus	-	-	+	-	0.2	0.04	+87°	-	-	-	-	11/0	18/0	V_1 - V_3	III, aVF	0.46	
A. O.	140	Sinus	-	-	+	-	0.12	0.06	+80°	+	-	-	-	16/0	20/2	II, III, aVF	aVL	0.43	
I. O.	100	Sinus	-	-	+	-	0.16	0.10	+54°	+	-	-	-	25/0	25/0	V_1 - V_3	aVL	0.52	
T. O.	96	A. F.	-	-	-	-	0.12	0.04	+60	-	-	-	-	11/1	9/0	I, aVL, V_1 - V_6	-	0.41	
E. O.	110	Sinus	-	-	+	+	0.14	0.08	+83°	+	-	-	-	28/5	12/1	-	-	0.39	

LAE = Left atrial hypertrophy
RAE = Right " "
VES = Ventricular extrasystoles
ASE = Atrial extrasystoles
LBBB = Left bundle branch block
RBBB = Right bundle branch block
LVH = Left ventricular hypertrophy
RVH = Right " "

TABLE 46

The Electrocardiographic Changes in Group A2 patients

Name	Rate	Rhythm	VES	ASE	LAE	RAE	P-R	QRS dur.	QRS axis	LVH	RVH	LBBB	RBBB	R/S V_5	R/S V_6	ST-T	Low T	Q-To	Remarks
J. P.	110	Sinus	-	-	-	-	0.20	0.04	-52°	-	-	-	-	17/5	10/6	I, aVL, V4 - V6, ST	III, aVF	0.41	
L. L.	100	Sinus	++	+	+	+	0.18	0.08	+82	-	-	-	-	5/0	12/0	V5 - V6	I,II,III,aVF,aVL	0.43	
T. O.	120	Sinus	-	-	+	-	0.16	0.06	-42	-	+	-	-	16/0	14/0	I, aVL, V4-V6	II, aVF	0.47	Low voltage
O. O.	90	Sinus	++	-	+	-	0.18	0.08	-18	-	-	-	-	4/3	8/4	aVL, V6	II, III, aVF	0.51	
K. A.	105	Sinus	-	-	+	-	0.16	0.06	-44	-	-	-	-	14/0	16/0	I, aVL, V4 - V6	II, aVF	0.41	
O. F.	100	Sinus	-	-	-	-	0.15	0.06	+80	-	-	-	-	14/2	15/1	aVL, V6	II, III, aVF	0.42	
I. A.	96	Sinus	+	-	+	-	0.20	0.08	-[illegible]	-	-	-	-	13/0	8/0	-	III leads	0.42	
I. A.	120	Sinus	-	-	-	+	0.16	0.04	+105°	-	+	-	-	12/4	12/7	III, aVF	-	0.44	
O. O.	150	Sinus	-	-	+	-	0.10	0.04	+[illegible]°	+	-	-	-	17/0	12/0	II, III, aVF, V6	I, V4, V5	0.[illegible]	
T. A.	56	Sinus	-	-	-	-	0.28	0.10	-60°	-	-	-	-	3/5	3/5	-	I,II,III,aVR,aVL, aVF, V4-V6	0.[illegible] sec.	
F. L.	92	Sinus	-	-	-	-	0.16	0.14	-12°	-	-	-	+	3/1	2/1	V1 - V6	III, aVF	0.53	Low voltage
A. I.	100	Sinus	-	-	+	-	0.18	0.08	-43°	+	-	-	-	22/0	22/0	I,II,III,aVL,aVF,V4-V6	-	0.47	
																		0.44	

LAE = Left atrial hypertrophy
RAE = Right atrial hypertrophy
VES = Ventricular extrasystoles
ASE = Atrial extrasystoles
LBBB = Left bundle branch block
RBBB = Right bundle branch block
LVH = Left ventricular hypertrophy
RVH = Right ventricular hypertrophy

TABLE 47

The Electrocardiographic Changes of Patients in Groups A1, B1 and B2

Name	Rate	Rhythm	P1V1	LAT	LAH	RAH	P-R	QRS dur.	QRS axis	LVH	RVH	LBBB	RBBB	S/3 T3	S/3 V6	ST-T	Low-Ta	Q-Ta	Remarks
A.O.	90	Sinus	-	-	+	-	0.22	0.08	+80°	+	-	-	-	16/0	16/0	II, III, aVF, V4-V6	I, aVL	0.43 sec.	
A.O.	110	Sinus	-	-	+	-	0.14	0.08	-80°	-	+	-	-	3/7	4/6	-	II, III, aVF	0.46 sec.	
E.A.	88	Sinus	-	-	+	-	0.16	0.16	+16°	-	-	+	-	12/0	16/0	-	-	0.51 sec.	
A.O.	90	Sinus	-	-	+	-	0.16	0.10	+45°	+	-	-	-	25/0	24/0	III	aVF	0.51 sec.	
A.O.	110	Sinus	-	-	+	-	0.20	0.08	-20°	+	-	-	-	8/7	9/7	I, aVL	II, III	0.44 sec.	
J.A.	96	Sinus	+	-	+	-	0.16	0.14	-45°	+	-	-	+	20/4	22/5	I, aVL, V1-V6	-	0.5 sec.	
T.E	110	Sinus	+	-	-	-	0.2	0.16	+140°	-	+	+	-	1/14		II, III, aVF	I, aVL	0.38 sec.	
I.T.	100	Sinus	-	-	-	-	0.16	0.04	-3°	-	-	-	-	5/0	8/0	I, II, aVL, aVF, V5-V6	-	0.50 sec.	
E.T.	100	Sinus	-	-	+	-	0.16	0.10	-30°	+	-	-	-	23/7	24/1	I, aVL, V5-6 ST	-	0.43 sec.	
E.A.	100	Sinus	-	+	+	-	0.14	0.08	+30°	-	-	-	-	12/0		I, II, aVL, V5-V6	III, aVF, V6	0.42 sec.	
S.F.	110	Sinus	+	-	+	-	0.16	0.08	-70	+	-	-	-	25/0	22/0	I, II, aVL, V5-V6	V6, aVF	0.42 sec.	
S.L.	160	Junctional	-	-	-	-	0.14	0.04	+60°	-	-	-	-	15/0	12/0	V6	-	0.34 sec.	
E.E.	110	Sinus	++	-	+	-	0.20	0.08	+23°	+	0	-	-	15/0	20/0	I, II, III, aVF, V5-V6.	-	0.43 sec.	
B.O.	100	Sinus	+	-	+	+	0.16	0.06	+2°	+	-	-	-	25/0	24/0	I, II, aVL, aVF, V4-V6	-	0.44 sec.	
E.A.	120	Sinus	-	-	-	-	0.12	0.06	+36°	+	-	-	-	33/1	29/0	I, II, III, aVF, V4-V6	-	0.46 sec.	
I.O.	96	Sinus	-	+	+	-	0.18	0.06	+12	+	-	-	-	14/3	9/0	I, aVL, V4-V6	-	0.45 sec.	
E.E.	100	Sinus	+	-	+	-	0.16	0.08	-70°	-	-	-	-	7/9	2/10	II, III, aVF, V4-V5	aVL	0.52 sec.	
A.A.	150	Sinus	-	-	+	-	0.12	0.04	-30°	+	-	-	-	19/3	24/0	I, II, aVL, V4-V6	III, aVF	0.49 sec.	
E.E.	160	Sinus	-	-	+	+	0.12	0.08	-15	+	-	-	-	27/2	26/2	-	II,III,aVF,V6	0.42 sec.	
L.A.	110	Sinus	-	-	+	-	0.14	0.08	+105°	+	+	-	-	10/16	11/4	II, III, aVF	-	0.52 sec.	
J.O.	130	Sinus	-	-	+	-	0.16	0.08	-21	+	-	-	-	20/0	19/0	I, aVL, V4-V5	-	0.48 sec.	
E.O.	105	Sinus	-	-	+	-	0.20	0.10	-66	+	-	-	-	15/0	12/0	-	I, aVL	0.11 sec.	
J.E.	125	Sinus	-	-	+	-	0.14	0.04	+105	-	+	-	-	9/2	5/4	V1 - V4	I,aVL,III,aVF	0.44 sec.	
E.O.	100	Sinus	-	-	-	-	0.16	0.14	+54	-	-	+	-	2/0	4/0	II, III, aVF	V5 - V6	0.47 sec.	
O.O.	90	Sinus	-	-	+	-	0.24	0.08	-30°	+	-	-	-	7/8	25/6	II, III, aVF, V6	V5, I, aVL	0.44 sec.	
J.T.	110	Sinus	-	-	+	-	0.16	0.04	+03	-	-	-	-	10/3	6/0	-	-	0.44 sec.	
E.I.	120	Sinus	-	-	+	+	0.16	0.04	-90°	-	+	-	-	11/11	7/7	V1-V6	I,II,III,aVL,aVF	0.43 sec.	
E.E.	96	Sinus	+	-	-	-	0.18	0.14	-40°	-	-	-	+	8/3	6/2	V1-V5	-	0.50 sec.	
A.T.	86	Sinus	-	-	+	-	0.14	0.08	-30	+	-	-	-	16/6	22/2	I,aVL,II,V4-V5	III, aVF	0.43 sec.	
E.A.	105	Sinus	+	-	+	-	0.18	0.08	-23°	+	-	-	-	29/2	20/0	-	I,II,III,aVL, aVF, V1-V5	0.43 sec.	
E.T.	110	Sinus	+	-	+	-	0.16	0.04	-43°	+	-	-	-	34/5	32/0	I, aVL, V5-6	V4	0.47 sec.	
A.E.	80	Sinus	-	-	+	-	0.14	0.08	+30°	+	-	-	-	19/3	17/0	I,II,III,aVF,aVL, V1-V5	-		

LAH - Left atrial hypertrophy RAH - Right atrial hypertrophy VES - Ventricular extrasystoles ASS - Atrial extrasystoles

LBBB - Left bundle branch block RBBB - Right bundle branch block LVH - Left ventricular hypertrophy RVH - Right ventricular hypertrophy.

Group A2: All the patients in this group were in sinus rhythm. 3 had ventricular extrasystoles; 1 of these 3 patients had atrial extrasystoles in addition. 7 patients had left atrial enlargement and 2 right atrial enlargement. The P-R interval of 1 patient was prolonged beyond 0.20 seconds; 1 had right bundle branch block and 1 left anterior hemiblock. Only 2 patients had left ventricular hypertrophy. 1 had right ventricular hypertrophy. One had q waves in the inferior leads though he never had chest pain. All the patients had ST-T changes while the Q-Tc was prolonged beyond 0.44 seconds in 4 patients. Two patients had low voltage complexes.

Group A3, B1 and B2: All the patients in these groups except one were in sinus rhythm. 9 had ventricular extrasystoles, 2 atrial extrasystoles. 26 left atrial enlargement and 3 right atrial enlargement. The P-R interval was prolonged in 2 patients, 3 had left bundle branch block and 2 right bundle branch block. 5 of them had left anterior hemiblock. One had left posterior hemiblock and another had significant q waves in the inferior leads though he had never complained of chest pain. It was thought to be due to myocardial fibrosis which has been reported to produce q waves similar to myocardial infarction (Bahl and Massie, 1972). 20 had

left ventricular hypertrophy while 5 had right ventricular hypertrophy. ST-T changes were present in all the patients with the exception of two. 23 patients had prolonged Q-Tc.

RADIOLOGICAL FINDINGS (tables 48-51)

Cardio-thoracic Ratios: The mean cardio-thoracic ratio of the patients in group A1 was 0.63 ± 0.059, that of group A2 was 0.66 ± 0.064 and that of groups A3, B1 and B2 0.66 ± 0.065. There was no statistically significant difference between the three groups ($P > 0.05$). However, there was a significant decrease in the heart sizes of those who had repeat chest x-rays at 6 months and 1 year.

Aortic Diameter: The mean aortic diameter on plain film of patients in group A1 was 5.73 cm ± 0.045 while that of group A2 patients was 5.78cm ± 1.29. The mean aortic diameter of patients in groups A3, B1 and B2 was 6.98cm ± 0.83. This value was significantly higher than those of groups A1 and A2 ($P < 0.05$). There was no significant difference between the values obtained for group A1 and group A2 patients.

On angiography, the mean aortic diameter of patients in group A1 at the root level was 3.47 cm ± 0.43, that of group A2 was 3.70cm ± 0.5 while that of patients in groups A3, B1 and B2 was 4.01 cm ± 0.38. This latter value was significantly higher than that of group A1 ($P < 0.05$) but

TABLE 40

THE RADIOLOGICAL STUDIES IN GROUP A1 PATIENTS

Name	Surface Area	C. T. RATIOS			Aortic diameter (plain film)	Aortic diameter (angios)			Heart Volume (Plain film)			Heart Volume angios		W	I/I	EF		
		Admission	6/12	1 yr. A +		Root level	Mid cav.	Mid dcav.	Admission	6/12	1 yr. A +	[illegible]	[illegible]					
L. L.	1.8	0.54	0.57	0.60	5.8cm.	3.6cm.	4.3cm.	2.2cm.	342.2	307.0	400.4	[illegible]	165.8	1.2cm	[illegible]	67%		
O. E	1.50	0.67	0.57	0.64	6.0cm.	4cm.	3.6cm.	2.2cm.	697.3	615.9	587	[illegible]	220.5	1.27	[illegible]	73.2		
E. C.	1.44	0.61	0.51	0.67	6.2cm.	3cm.	3.6cm.	2.5cm.	740.5	670.1	[illegible]	201.4	400.7	1.23	[illegible]	[illegible]		
I. O.	1.75	0.66		0.65	5.5cm.	4cm.	3.6cm.	2.5cm.	476.3		[illegible]	118.1	302.1	1.6	[illegible]	65		
K. C.	1.26	0.59			5.7cm.	3cm.	3.4cm.	2.5cm.	800.3			200.1	470.6	1.7		70		
A. C.	1.35	0.72			4.8cm.	3.2cm.	3.6cm.	2.4cm.	794.2			70.5	250.6	1.4		72		

W = Left ventricular wall thickness. EF = Ejection fraction

TABLE 42

THE RADIOLOGICAL STUDIES IN GROUP A2 PATIENTS

Name	Surface Area	C. T. RATIOS			Aortic diameter (plain film)	Aortic diameter (angios)			Heart Volume (Plain film)			Heart Volume angios		W	I/I	EF		
		Admission	6/12	1 yr. A +		Root level	Mid cav.	Mid dcav.	Admission	6/12	1 yr. A +	[illegible]	[illegible]					
J. P.	1.75	0.68	0.53		7.2cm.	4.2cm.	4.[illegible]cm.	3.1cm.	877.2	696.9		234.3	340.1	0.83	[illegible]	55.8		
E. L.	1.70	0.65		0.64	7.2cm.													
T. C.	1.7	0.59			5.6cm.	4.1cm.	3.4cm.	2.4cm.	866.5		784.2							
C. C.	1.7	0.74	0.70	0.77	6.5cm.	3.2cm.	3.6cm.	2.5cm.	990.8			276.3	314.7	0.59	[illegible]	53.2		
V. E.	1.35	0.68			6.4cm.	4.6cm.	4.6cm.		852	707.8	189.1	325.6	470.8	1.19	[illegible]	74.7		
C. A.	1.60	0.77			5.6cm.				804.1			188.8	322.4	0.78	[illegible]	67.6		
B. E.	1.72	0.62			3.4cm.				1030.6			360.4	399.2	0.63	[illegible]	7.7		
C. C.	1.62	0.60		0.51	3.7cm.	3.2cm.	2.6cm.	2.1cm.	600.5			92.5	199.8	2.21	[illegible]	69.7		
T. A.	1.77	0.67			7.5cm.	3.7cm.	2.9cm.	2.4cm.	971.1		629.9	77.8	198.7	1.07	[illegible]	56.4		
T. L.	1.62	0.60	0.50		5.7cm.				871.2									
L. I.	1.35	0.68			5cm.	3cm.	3.6cm.	2.3cm.	461.0	419.1		83	207	0.93	[illegible]	59.2		
F. C.	1.76	0.52			5.8cm.	3.5cm.	3.5cm.	2cm.	640.8			237.8	317.3	1.11	[illegible]	3.8		
									433.7									

W = Left ventricular wall thickness. EF = Ejection fraction.

THE RADIOLOGICAL FINDINGS IN PATIENTS BELONGING TO GROUPS A3, B1 AND B2

NAME	SURFACE AREA	CARDIO-THORACIC RATIOS			Aortic diameter (Plain film)	Aortic diameter (angios)			Heart Volume (Plain film)			Heart Volume angios (V)		W	V/W	EF	RENAL SIZE	
		ADMISSION	6/12	1 yr. & +		Root level	Mid asc.	Mid desc.	Admission	6/12	1 yr. & +	SYST.	DIAST.				Right	Left
A. O.																		
A. O.	1.74	0.58	0.61		7.3cm.				624.2	520.9							L = 10.3 B = 5.5	L = 10.3 B = [illegible]
E. A.	1.82	0.57	0.65	0.80	5.0cm.	4cm	4.3cm	2.7cm	576.4	522.0	456.2	268.4	335.2	0.5[illegible]	S = 305.3 D = 301.3	205	L = 10.3cm B = 4.1cm	L = [illegible] B = [illegible]
A. O.	1.56	0.71	0.69		8.0				795.4	700.0							L = 10.[illegible]cm B = 4.[illegible]	L = 1[illegible] B = [illegible]
A. O.	1.63	0.71	0.66	0.63	6.7cm	4.1cm	4.5cm		646	623.1	530.6	725.8	[illegible]	0.60	S = 1075.6 D = 1473.2	27	L = 11.1cm B = 5.5cm	L = 11.[illegible] B = [illegible]
J. A.	1.80	0.69			7.6cm				745.9								L = 11.8cm B = 5.[illegible]	L = 11.[illegible] B = [illegible]
T. R.	1.70	0.71	0.65	0.60	6.5cm	3.5cm	3.0cm.	3.0cm	600.3	755.0	706.2	62[illegible].4	651.6	0.58	S = 1000.3 D = 1005.8	1.5		
G. O.	1.16	0.76			6.8cm				773.3									
E. T.	1.50	0.72			6.5cm	3.5cm	4.7cm	2.8cm	534.1			551.0	455.8	0.80	S = 551.7 D = 759.6	27.4	L = 10.1cm B = 5.5cm	L = 11cm. B = 5.[illegible]
K. A.	1.46	0.75			6.9cm	3.5cm	4.2cm	3.0cm	592.5			352.0	376.3	0.75	S = 467.2 D = [illegible]	6.6		
S. F.	1.84	0.71	0.62	0.67	7.9cm				669.6	663.9	697.2						L = 11.3cm B = 5cm	L = 11[illegible] B = 5.[illegible]
S. L.	1.4	0.65			8.0cm	4.0cm	3.9cm	2.4cm	629.6			271.2	349.4	0.57	S = 414.3 D = 410	22.2		
F. E.	1.98	0.67			8.2cm				678.9									
D. C.	1.70	0.67	0.58		6.0cm	4.3cm	4.0cm	3.1cm	695.2	634.5		471.1	523.9	0.59	S = [illegible] D = [illegible]	10.6	L = 11.3cm B = 6cm	L = 11.[illegible]cm B = [illegible]
F. A.																	L = 12cm B = 7cm	L = 1[illegible] B = 6.[illegible]
L. O.	1.72	0.60	0.58		7.9cm				839.0	774.5								
R. S.	1.72	0.71		0.63	7.6cm				979.9		636.9							
A. A.	1.44	0.75			8.2cm	4.0cm	4.0cm	[illegible].6cm	406.7			291.2	477	0.63	S = 465.9 D = [illegible]	59	L = 10.2cm B = 4.6cm	L = 10.[illegible]cm B = 5.7cm
S. H.	1.36	0.73	0.52		6.5cm	3.8cm	4.[illegible]cm	2.3cm	671.0			153.5	350.8	0.74	S = 283.6 D = 477.1	44.8	L = 10.1cm B = 5.7cm	L = 1[illegible] B = [illegible]
L. A.	1.5	0.50			6.6cm	3.8cm	4.[illegible]cm	2.7cm	571.4			245.3	413.3	0.87	S = 186.3 D = 471.2	40.5		L = 11.[illegible]cm B = 4.[illegible]cm
J. O.	1.54	0.66			7.6cm	4.6cm	5.2cm	3.6cm	693.4			255.4	485.3	0.65	S = 311.3 D = 722.7	45.4	L = 10.7cm B = 5.4cm	
S. O.	1.77	0.55	0.54	0.54	5.9cm	4.0cm	5.0cm	3.5cm	559.6	504.2		122	362.3	1.30	S = 83.9 D = 279.5	64.6		
J. S.	1.76	0.62	0.67	0.57	6.8cm				657.7	707.9	644.2							
J. D.	1.80	0.50		0.53	6.7cm				696.7		639.4							L = 1[illegible] B = [illegible]
O. D.	1.64	0.61			6.2cm				785.3									
J. S.	1.40	0.60			4.0cm							327.1	375.3	0.68	S = [illegible] D = [illegible]	12.3	L = 9.2cm B = 4.7cm	
Z. [illegible]	1.34	0.63			6.6cm				647.0									
R. B.	1.48	0.52			6.3cm	4cm	5.2cm	2.8cm	596.6			109.4	[illegible]	0.54	S = [illegible] D = [illegible]	34.6	L = 1[illegible].5cm B = [illegible]	L = 1[illegible] B = [illegible]
A. T.	1.72	0.64	0.50		7.3cm	3.7cm	4.4cm	2.5cm	581.7	440		159.2	[illegible]	0.70	S = [illegible] D = [illegible]	51.4	L = [illegible] B = [illegible]	L = [illegible] B = [illegible]
S. A.	1.67	0.63			5.6cm	4cm.	3.8cm	2.0cm	771.0			452.4	339.3	0.66	S = [illegible] D = [illegible]	14.7	L = 11.[illegible] B = [illegible]	L = [illegible] B = [illegible]
B. T.	2.0	0.70	0.61		6.6cm	4.5cm	4.9cm		700.4	659.0		376.9	807.1	0.59	S = 1153.[illegible] D = [illegible]	16		
A. E.	1.82	0.75			7.2cm				893.9									

W = Left ventricular wall thickness, EF = Ejection fraction.

TABLE 51

THE MEAN VALUES OF THE THREE GROUPS

	Cardio-thoracic ratio	Aortic diameter (plain film)	Aortic diameter (angio) Root	Mid asc.	Mid desc.	Heart volume (plain film)	Heart volume (angio) Syst.	Diast.	W	EF
Group A1	0.632±0.059	5.73±0.045	3.47± 0.43	3.68 ± 0.29	2.38±0.134	641.8±172.4	61.4± 25.1	310.4± 123.3	1.44 ± 0.16	62.4 ± 11.4
Group A2	0.657±0.064	5.78±1.29	3.7 ± 0.5	3.59 ± 0.58	2.4 ± 0.33	727.04±178.8	200.9± 66.96	352.9± 181.8	1.04 ± 0.5	32.52 ± 24.34
Groups A3, B1 and B2	0.661±0.065	6.98±0.83	4.01± 0.38	4.38 ± 0.57	2.89±0.42	689.1±127.3	167.8± 40.7	464.5± 171.9	0.702± 0.18	28.12 ± 17.13

W = Left ventricular wall thickness. EF = Ejection fraction

C.T. ration:- The mean CT ratios of the patients on admission were 0.632 (Group A1), 0.657 (A2), 0.661 (Groups A3, B1 and B2). There was no significant difference between the three groups (P>0.05). Significantly, the heart sizes decrease in 6/12 and 1 year.

Aortic diameter:- The mean aortic diameters were 5.73 for group A1, 5.78 for group A2 and 6.98 for groups A3, B1 and B2.

not of group A2 ($P > 0.05$). There was no significant difference between the values of groups A1 and A2 ($P > 0.05$).

At the mid-ascending level, the mean values were 3.68 cm ± 0.29 (Group A1), 3.59 cm ± 0.58 (group A2) and 4.38cm ± 0.57 (groups A3, B1 and B2). The value for groups A3, B1 and B2 was significantly higher than those of groups A1 and A2 ($P < 0.05$); there was no significant difference between those of group A1 and group A2 ($P > 0.05$).

The mean aortic diameters at the mid-descending level on angiography were 2.38cm ± 0.134 (group A1), 2.4cm ± 0.33 (group A2) and 2.89cm ± 0.42 (groups A3, B1 and B2). The latter value was also significantly higher than those of group A1 and group A2 ($P < 0.05$). There was no significant difference between those of groups A1 and A2 ($P > 0.05$).

Heart Volumes: The mean total heart volumes on plain chest x-rays were 641.8c.cm ± 172.4 (group A1), 727.04c.cm ± 178.82 (group A2) and 689.1c.cm ± 127.3 (groups A3, B1 and B2). There was no significant difference between the three groups ($P > 0.05$).

The mean left ventricular systolic volume of patients in group A1 was 61.4c.cm ± 25.1, that of group A2 was 200.9c.cm ± 66.96 while the value for groups A3, B1 and B2 was 167.8c.cm ± 40.7. The value obtained for the patients

in the latter group was significantly higher than that of group A1 patients ($P<0.05$). There was no significant difference between the mean systolic volumes of patients in groups A3, B1 and B2 and patients in group A2. The value for group A2 patients was also not different statistically from that of patients in group A1 ($P>0.05$).

The mean left ventricular end-diastolic volumes were 310.4c.cm ± 123.3 (group A1), 352.9c.cm ± 181.8 (group A2) and 464.5c.cm ± 171.9 (groups A3, B1 and B2). There was no significant difference between these values ($P>0.05$).

Left ventricular wall thickness: The mean left ventricular wall thickness of group A1 patients was significantly higher (mean = 1.44mm ± 0.16) than group A2 patients (mean = 1.04mm ± 0.48) and groups A3, B1 and B2 patients (mean = 0.70mm ± 0.18; $P<0.05$). Group A2 patients also had significantly thicker left ventricular walls than patients in groups A3, B1 and B2 ($P<0.05$).

Ejection Fraction: There was no significant difference between the mean ejection fractions of patients in groups A3, B1, B2 (28.12 ± 17.13) and group A2 patients (32.52 ± 24.34; $P>0.05$). However, the mean value obtained in patients belonging to groups A3, B1 and B2 was significantly less than that of group A1 patients (62.4 ± 11.4; $P<0.05$

Similarly, group A2 patients had significantly lower mean ejection fraction than patients in group A1 ($P < 0.05$).

CHAPTER 6

DISCUSSION

Lone mitral incompetence, a common valvular lesion in Ibadan (Carlisle and Ogunlesi, 1972) often presents in a similar clinical setting whether it is due to chronic rheumatic heart disease or to endomyocardial fibrosis (Carlisle and Ogunlesi, 1972; Falase et al, 1976). The differentiation between these two diseases and HMD with mitral incompetence is often difficult or sometimes impossible (Parry, 1968; Carlisle and Ogunlesi, 1972; Brockington, 1974; Falase et al, 1976). A history strongly indicative of rheumatic fever (Carlisle and Ogunlesi, 1972), additional murmurs (Parry, 1968; Brockington, 1974), definite left atrial enlargement, valvular calcification or intracardiac calcification on radiography (Carlisle and Ogunlesi, 1972; Brockington, 1974) and disappearance of murmurs with improvement of heart failure (Parry, 1968) have been suggested as distinguishing features. To these should be added, as shown in this study, poor quality first heart sound and soft apical systolic murmurs. This is not surprising as one of the factors controlling the amplitude of the first heart sound and the loudness of the murmur of mitral incompetence is the force of ventricular contraction

(Wayne, 1973). Diffuse or localised disease of the myocardium reduces the rate of pressure rise in the left ventricle (dp/dt), the resulting intensity of the first heart sound and of the regurgitant murmur (Wayne, 1973). In the absence of obesity and emphysema, extracardiac factors that affect the amplitude of the first heart sound, and in the absence of a mitral valve that is significantly damaged, pericardial effusion and a prolonged P-R interval, a soft first heart sound implies reduced left ventricular dp/dt and most probably a myocardial disease.

In one patient, the murmur of mitral regurgitation was absent despite the fact that he had significant incompetence on angiography. This was due to the fact that the myocardial function was so poor and not forceful enough to generate audible vibrations.

The presence of apical systolic thrills, regarded as a feature of HMD (WHO, 1965; Brockington, 1974) therefore, implies a forceful ventricular contraction and is probably not a feature of HMD. As shown in this study, only patients with organic mitral incompetence had apical systolic thrills.

The six patients with organic MR were younger, had loud murmurs, a good ejection fraction on left ventricular angiography and absence of severe myocardial damage on the

ECG. These suggest that the patients are probably in a relatively early phase of their disease. It is therefore possible for each to progress, if untreated as is often the case in Nigeria, to a stage in which the ventricle is so dilated and flabby that its contractile force is poor. Such patients if seen at this stage will be diagnosed as HMD; cardiac catheterisation will show a high left ventricular end-diastolic pressure and angiography will confirm a poorly contractile left ventricle. Since lone mitral incompetence is very common in Nigerians (Carlisle and Ogunlesi, 1972) and there are no facilities for open heart surgery, it is possible that some of the patients diagnosed and confirmed as HMD are in the advanced stages of untreated organic mitral incompetence.

This was observed in two of the patients in this study (K.O. and L.L., table 1). The first patient (K.O) presented initially in congestive cardiac failure with a loud murmur of mitral incompetence and a third sound. The left ventricular end-diastolic pressure was 6mmHg; left ventricular angiography showed a slightly dilated ventricle with a fairly good contraction and florid mitral incompetence (fig. 23). His systolic ejection fraction was 58.2%. He improved on digitalis and frusemide both as in-patient and out-patient. He was reinvestigated

A

B

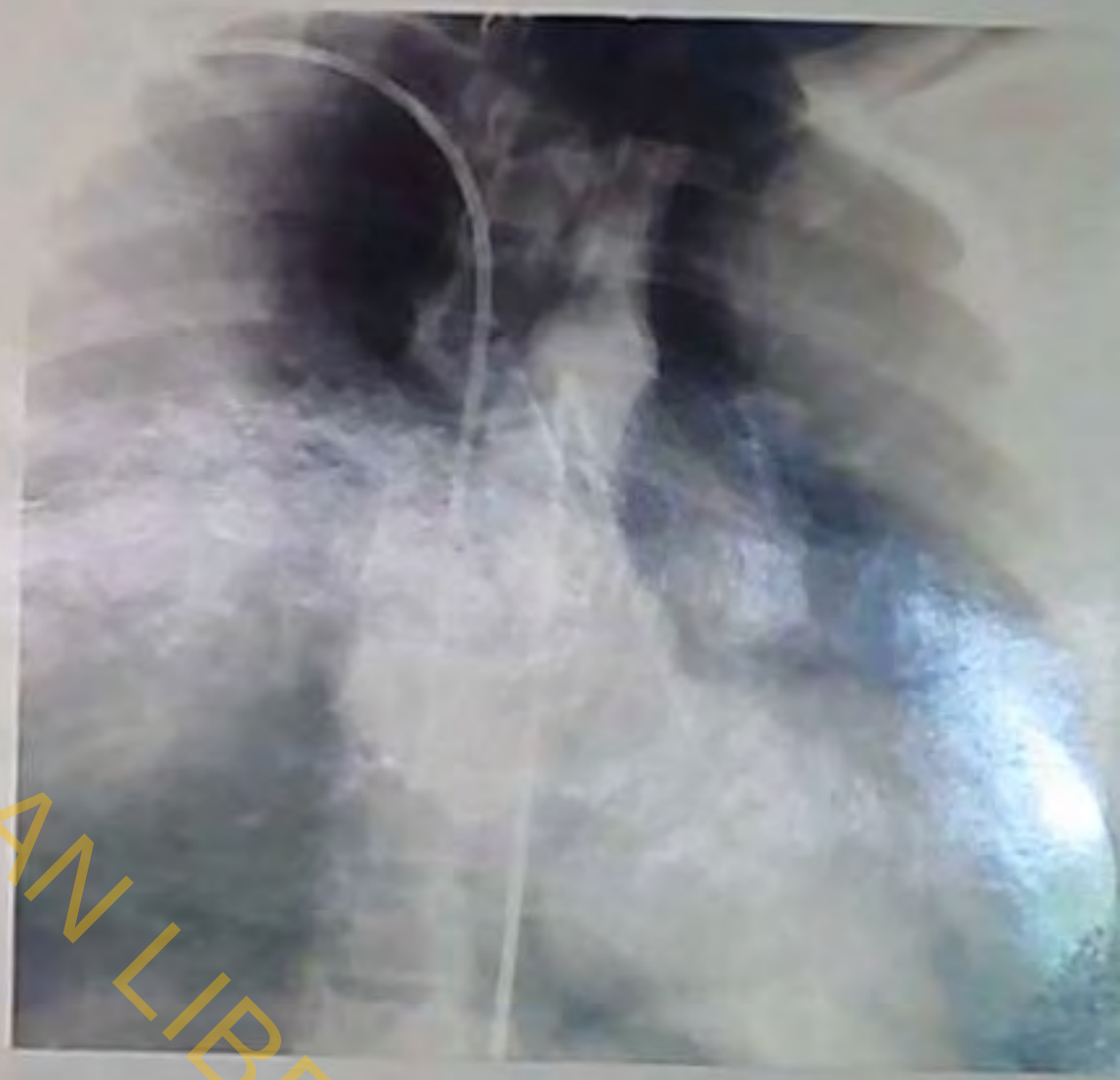
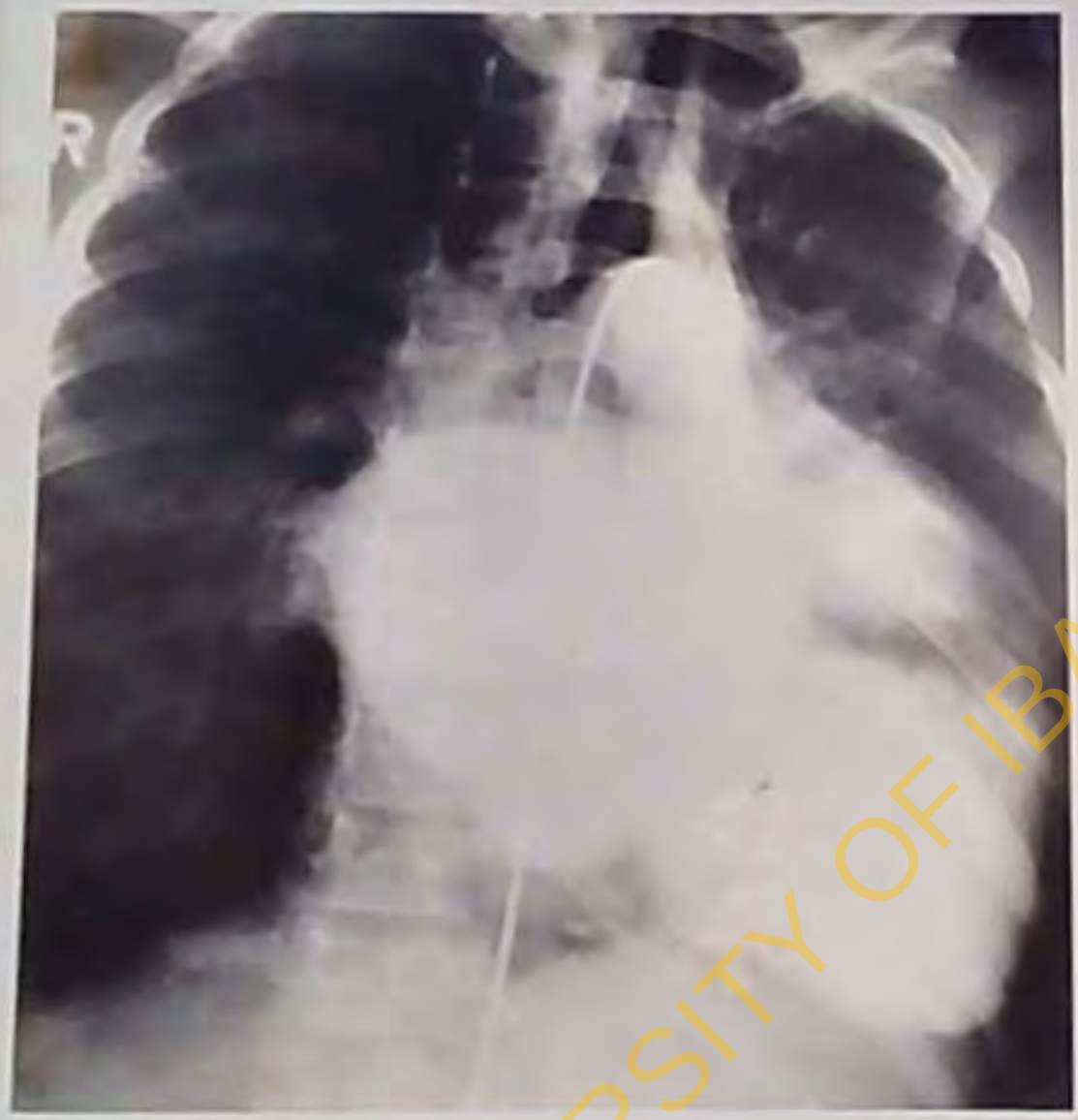


Fig. 23: Case 5. Left ventricular angiogram during systole (A) and diastole (B) showing a dilated left ventricle with fairly good myocardial contraction. There is florid mitral incompetence.

a year afterwards by which time he had worsened, developed tricuspid incompetence and required higher doses of frusemide to keep him out of heart failure. His murmur was soft and midsystolic; he still had a third sound. His left ventricular end-diastolic pressure had risen to 30 mmHg; an angiogram showed a grossly dilated poorly contractile left ventricle (fig. 24). The systolic ejection fraction was 19.5%. He died at home a year afterwards. If he had just be referred to us at the time of his second heart failure, our diagnosis would justifiably have been HMD.

The second patient (L.L.) similarly presented in congestive heart failure with a loud apical pansystolic murmur. Her angiograms (fig. 25) showed a dilated left ventricle but with a good ejection fraction (67%). A year later, she developed tricuspid incompetence and needed higher doses of frusemide to keep her out of heart failure. Her murmur was softer and mid-systolic. Her cardiothoracic ratio had increased; she did not consent to a repeat left ventricular angiogram.

The behaviour of the blood pressure of Group A1 patients on digitalis and frusemide in this study was similar to that of the patients in group A2. Both groups responded to routine management of heart failure on admission with frusemide as the diuretic. On discharge,



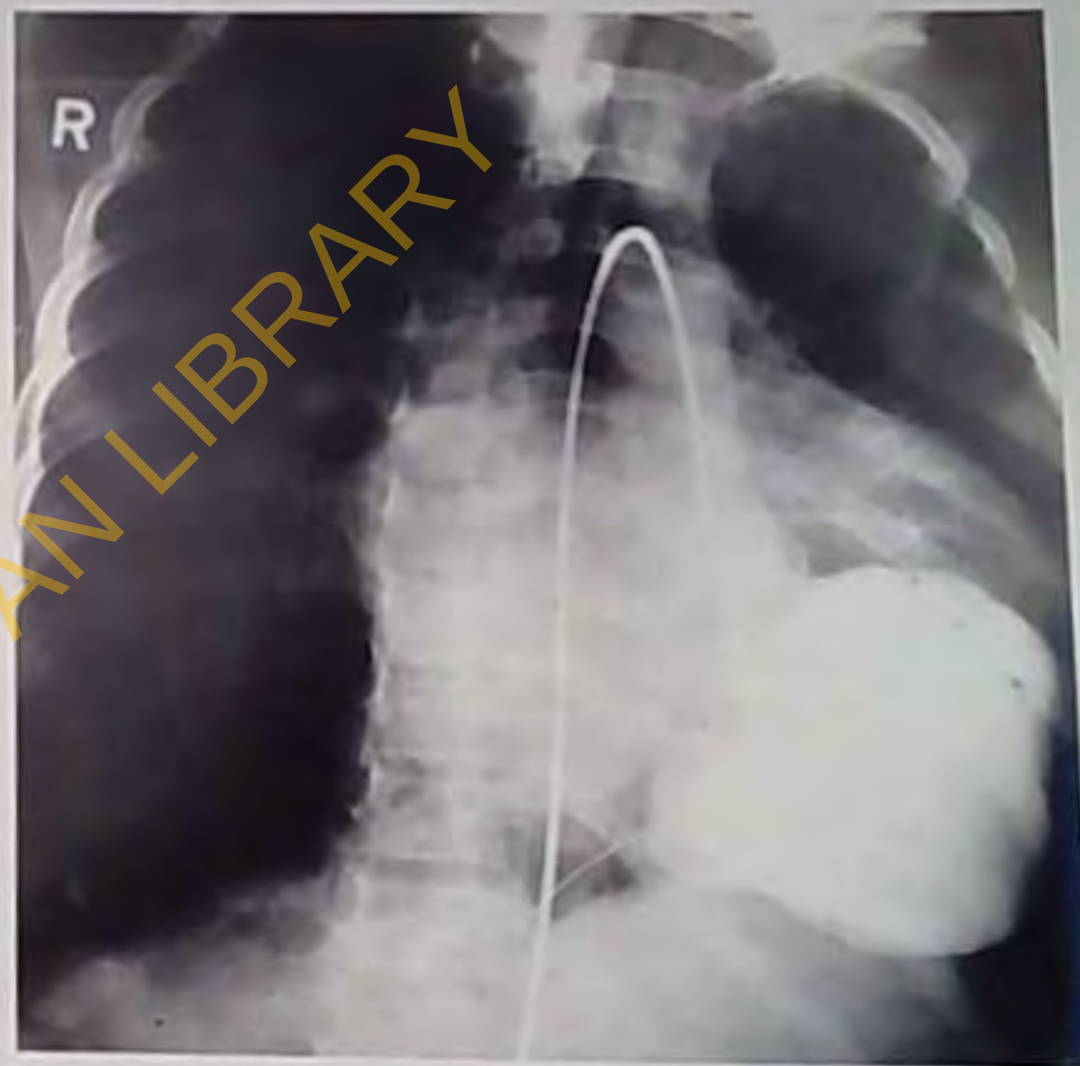
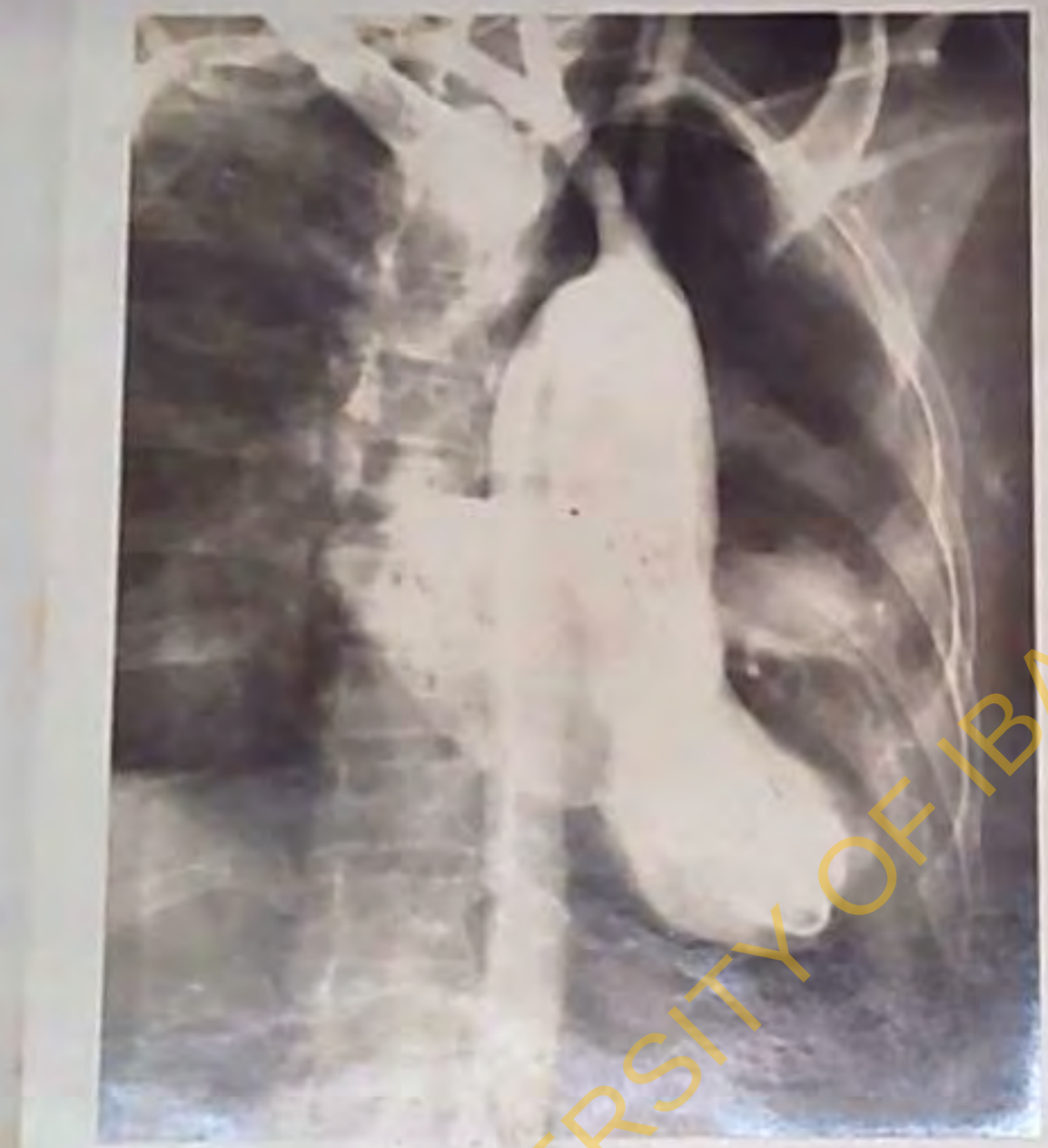


Fig. 24: Case 5. Left ventricular angiogram (a year afterwards) during systole (A) and diastole (B) showing a dilated ventricle with poor contraction. There is severe mitral incompetence.



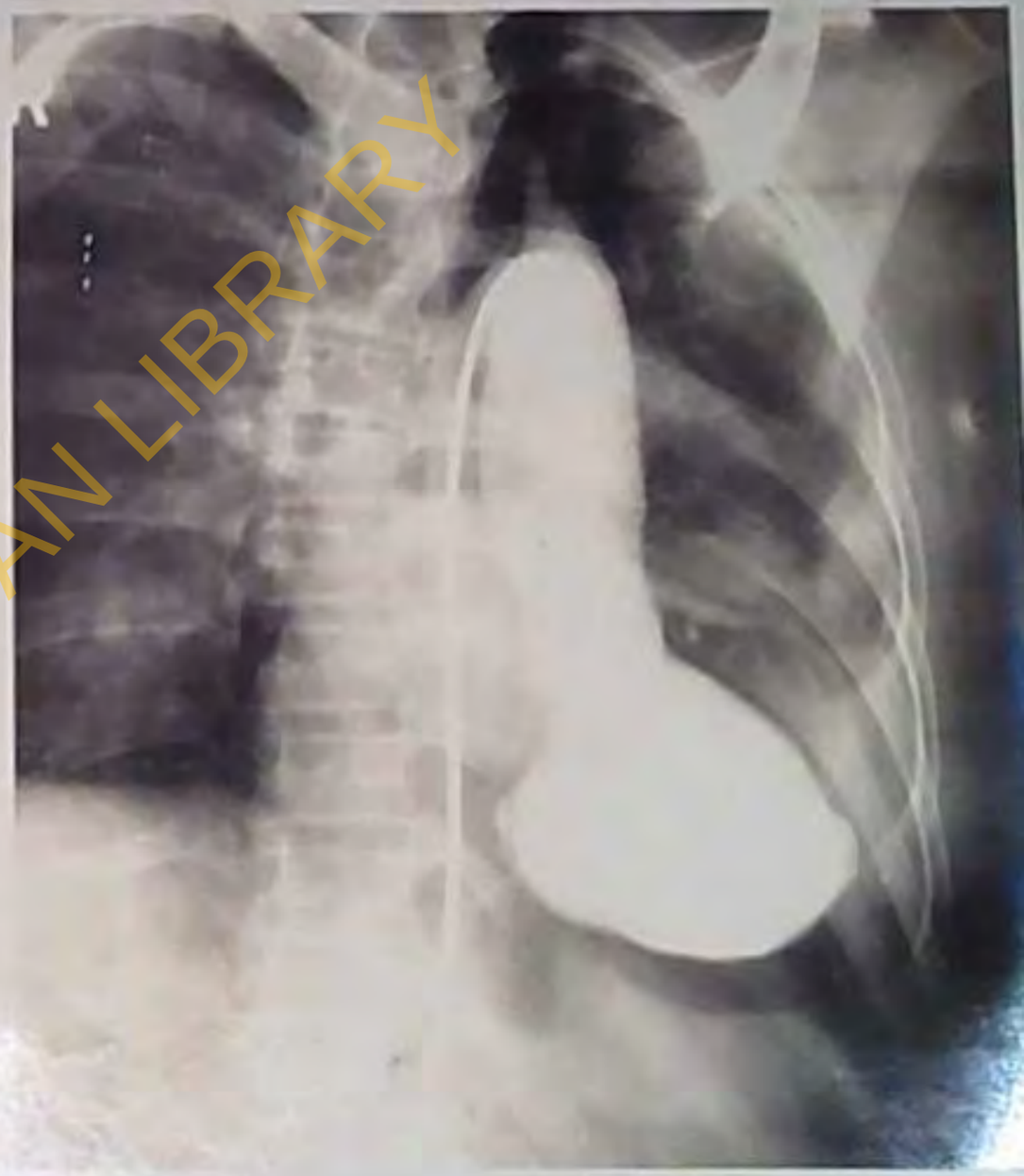
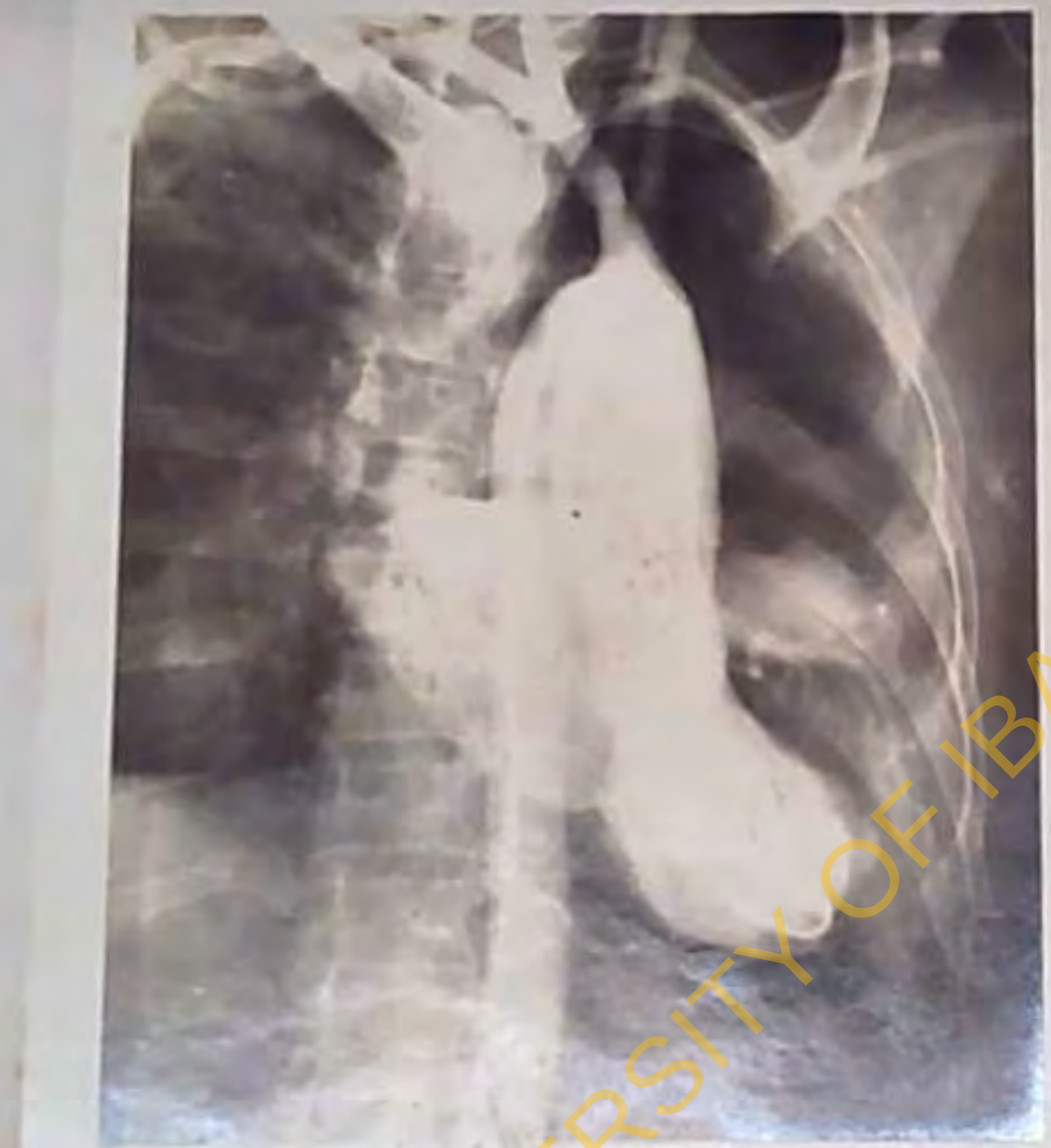


Fig. 25: Case 2. Left ventricular angiogram during systole (A) and diastole (B) showing a slightly dilated left ventricle, good myocardial contraction in systole and moderate mitral incompetence.



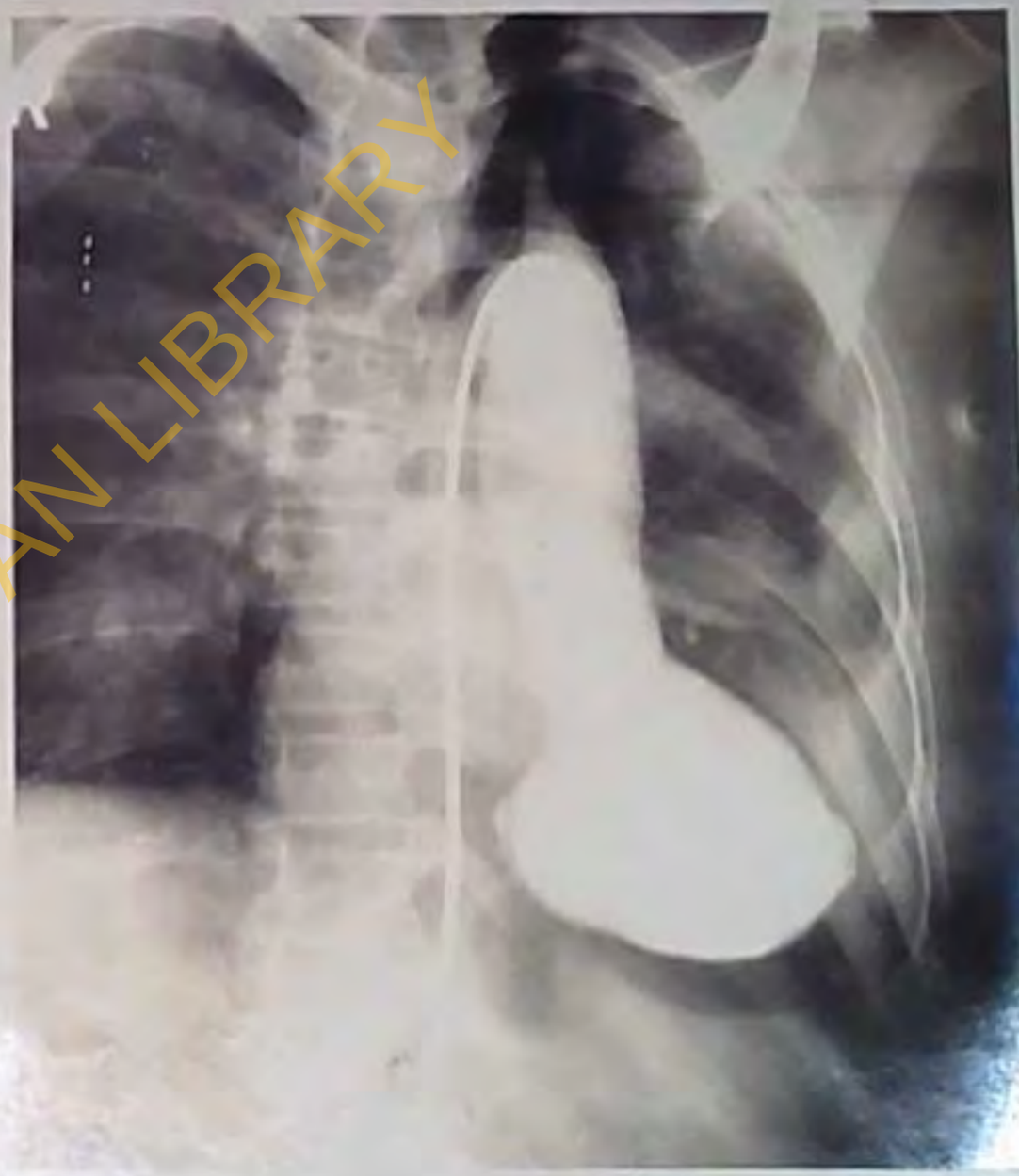


Fig. 25: Case 2. Left ventricular angiogram during systole (A) and diastole (B) showing a slightly dilated left ventricle, good myocardial contraction in systole and moderate mitral incompetence.

with the therapy unchanged, both groups continued to do well. Although group A3 patients presented in heart failure without elevated blood pressure, their clinical course resembled group B1 patients who presented with elevated blood pressures. The two groups improved in hospital on digitalis and frusemide but relapsed with elevated blood pressure on discharge. They improved only when the diuretic was changed to a thiazide and in some cases on the addition of methyl dopa. Group B2 patients did not respond even as in-patients to digoxin and frusemide but improved when the diuretic was changed to a thiazide and in many of them on the addition of methyl dopa.

These results show that not all Nigerians with HMD have raised blood pressure when they are in heart failure. They also show that the clinical course of many patients who are normotensive when in heart failure is different from those with mild hypertension. If hypertension is a consequence of their heart failure, it is difficult to explain why all the patients including the patients with organic mitral incompetence did not present with mildly raised blood pressure and why their clinical course was different. It seems more likely that hypertension was contributory to the morbidity of the patients in groups A3,

B1 and B2 and that the improvement in their heart failure was consequent upon lowering of their blood pressure. The factors which lowered their blood pressure in hospital were bed rest, low salt diet and frusemide. As out-patient, because of the unrestricted activity and salt intake and the lack of effective control of the blood pressure by frusemide, their condition worsened. They, however, improved when a thiazide diuretic, a more effective hypotensive (Anderson et al, 1971), was substituted. Such patients if treated with thiazides initially and as out-patients, may continue to maintain normal blood pressures and remain out of heart failure. If, however, the diuretic is discontinued, a rise in blood pressure may occur tilting them into heart failure. This probably explains why the hypertension in HMD is transient, occurs only when the patient is in heart failure and improves with treatment.

Other evidence also support the hypothesis that hypertension contributed to the morbidity of patients in groups A3, B1 and B2. Some of the patients required methyl dopa, a known hypotensive, to improve their heart failure. This effect is striking in group B2 patients, who, on digitalis and frusemide remained in heart failure in hospital with raised blood pressures and improved only on addition of methyl dopa. Also as shown in table 18 and case 32, those

who failed to respond to frusemide as out-patients improved on addition of methyl dopa. This improvement was always associated with a lowering of the blood pressure.

In some patients, the control of blood pressure became more difficult with recovery implying that it fell with onset of heart failure and continued to rise with myocardial recovery. This is not surprising as the blood pressure is a direct correlate of cardiac output and peripheral resistance. Therefore if the cardiac output falls, a fall in blood pressure without a change in peripheral resistance may occur (Oakley, 1972). Such a situation exists in a hypertensive patient who sustains a major infarction. His blood pressure may become normal (Goodwin, 1972). Brockington (1972) has also observed such changes in a Nigerian who initially had hypertensive heart failure but who, after defaulting twice, was seen later in heart failure but almost normotensive. A patient seen recently in the clinic also confirms this observation.

She was a 56 year old lady with angina pectoris and a blood pressure of 150/115 mmHg. She was not in heart failure and her blood pressure was easily controlled on hydrochlorothiazide 100mg daily. She then defaulted and was seen three months later in congestive cardiac failure with a blood

pressure of 120/100 mmHg. She had a loud third sound and an apical soft pansystolic murmur. She improved on digoxin and hydrochlorothiazide 100mg daily and then travelled to another part of the country. When her drugs finished she was given digoxin and frusemide 120mg daily instead of hydrochlorothiazide. Her blood pressure at the time was 120/80 mmHg. Three weeks afterwards she relapsed into congestive cardiac failure and came back to our clinic. On examination, we found that she was in congestive cardiac failure with a blood pressure of 110/90 mmHg. She responded again to digoxin and hydrochlorothiazide; she has since remained well.

The 12 patients from groups A3, B1 and B2 observed on digoxin alone after recovery from heart failure showed an initial rise in blood pressure before they had symptoms of heart failure while the 8 patients from groups A1 and A2 remained normotensive throughout. This suggested that the rise in blood pressure was not sequel to the development of heart failure.

Many patients from groups A3, B1 and B2 had small kidneys on intravenous pyelography. They may thus have good reasons to be hypertensive, as is typefied by case 38. This patient presented in congestive cardiac failure without uraemia but with a mildly raised blood pressure.

His blood pressure improved with treatment of his heart failure, although he did not do well on frusemide as outpatient. Each time he failed to use his drugs, he relapsed into congestive cardiac failure with mildly elevated blood pressure. Terminally, he became uraemic and autopsy showed a heart similar to HMD and kidneys that were bilaterally small and contracted. He was an alcoholic and the significance of this will later be discussed.

The patients in groups A3, B1 and B2 had significantly higher mean aortic diameters on plain chest x-ray and on angiography than patients in the other groups. The ages of patients in groups A3, B1 and B2 was comparable to those of group A2 patients; group A1 patients were, however, younger. Hypertension leaves its mark on the arterial tree in many ways and one of these is to cause dilatation of the aorta (Remington et al, 1948). Enlargement of the aortic shadow on radiography is therefore a useful confirmatory sign of hypertension.

This study also shows that large flabby hearts are not confined to HMD. Although the classic cardiac finding in patients with hypertension is more of concentric hypertrophy and less of cavity dilatation (Goodwin, 1972), some can have hearts resembling HMD.

The above therefore strongly suggest that the mild hypertension seen in some of the patients with HMD contributes to their morbidity and is not a result of their heart failure. They also provide an explanation as to why the hypertension is transient, occurring when the patients are in heart failure. It is, however, difficult to believe that such a mildly raised blood pressure can be responsible for biventricular failure. Also why do certain patients with mild to moderate hypertension develop dilated, hypertrophied hearts and cardiac failure whereas others living in the same area are able to sustain prolonged severe hypertension without these effects.

There are 3 possible reasons to explain why the presenting blood pressures of the patients were low. As argued previously, there is a tendency for the blood pressure to fall with onset of heart failure. Secondly, some of the patients had been started on diuretics, which can lower the blood pressure, before they were seen in the clinic. Significantly, all the patients in group A3 who presented with normal blood pressures but subsequently behaved like hypertensives had received treatment before they were seen. It is therefore probable that their blood pressures had been lowered with this prior treatment. Thirdly, as shown in this study, some of the patients were

also alcoholics, malnourished, thiamine deficient and some had antibody titres to toxoplasma gondii and Coxsackie B viruses. It is therefore possible for these patients to sustain previous myocardial damage but remain compensated. If they subsequently develop hypertension, their hearts become unable to withstand the new afterload and failure will supervene at a relatively low level of diastolic blood pressure. Hypertensives living in this area who are able to sustain prolonged severe hypertension without cardiac failure probably have little or no additional assault on the myocardium from the injurious factors enumerated above.

Apart from hypertension, this study showed that alcoholism was not as rare as suggested by Brockington (1974). Many of the alcoholics, including those in the high socio-economic group, were thiamine deficient though without high output failure. A few patients in the study and control groups had thiamine deficiency without alcoholism. Presumably their deficiency was caused by inadequate intake of the vitamin. One of them had a reversible high output failure.

Although the cobalt content of the alcoholic beverages was not determined, the general impression is that cobalt is not present. None of the alcoholic beverages analysed

contain other alcohols apart from ethyl alcohol. The mineral contents of the beverages were probably harmless.

Patients with HMD were significantly malnourished as reflected in the low serum albumin levels compared with controls. Presumably those in the high socio-economic group were malnourished because all but one of them were alcoholics.

Potassium deficiency cannot be implicated as a cause of the myocardial damage of patients with HMD in this study as there was no significant difference between them and the controls. However, it would have been more informative if the total body potassium had also been measured as this would be a more accurate index of potassium deficiency. Facilities for this were, however, not available when the study was conducted.

Toxoplasma gondii infection seemed to be endemic. This is in conflict with the view of Brockington (1974) that it was non-existent in the community. Olurin et al (1972) had also shown in their study on chorio-retinitis that toxoplasmosis was highly endemic. Although there was no difference between the frequency of infection of the patients with HMD and controls, the two cases described highlight the fact that the infection may become virulent and precipitate heart failure in the presence of stressful

situations such as pregnancy. It is well-recognised that toxoplasma infection can become virulent in such conditions including patients with secondary immunologic deficiency states (Theologides and Kennedy, 1969).

Coxsackie B viral infection is endemic in the community as shown in this study and in the study by Fabiyi and Odegbo-Olukoya (1974). These again are in conflict with the views of Brockington (1974) that they are non-existent. In this study more patients with HMD had significant infection compared with controls. Patients with HMD also had significantly higher levels of antibody titres; antibodies to Coxsackie viruses B2, B3 and B6 were significantly present in their sera than in controls. These findings, however, do not prove a Coxsackie B viral aetiology of the Nigerian HMD. It is also likely that most adults would have been immune from infection early in life. However, it is possible that the first exposure of some of the patients with HMD to the viruses resulted in severe myocarditis leaving the heart damaged though compensated. As concluded by Sanders (1963), patients with HMD are therefore probably "far removed from their initial insult". Any further insult in later life, therefore, may tilt them easily into heart failure and produce HMD. This study did not attempt to examine the role of other viruses and

rickettsial diseases although it is possible that they are important in the aetiology of HMD.

There was no evidence to implicate Trypanosoma cruzi as a cause of heart failure in Nigerians. There was also no evidence to incriminate other parasites and eosinophilia as important causes of HMD in Nigeria. However, as pointed out above, it is difficult to underplay the role of parasitic and bacterial infections in their contribution to the final cardiac pathology in those states.

No case of haemochromatosis, amyloidosis or sarcoidosis was identified in the study. They may occur, though rarely, and it is possible that some of the patients diagnosed as H MD at Ibadan actually have one of these conditions. One case of hypothyroidism was discovered to have been misdiagnosed clinically as HMD. An associated cardiomyopathy could not, however, be excluded.

High parity was common among the female patients with HMD but post-partum cardiac failure was not as common as reported from Northern Nigeria. One of the patients who became ill during the puerperium was hypertensive, her blood pressure on long term follow up becoming difficult to control. The remaining 2 patients had toxoplasma cardiomyopathy. It is unlikely that pregnancy itself causes HMD. It is more likely to contribute to the demise

of a heart that is on the verge of failing and, by lowering immunity, allow infections to be more virulent. Significantly, peripartum cardiomyopathy rarely occurs in more priviledged communities (Goodwin and Oakley, 1972). If peripartum cariomyopathy is caused by pregnancy alone, it should occur more frequently in such societies or, at least, in those of them with high parity. The high incidence in Northern Nigeria has been attributed to the fact that many of these patients are exposed to a hot and humid environment during the puerperium. They also consume large amounts of salt (Adesanya and Parry, 1976). These, as the authors admitted, may merely be contributory to a whole variety of interacting factors still altogether obscure.

Although each of the various injurious factors identified in the study may independently cause the myocardial damage of HMD, it is also possible that HMD is a multicausal syndrome. For example, it is believed that the heart does not fail in hypertension unless it is exposed to some additional injuries. In a series of 445 patients with high blood pressure and heart failure, Mickerson (1963) found additional cause of heart failure in all but 12. Fowler (1972) too found that cardiac failure in Ugandan hypertensives was rare in the presence of

normal renal function and absence of anaemia or valvular heart disease. In the autopsy study on patients with established hypertension reported in Chapter 5, anaemia was identified as a possible additional cause of the large, flabby hearts. And in this study, some of the patients who were hypertensive were also alcoholics. Some had thiamine deficiency in addition while many had evidence of previous or recent infection from toxoplasma gondii and the Coxsackie B viruses. It is, therefore, possible that the heart failed from exposures to combinations of these adverse factors.

In conclusion, HMD in Nigerians was not caused by a single disease process. Many were hypertensives and alcoholism was common especially among those in the high socio-economic group. Many had a background of protein malnutrition and a number were thiamine deficient. Majority of the female patients were of igh parity. Toxoplasma and Coxsackie B viral infections were endemic and might have been responsible or contributory to the heart failure of some of the patients. Organic mitral incompetence presented some difficulty in differential diagnosis; one patient had hypothyroidism. Chaga's disease was not existent in the community. HMD can therefore be regarded as the end-stage of myocardial

damage produced by various factors acting independently of each other or in combination.

SUMMARY AND CONCLUSIONS

The prevalence, pathology, clinical and the radiological features of heart muscle disease (HMD) in Ibadan were discussed. A critical review of previous studies in Ibadan aimed at finding its cause was made. Other disorders that have been incriminated in causing myocardial damage were also reviewed. A study was then undertaken, using a multifactorial approach, to assess the role of these disorders in the aetiology of HMD. The role of malnutrition, hypertension and thiamine deficiency, factors that have been suggested as possible causes in Ibadan were also evaluated.

50 Nigerians with HMD defined as congestive cardiac failure and cardiac enlargement of unknown cause but with a presenting diastolic blood pressure of 100mmHg and below were studied. Initial assessment included a comprehensive history and physical examination. A wide range of investigations was also carried out. The patients were treated on admission with digitalis and frusemide and maintained on the same dose of drugs on discharge from hospital. Thiazides, and when necessary, alpha methyldopa were substituted for frusemide if at any stage there was no improvement or if the blood pressure remained elevated. Each patient was followed up for at least a year.

Of the 50 patients, 6 were found on left ventricular angiography to have organic mitral incompetence. 18 of the remaining 44 patients presented with a normal blood pressure (diastolic blood pressure below 90 mmHg) and 26 with a diastolic blood pressure of 90 - 100 mmHg. Of the 18 normotensive patients, 12 remained normotensive throughout the entire observation period. Their heart failure was controlled with digoxin and frusemide both as in-patient and in the subsequent out-patient follow up. The heart failure of the remaining six patients was controlled while in hospital but they developed elevated blood pressures and relapsed into heart failure during out-patient follow-up on digoxin and frusemide. They needed antihypertensive therapy in the form of thiazides or methyldopa with thiazides to keep them out of heart failure. 20 patients with initially raised blood pressures responded to inpatient treatment with a fall in blood pressure and remission of their cardiac failure. During out-patient follow-up the blood pressure became elevated again and cardiac failure reappeared. These patients needed anti-hypertensive therapy to produce a sustained fall in blood pressure and relief of their heart failure. 6 other patients who presented with elevated blood pressures did not respond even as in-patients until

antihypertensive therapy had been instituted. Those who needed antihypertensive treatment to improve their heart failure had significantly enlarged aortic shadows on plain chest x-ray and on angiography. Many of them also had small kidneys on intravenous pyelography.

20 of the 44 patients with HMD were alcoholics. All but one of the patients in the high socio-economic group were alcoholics. Many of the patients with HMD had a background of protein malnutrition as reflected in their significantly low serum albumin. They were also significantly thiamine deficient, only 1 patient had a high cardiac output reversed by thiamine administration. There was no significant difference between their serum potassium and controls.

There was also no significant difference in the frequency of toxoplasma infection between patients with HMD and controls. Two female patients with HMD had toxoplasma cardiomyopathy. They became ill in early puerperium and had very high titres against toxoplasma gondii.

Patients with HMD had a significantly higher incidence of infection from Coxsackie B viruses than controls. They also had higher levels of antibody titres. Antibodies to Coxsackie viruses B2, B3 and B6 were also more commonly

identified in their sera than in controls.

There was no evidence implicating Trypanosoma cruzi as a cause of heart failure in Nigerians. There was also no evidence to incriminate other parasites and eosinophilia as causes of HMD in Nigeria. One patient had hypothyroidism.

83% of the female patients had a high parity although only three were ill during pregnancy or early puerperium. Two of these had toxoplasma cardiomyopathy; the third had hypertension in addition.

No case of haemochromatosis, amyloidosis or sarcoidosis was identified in the study.

It is concluded that HMD in Nigerians is not caused by a single disease process but is the end-result of myocardial damage produced by a variety of factors. The mild hypertension seen in some of them contributes to their morbidity and is not a result of their heart failure.

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APPENDIX 1

STUDIES ON HEART MUSCLE DISEASE

INITIAL REPORT/HISTORY

I. GENERAL INFORMATION

STUDY NO ☐☐☐☐☐

UNIT NO ☐☐☐☐☐☐

Date of Registration ☐☐☐☐

1. Name

2. Sex Male 1 ☐

Female 2 ☐

3. Age ☐☐

4. Occupation

Unskilled labourer 1 ☐

Housewife 2 ☐

Farmer 3 ☐

Artisan 4

Driver, Tailor, Bricklayer
Carpenter, Cook etc. ☐

Trader 5 ☐

Clerical 6 ☐

Medium Professional 7 ☐

High Professional 8 ☐

Unemployed/Retired 9 ☐

5. Home Address .....

.....

6. Religion:

Christian 1 ☐

Moslem 2 ☐

Others 3 ☐

7. Nationality:

Nigerian 1 ☐

Other African 2 ☐

Caucasian 3 ☐

Asian 4 ☐

Other 5 ☐

II PRESENTING SYMPTOMS

1. Dyspnoea

Yes, Grade 1 ☐

2 ☐

3 ☐

4 ☐

No 5 ☐

2. Orthopnoea Yes ☐

No ☐

Duration ☐

3. Paroxysmal nocturnal dyspnoea

Yes 1 ☐

No 2 ☐

Duration ☐

4. Fatigue

Yes 1 ☐

No 2 ☐

Duration ☐☐

5. Oedema

Yes 1 ☐

No 2 ☐

Duration ☐☐

6. Chest Pain

Angina 1 ☐

Pleuritic 2 ☐

Pericarditic 3 ☐

Vague 4 ☐

Duration ☐☐

7. Abdominal Swelling

Yes 1 ☐

No 2 ☐

Duration ☐☐

8. Pain in the (R) hypochondrium

Yes 1 ☐

No 2 ☐

Duration ☐☐

9. Fever

Yes 1 ☐

No 2 ☐

Duration ☐☐

10. Cough

Yes 1 ☐

No 2 ☐

Duration ☐☐

11. Paraesthesiae of hands and feet

Yes 1 ☐

No 2 ☐

Duration ☐☐

12. Polyuria

Yes 1 ☐

No 2 ☐

Duration ☐

13. Oliguria

Yes 1 ☐

No 2 ☐

14. Other symptoms

a .....
Duration

b .....
Duration

c .....
Duration

d .....
Duration

III PAST MEDICAL HISTORY

1. a. Dyspnoea

Yes 1 ☐

No 2 ☐

b. How long ago (did it start) ☐

c. Treatment

Native	1	☐
Hospital	2	☐
Both	3	☐
None	4	☐

2. a Orthopnoea

Yes	1	☐
No	2	☐

b How long ago (did it start) ☐

c Treatment

Native	1	☐
Hospital	2	☐
Both	3	☐
None	4	☐

3. a P.N.D.

Yes	1	☐
No	2	☐

b How long ago (did it start) ☐

c. Treatment

Native	1	☐
Hospital	2	☐
Both	3	☐
None	4	☐

4. a. Ankle oedema

Yes	1	☐
No	2	☐

b. How long ago (did it start) ☐

c. Treatment

Native	1	☐
Hospital	2	☐
Both	3	☐
None	4	☐

5. a Abdominal Swelling

Yes	1	☐
No	2	☐

b. How long ago (did it start) ☐

c. Treatment

Native 1 ☐

Hospital 2 ☐

Both 3 ☐

None 4 ☐

6. a. Fever

Yes 1 ☐

No 2 ☐

b. How long ago (did it start) ☐

Native 1 ☐

Hospital 2 ☐

Both 3 ☐

None 4 ☐

7 a. Chest Pain and fever

Yes 1 ☐

No 2 ☐

b. How long ago (did it start) ☐

c. Treatment

Native 1 ☐

Hospital 2 ☐

Both 3 ☐

None 4 ☐

8 a. Fever with symptoms of heart failure

Yes 1 ☐

No 2 ☐

b. How long ago (did it start) ☐

c. Treatment

Native 1 ☐

Hospital 2 ☐

Both 3 ☐

None 4 ☐

9. a Other Illness 1 ☐

2 ☐

3 ☐

b. Treatment

Native 1 ☐

Hospital 2 ☐

Both 3 ☐

None 4 ☐

IV. DIETARY HISTORY

1. FOOD

a. Gari/Eba Frequency per week ☐☐

b. Amala ☐☐

c. Meat/Fish ☐☐

d. Yams

e. Beans

f. Fish

g. Vegetables

h. Bread

i. Others

i

ii

iii

2. Alcoholic intake 1 Yes 2 No

a. Palmwine - No. of bottles per week

b. Beer

c. Gin

d. Other wines

3. a. Cigarettes and tobacco Yes 2

No 1

b. Frequency per day ☐

V. SOCIO-ECONOMIC STATUS

1. Average Income per Year

Above ₦4,000	1	☐
₦3,000 - ₦4,000	2	☐
₦2,000 - ₦3,000	3	☐
₦1,000 - ₦2,000	4	☐
₦500 - ₦1,000	5	☐
Below ₦500	6	☐

2. No. of wives ☐

3. No. of children ☐

IV. HOUSING

1. Type of House

Mud	1	☐
Cement Plastered	2	☐

2. How many sleep in a room with the patient ☐

3. Which of the following do you keep

Goats 1 Yes/2 No ☐

Sheep 1 Yes/2 No ☐

Hen 1 Yes/2 No ☐

Others 1 Yes/2 No ☐

VII PREGNANCY HISTORY (FOR FEMALES ONLY)

1. How many pregnancies ☐☐

2. How many abortions ☐☐

3. Do you have any symptom of the following during pregnancy

a. Exertion dyspnoea Yes 1 ☐

No 2 ☐

b. Orthopnoea Yes 1 ☐

No 2 ☐

c. Paroxysmal Nocturnal dyspnoea

Yes 1 ☐

No 2 ☐

d. Ankle Swelling Yes 1 ☐

No 2 ☐

e. Cough Yes 1 ☐

No 2 ☐

4. Do you have any symptoms of the following after delivery

a. Exertional dyspnoea

Yes 1 ☐

No 2 ☐

b. Orthopnoea Yes 1 ☐

No 2 ☐

c. Paraxysmal nocturnal dyspnoea

Yes 1 ☐

No 2 ☐

d. Ankle Swelling Yes 1 ☐

No 2 ☐

e. Cough Yes 1 ☐

No 2 ☐

VIII FAMILY HISTORY

1. Has any of your relatives suffered from

a. Exertional dyspnoea

Yes 1 ☐

No 2 ☐

b. Orthopnoea Yes 1 ☐

No 2 ☐

c. Ankle Swelling Yes 1 ☐

No 2 ☐

d. Cough Yes 1 ☐

No 2 ☐

IX PHYSICAL SIGNS

1. General State

Quite well 1 ☐

Not very well 2 ☐

Poor 3 ☐

Very Poor 4 ☐

2. Nutritional Status

Good 1 ☐

Fair 2 ☐

Poor 3 ☐

3. Weight kg ☐☐☐

4. Height cc ☐☐☐

5. Temperature °F ☐☐☐

6. Pallor of N N Yes 1 ☐

No 2 ☐

7. Jaundice Yes 1 ☐

No 2 ☐

8. Glands

Yes 1 ☐

No 2 ☐

9. Peripheral Pulse ☐☐☐

a. Rhythm

Normal 1 ☐

Irregular 2 ☐

Irregularly irregular 3 ☐

Pulsus alternans 4 ☐

Not easily palpable 5 ☐

b. Character Normal 1 ☐

Abnormal 2 ☐

Specify .....

c. Volume Normal 1 ☐

Abnormal 2 ☐

Specify .....

10. Jugular Vein

a. Pressure Normal 1 ☐

Raised 2 ☐

Height in cc ☐☐

b. Pulsation

Normal 1 ☐

Abnormal 2 ☐

If abnormal

prominent 'a' wave 1 ☐

prominent systolic wave ....2 ☐

both 3 ☐

11. Congestive cardiac failure

Yes 1 ☐

Suspect 2 ☐

No 3 ☐

Degree:

Gross 1 ☐

Severe 2 ☐

Moderate 3 ☐

Mild 4 ☐

12. Pulmonary congestion

Yes	1	☐
Suspect	2	☐
No	3	☐

Degree:

Gross	1	☐
Severe	2	☐
Moderate	3	☐
Mild	4	☐

13. Chest findings in general ☐

14. Apical impulse

a. Location

Mid clavicular	1	☐
Outside MCL	2	☐
Inside MCL	3	☐
4th Intercostal space	4	☐
5th Intercostal space	5	☐

6th intercostal space 6 ☐

Not palpable 7 ☐

b. Character:

Normal 1 ☐

Heaving and diffuse 2 ☐

Heaving but not diffuse 3 ☐

15. Right ventricular impulse

Palpable 1 ☐

Not palpable 2 ☐

Heaving 3 ☐

16. Pulmonary artery pulsation palpable

Yes 1 ☐

No 2 ☐

17. Pulmonary artery closure palpable

Yes 1 ☐

No 2 ☐

AUSCULTATION

18. Rhythm

Regular Yes 1 No 2 ☐

Ectopics ..... per minute ☐

Atrial Fibrillation Yes 1 No 2 ☐

Gallop rhythm (RV) Yes 1 No 2 ☐

Gallop rhythm (LV) Yes 1 No 2 ☐

19. Heart sounds

a. Normal

S1 ☐

S2 ☐

b. Distant

S1 ☐

S2 ☐

c. Pathological S3

Yes 1 ☐

No 2 ☐

20. Individual Heart sounds

a. A2

Normal	1	☐
Accentuated	2	☐
Diminshed	3	☐

b. P_2

Normal	1	☐
Accentuated	2	☐
Diminished	3	☐

21. Murmurs

a. Mitral Incompetence

	1	☐
Present	2	☐
Absent	3	☐

b. Tricuspid Incompetence

Present	1	☐
Absent	2	☐

22. SKIN

a. Exfoliation — Yes 1 ☐ — No 2 ☐

b. Onchocercal changes

i White nails — Yes 1 ☐ — No 2 ☐

ii Cheilosis — Yes 1 ☐ — No 2 ☐

iii Colour — Light 1 ☐ — Dark 2 ☐ — Very dark 3 ☐

iv Angular stomatitis — Yes 1 ☐ — No 2 ☐

v Others ☐

23. Peripheral Oedema

Present 1 ☐

Absent 2 ☐

24. Ascites

Present		1	☐
Absent		2	☐

25. Pleural effusion

Present	R sided	1	☐
	L sided	2	☐
Absent			☐

26. Pericardial effusion

Present	1	☐
Absent	2	☐

27. Blood Pressure

Systolic	☐☐☐
Diastolic	☐☐☐

28. Liver

a. Palpable	Yes	1	☐
	No	2	☐

If yes, cms below costal margin

b. Systolic Pulsation

Present	1	☐
Absent	2	☐

c. Pre-systolic Pulsation

Present	1	☐
Absent	2	☐

29. Spleen

Enlarged	1	☐
Not enlarged	2	☐

30. Peripheral neuritis

Motor	1	☐
Sensory	2	☐
Sensorimotor	3	☐
Absent	4	☐

31. Fundoscopy

(a) Arterial narrowing	Yes	1	☐
	No	2	☐
(b) A - V nipping	Yes	1	☐
	No	2	☐
(c) Haemorrhages	Yes	1	☐
	No	2	☐

d. Exudates

Yes 1 ☐

No 2 ☐

e. Papilloedema

Yes 1 ☐

No 2 ☐

32. LABORATORY FINDINGS

I Electrocardiogram

a. Atrial Fibrillation/Flutter

Yes 1 ☐

No 2 ☐

b. Sinus Rhythm

Yes 1 ☐

No 2 ☐

c. Supraventricular tachycardia

Yes 1 ☐

No 2 ☐

d. Ventricular tachycardia

Yes 1 ☐

No 2 ☐

e. Atrial/Nodal focus

Yes 1 ☐

No 2 ☐

f. Supraventricular ectopics

Yes	1	☐
No	2	☐

g. Ventricular ectopics

Coupled	1	☐
Runs of	2	☐
Frequent	3	☐
Occasional	4	☐
None	5	☐

h. Right atrial hypertrophy

Present	1	☐
Probable	2	☐
Absent	3	☐

i. Left atrial hypertrophy

Present	1	☐
Probable	2	☐
Absent	3	☐

j. P-R interval

Short	1	☐
Normal	2	☐
Prolonged	3	☐

k. Complete A - V block

Present	1	☐
Absent	2	☐

l. Partial A - V block

Present	1	☐
Absent	2	☐

m. QRS axis

Normal	1	☐
Left	2	☐
Right	3	☐

n. Left anterior fascicular block

Present	1	☐
Absent	2	☐

o. Left posterior fascicular block

Present	1	☐
Absent	2	☐

p. R BBB

Present	1	☐
Absent	2	☐

q. L BBB

Present 1 ☐

Absent 2 ☐

r. Right ventricular hypertrophy

Present 1 ☐

Probable 2 ☐

Absent 3 ☐

s. Left ventricular hypertrophy

Present 1 ☐

Probable 2 ☐

Absent 3 ☐

t. Injury ST - T

		Yes 1 No 2	
1	Lead I		☐
2	II		☐
3	III		☐
4	aVR		☐
5	aV_L		☐
6	aV_F		☐
7	V1		☐
8	V_2		☐

9	V_3	
10	V_4	
11	V_5	
12	V_6	

u. Inverted T waves

1	Lead	I	Yes 1	No 2	
2		II			
3		III			
4		aV_R			
5		aV_L			
6		aV_F			
7		V_1			
8		V_2			
9		V_3			
10		V_4			
11		V_5			
12		V_6			

v. Low T-waves

1	lead	I	Yes 1	No 2
2		II		
3		III		
4		aV_R		
5		aV_L		
6		aV_F		
7		V_1		
8		V_2		
9		V_3		
10		V_4		
11		V_5		
12		V_6		

w. Q - To

Normal	1	
Increased	2	
Decreased	3	

x. Other comments (state)

II Chest X-Ray

a. Cardiac shadow

Enlarged	1	☐
Normal	2	☐

b. Left atrium

Enlarged	1	☐
Normal	2	☐

c. Evidence of Pulmonary venous hypertension

Yes	1	☐
Doubtful	2	☐
No	3	☐

d. Pulmonary artery

Dilated	1	☐

e. Pleural effusion

R sided	1	☐
L sided	2	☐
Bilateral	3	☐
Absent	4	☐

f. Others (specify)

III Biochemical and Haematological measurement

1. Hb ☐☐☐

2. PCV ☐☐☐

3. MCHC ☐☐☐

4. WBC ☐☐☐ (thousands)

Neutrophils ☐☐☐

Eosinophils ☐☐☐

Basophils ☐☐☐

Lymphocytes ☐☐☐

Monocytes ☐☐☐

Reticulocyte ☐☐☐ %

5. Sickle cells

Present 1 ☐

Absent 2 ☐

6. Anisocytosis

Present 1 ☐

Absent 2 ☐

7. Poikilocytosis	Present	1	☐
	Absent	2	☐
8. Macrocytosis	Present	1	☐
	Absent	2	☐
9. Target cells	Present	1	☐
	Absent	2	☐
10. Hypochromia	Present	1	☐
	Absent	2	☐
11. Hb Genotype	AA	1	☐
	AS	2	☐
	SS	3	☐
	SC	4	☐
	Others	5	☐

12. Na^+ ☐☐☐

13. K^+ ☐☐

14. Cl^- ☐☐☐

15. HCO_3 ☐☐

16. Urea ☐☐

17. Bilirubin

Total ☐☐

Direct ☐☐

18. Alkaline Phosphatase ☐☐

19. Cholesterol ☐☐

20. Thymol Turbidity ☐☐

21. Serum Proteins

Total ☐☐

Albumin ☐☐

Globulins ☐☐

22. ABO titre ☐☐

23. ESR ☐☐

24. Toxoplasma

Positive	1	☐
Doubtful	2	☐
Negative	3	☐

25. Viral Isolation

a. Poliomyelitis	Positive	1	☐
	Negative	2	☐
b. Coxsackie B	Positive	1	☐
	Negative	2	☐
c. Influenza	Positive	1	☐
	Negative	2	☐
d. Mumps	Positive	1	☐
	Negative	2	☐
e. Others (specify)			
.....			

26. Serology for viruses (Acute & Convelescent)

a. Poliomyelitis	Positive	1	☐
	Doubtful	2	☐
	Negative	3	☐

b. Coxsackie B — Positive 1 ☐

Doubtful 2 ☐

Negative 3 ☐

c. Influenza — Positive 1 ☐

Doubtful 2 ☐

Negative 3 ☐

d. Mumps — Positive 1 ☐

Doubtful 2 ☐

Negative 3 ☐

e. Others (specify) .....

.....

27. Serology test for chagus disease

Positive 1 ☐

Doubtful 2 ☐

Negative 3 ☐

28. Blood film for filariasis

Positive 1 ☐

Negative 2 ☐

29. Other parasites isolated (specify)

.....

.....

30. VDRL

Strongly positive	1	☐
Weakly positive	2	☐
Negative	3	☐

31. Stool

a. Hookworm	Present	1	☐
	Absent	2	☐
b. Ascaris	Present	1	☐
	Absent	2	☐

32. RBC transketolase

a. TPP effect ☐☐ %

b. Severely deficient	1	☐
Marginally deficient	2	☐
Normal	3	☐

33. Plasma thiocyanate

Increased	1	☐
Doubtful	2	☐
Normal	3	☐

34. Riboflavine status — Normal 1 ☐

Deficient 2 ☐

35. Cardiac output ☐☐ Litres/min

IV HAEMODYNAMICS

1. a. P A W — Systolic ☐☐☐

Diastolic ☐☐☐

Mean ☐☐☐

b. P.A. — Systolic ☐☐☐

Mean ☐☐☐

c. R. V. — Systolic ☐☐☐

Diastolic ☐☐☐

Mean ☐☐☐

d. P.C. — Systolic ☐☐☐

Diastolic ☐☐☐

Mean ☐☐☐

e. L.V.

Systolic

Diastolic

Mean

f. A.O.

Systolic

Diastolic

Mean

2. LV + PAW simultaneous EDG

3. LV -> AO Systolic gradient

4. Pulmonary arteriolar resistance

5. Total pulmonary resistance

6. Angiographic findings

Specify:

V LIVER BIOPSY:

a. Nutritional changes:

Present 1

Absent 2

Specify changes

b. Hepatitis — Present 1 ☐

Absent 2 ☐

c Amyloid — Present 1 ☐

Absent 2 ☐

d. Iron content — Excessive 1 ☐

Normal 2 ☐

e. Other changes (Specify)

VI Rectal biopsy

Amyloid — Present 1 ☐

Absent 2 ☐

VII Tz-resin uptake (Normal = 90 - 110%)

Increased 1 ☐

Normal 2 ☐

Decreased 3 ☐

VIII (a) Blood Pyruvate — Low 1 ☐

Normal 2 ☐

Raised 3 ☐

(b) Pyruvate Metabolism test

Normal 1 ☐

Abnormal 2 ☐

(c) Blood lactate Normal 1 ☐

Raised 2 ☐

IX AUTOPSY FINDINGS .....

☐☐

X Final Diagnosis and Aetiology

a. Specify .....

☐☐

b. State whether Clinical 1 ☐

Clinical + Autopsy 2 ☐

XI Treatment with dates

	Drug	Dose	Date started	Date stopped	Duration
a.	Digoxin				
b.	Frusemide				
c.	Thiazides				
d.	Thiamine				
e.	Others				
	1				
	2				
	3				

APPENDIX 2

THE STUDENTS TO WHOM WE GAVE QUESTIONS

NAME	SEX	AGE	SOCIO-ECONOMIC	ALCOHOL INTAKE	TOTAL SERUM PROTEIN	SERUM ALBUMIN	TRYPANOSOMIA		COEFFICIENTS & VIRULENCE									
							INITIAL	RECALLED	B_1		B_2		B_3		B_4		B_5	B_6
F. E.	M	60	II	-	11.[illegible]	4.0	-	-	-	-	-	1:4	-	-	-	-	-	-
J. I.	F	30	I	-	3.[illegible]	4.0	-	1:4	-	-	1:8	1:4	1:8	1:8	-	-	-	-
K. C.	F	71	I	-	7.2[illegible]	3.4	-	-	-	-	-	-	-	-	1:8	1:32	1:32	1:4
E. F.	M	27	I	-	20.8[illegible]	3.8	1:4	1:8	-	-	-	-	-	-	-	1:4	-	-
F. C.	M	30	I	-	2.[illegible]	3.3	-	-	-	-	-	1:4	-	-	-	1:4	-	-
E. C.	M	25	II	-	10.2[illegible]	4.0	1:4	1:16	-	-	1:32	1:8	1:8	1:8	1:4	1:4	1:16	1:16
A. A.	F	64	I	-	[illegible]	3.7	1:4	-	1:8	-	1:16	-	-	-	-	-	-	-
M. C.	M	30	II	+	3.9[illegible]	3.8	-	-	1:8	-	1:4	1:16	1:16	1:16	1:8	-	-	-
K. A.	M	40	I	-	37.3[illegible]	3.2	-	1:32	-	-	-	-	-	-	-	-	-	-
J. A.	F	63	I	-	10.7[illegible]	3.1	1:8	-	-	-	1:4	1:8	1:16	1:32	1:8	1:32	1:32	-
E. C.	F	40	I	-	7.6[illegible]	3.4	-	-	-	-	1:32	1:32	1:8	-	-	1:4	1:4	1:32
A. F.	M	74	I	-	7.2[illegible]	3.5	-	-	1:16	-	1:8	1:32	1:4	-	1:4	1:16	1:8	-
F. F.	F	62	I	-	8.1[illegible]	4.0	-	-	1:8	-	1:4	-	1:4	-	-	-	-	-
J. C.	F	46	I	-	10.7[illegible]	3.5	1:4	-	-	-	-	-	-	-	-	-	1:4	1:32
J. A.	F	50	I	-	23.9[illegible]	3.8	1:32	1:8	-	-	-	-	-	-	1:4	-	1:4	-
C. C.	F	54	I	-	23[illegible]	3.9	-	-	-	-	-	-	-	-	1:4	-	1:4	-
E. L.	F	60	I	-	2.6[illegible]	3.7	1:4	-	-	-	-	-	-	-	1:4	-	-	1:4
A. J.	F	59	I	-	0.8[illegible]	3.5	-	1:4	1:8	1:4	1:4	1:4	1:4	1:4	1:8	1:4	1:8	-
A. I.	F	65	I	-	1.2[illegible]	3.7	-	-	-	-	-	-	-	-	-	-	1:8	1:4
O. A.	F	35	I	-	11.8[illegible]	3.5	-	1:4	-	-	-	1:8	1:4	-	1:4	-	1:4	-
I. E.	F	22	II	-	2.2[illegible]	4.0	1:16	-	-	-	-	-	-	-	-	-	1:4	-
E. A.	F	30	II	-	17.5[illegible]	3.9	1:8	1:4	-	-	-	-	-	-	-	-	1:8	1:4
B. I.	F	31	I	-	[illegible]	3.7	1:4	-	-	-	-	-	-	-	-	-	-	-
A. F.	F	37	I	-	12.8[illegible]	3.1	1:4	1:4	-	-	-	-	-	-	1:8	-	1:4	-
F. I.	F	38	II	-	64.6[illegible]	3.9	1:4	1:4	-	-	-	-	1:8	1:4	1:4	1:4	1:4	1:4
B. A.	M	60	II	-	12.5[illegible]	3.6	-	1:4	1:4	-	-	-	-	-	-	-	-	-
J. I.	M	42	I	-	8.6[illegible]	4.0	1:16	1:4	1:4	-	1:4	-	1:4	-	1:4	-	1:4	-
E. A.	M	60	I	-	[illegible]	2.7	-	1:4	-	-	-	-	-	-	-	-	-	1:4
P. A.	M	40	I	+	3.3[illegible]	4.0	-	-	-	-	-	-	-	-	-	-	-	-
E. I.	M	65	I	-	10.6[illegible]	3.8	-	-	-	-	1:16	1:4	1:4	-	1:4	-	1:8	1:16
C. E.	M	48	I	-	10.2[illegible]	3.6	1:8	1:2	-	-	-	-	-	-	-	-	-	1:4
A. I.	M	42	I	-	7.2[illegible]	4.3	-	-	-	-	1:4	-	1:4	1:4	-	-	-	-
F. A.	M	76	I	-	11.7[illegible]	3.8	-	-	-	-	-	-	-	-	-	-	-	1:4
A. C.	M	57	II	-	[illegible]	3.9	1:16	1:4	-	-	1:16	1:4	-	-	-	-	-	-
C. A.	M	59	I	-	5.2[illegible]	3.9	-	-	-	-	-	-	-	-	-	-	-	-
F. M.	M	59	II	+	3.2[illegible]	4.2	-	-	-	-	1:4	1:8	-	-	1:8	1:4	-	-
E. F.	F	55	II	-	8.4[illegible]	4.0	-	1:4	-	1:4	-	-	-	-	-	-	-	-
E. I.	M	57	I	-	11[illegible]	4.2	-	-	-	-	-	-	-	-	-	-	1:8	-
I. E.	M	24	II	-	[illegible]	3.9	1:4	1:16	1:4	1:4	-	-	-	-	-	-	-	-
I. D.	M	22	II	-	2.1[illegible]	3.9	1:4	1:32	1:8	[illegible]	1:8	-	1:4	-	1:8	-	-	-
																		1:8

NAME	SEX	AGE	SOCIO-ECONOMIC	ALCOHOL INTAKE	THIAMINE STATUS	SERUM ALBUMIN	TOXOPLASMA		COXSACKIE B VIRUSES											
							INITIAL	SECOND	B_1		B_2		B_3		B_4		B_5		B_6	
G. C.	F	40	L	-	21.6%	3.9	-	-	-		-		-		-		-		1:4	
Y. A.	M	60	L	-	13.7%				-	-	-	-	-	-	-	-	-	-	-	-
I. C.	F	40	L	-	11.0%	3.6	1:16	1:8	-	-	-	-	-	-	-	-	-	-	-	-
P. C.	M	56	H	-	12.0%	3.2	1:16	1:8	-		1:4		-		1:4		-		-	
A. C.	F	44	L	-	6.0%	3.6	1:16	1:8	-	-	-		-	-	1:4	-	-	-	1:4	-
J. C.	F	56	L	-	8.0%	3.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-
S. E.	F	60	L	-	9.0%	3.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-
S. S.	M	45	L	-	1%	3.0	1:8	1:4	-		-		-		1:4		-		-	
C. A.	F	33	L	-	19.0%	3.0	-	-	-		1:4		-		-		-		-	
A. A.	M	36	L	-	10.0%	4.9	1:8	1:4	1:4		-		-		-		-		1:4	
S. A.	M	55	H	-	4.2%	4.1	-	-		1:4		1:4		1:4		1:4		-		-
T. A.	M	60	H	-	2.6%	4.0	-	-	1:4	-	1:4	1:4	1:4	-	1:4	-	-	-	-	-