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Idiopathic Cardiomegaly in Ceylon

Congestive Cardiac Failure, Cardiomegaly, Hepatomegaly, and Portal Fibrosis Associated with Malnutrition

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Cardiomyopathy or primary myocardial disease is being recognized with increasing frequency and different clinical syndromes belonging to this group of diseases have been described from various parts of the world. Amongst the causes reported are familial, inflammatory, allergic, toxic, nutritional, metabolic, cardiomyopathy associated with various systemic diseases, blood dyscrasias, collagen, malignant, and neuromuscular disorders. However, in the vast majority of cases no definite cause can be attributed. While all patients who suffer from cardiomyopathy manifest a number of similarities, there are a number of important differences that help to distinguish them.

This paper describes a well-defined clinical syndrome seen in Ceylonese patients with poor nutritional background, manifesting signs of malnutrition, congestive cardiac failure, cardiomegaly of unknown aetiology, hepatomegaly with portal fibrosis, and abnormal serum proteins. They were thought to be suffering from idiopathic cardiomegaly. The clinical picture in 28 such patients, post-mortem appearances in 4, and a comparison of their incomes, dietary habits, liver biopsy appearances, plasma protein electrophoretic patterns, biochemical, and blood picture studies, with patients suffering from congestive failure secondary to ischaemic, rheumatic, and hypertensive disease, is described. The latter patients served as controls.

Subjects and Methods

Studies were made of 28 patients admitted to the Colombo South Hospital who were suffering from congestive cardiac failure and cardiomegaly of unknown aetiology. Selection of patients was originally based on exclusion of all known causes of cardiac enlargement and congestive cardiac failure which occur in Ceylon. These were systematically sought and excluded. Moreover, patients with cardiomegaly secondary to established causes of cardiomyopathy, such as viral, malignant disease, blood dyscrasias, and alcoholic heart diease, were excluded.

In the history, attention was devoted to familial occurrence of heart disease and past history of febrile illnesses, infectious disease, alcoholism, and exposure to noxious agents. Since dietary habits are largely controlled by income, the incomes of patients suffering from the four most common causes of heart failure: ischaemic, cardiomyopathy, rheumatic, and hypertensive heart disease, were compared. The family monthly income refers to the total emoluments earned by members of a patient's family. The *per capita* income was also determined. Dietetic histories were obtained by a questionnaire; from details of diet consumed per week, the daily intake of calories, protein, fat, and carbohydrate was calculated. The diets of patients suffering from heart failure secondary to idiopathic cardiomegaly, ischaemic, hypertensive, and rheumatic heart disease were compared.

The main clinical features, serial electrocardiograms, and chest *x*-ray films were studied. Needle liver biopsies were carried out on 65 patients suffering from congestive cardiac failure irrespective of cause. Four patients with idiopathic cardiomegaly came to necropsy and the findings are described.

Results

The aetiology of congestive cardiac failure in 150 consecutive patients admitted to Colombo South Hospital is given in Table I. Idiopathic cardiomegaly accounted for 21 per cent and occurred mainly in the older age-groups, i.e. 41–70 years, as did ischaemic and hypertensive disease. Cardiomyopathy due to other causes accounted for 5 per cent.

Investigations were made on 14 men and 14 women suffering from idiopathic cardiomegaly. There was no familial history either of heart disease

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TABLE I

AETIOLOGY OF CONGESTIVE CARDIAC FAILURE IN 150 CONSECUTIVE PATIENTS AGED BETWEEN 10 AND 70 YEARS ADMITTED TO COLOMBO SOUTH HOSPITAL

Aetiology	Age-group (yr.)												Total	Percentage incidence
	11–20		21–30		31–40		41–50		51–60		61–70			
	M	F	M	F	M	F	M	F	M	F	M	F		
Ischaemic					1		3	1	11	6	15	8	45	30·0
Cardiomyopathy (idiopathic)						1	1	3	9	5	4	8	31	20·7
Cardiomyopathy (other causes)	1 (haemolytic anaemia)				1 leukaemia (acute)		1 malignant disease)		3 (alcohol)		1 (virus)		7	4·7
Rheumatic	2	4	2	3	5	4	1	4		1	2	1	29	19·3
Hypertension					1		1	1	2	1	4	5	15	10·0
Congenital		1			1	2	1	1		1		2	9	6·0
Cor pulmonale						1		1	2		1	2	7	4·7
Pericardial disease		1		1		1							3	2·0
Thyrotoxic heart disease								1				2	3	2·0
Syphilitic aortitis												1	1	0·6
	3	6	2	4	9	9	7	13	27	14	27	29	150	100

M, male; F, female.

or sudden death, and no history of febrile illnesses, exposure to toxic agents, or consumption of alcohol. Filaria was endemic in the area, and 5 patients gave histories of having been afflicted by it, but repeated blood films examined for microfilaria were negative.

Incomes and Diets. The monthly family incomes of patients suffering from the common causes of heart failure, ischaemic, idiopathic cardiomegaly, rheumatic, and hypertensive heart disease, were determined and grouped under four categories—Rs. 0–50/-, 51–100/-, 101–500/-, and over 500/- (Table II). Of the patients suffering from idiopathic cardiomegaly, 94 per cent were in the two lower income groups, and 61 per cent were in the lowest group. Patients suffering from ischaemia, hypertension, and "cardiomyopathy from other causes" were equally distributed in all four groups, rheumatic heart disease occurring mainly in the lower three. Two patients suffering from idiopathic cardiomegaly earned over Rs. 100/- monthly. The diets of these patients, however, were inadequate. The incomes of patients calculated on a *per capita* basis gave similar results. Those suffering from idiopathic cardiomegaly earned significantly less than the others.

The mean daily dietetic intake of patients suffering from congestive cardiac failure secondary to idiopathic cardiomegaly, ischaemia, rheumatism, and hypertension is given in Table III. The mean calorie, protein, fat, and carbohydrate intake of patients suffering from this anomaly was significantly lower than that of patients in the other three groups taken together ($p < 0.001$) and individually ($p < 0.001$). There was no significant difference in the diets of patients with ischaemic, rheumatic, and hypertensive heart disease.

Clinical Features. The clinical picture was a combination of bilateral heart failure and malnutrition, and is summarized in Table IV.

The patients were malnourished and underweight. The mean weight of the male patients was 43·5 kg. (96 lb.) (range 36–50 kg.) and of the female patients 36 kg. (79 lb.) (range 28·5–44 kg.), about 20 per cent below average weight according to standard weight tables for Ceylonese adults (Nicholls, 1951). Hepatomegaly was a constant feature being 3–6 cm.

TABLE II

INCOME GROUPS OF PATIENTS SUFFERING FROM CONGESTIVE CARDIAC FAILURE

	Income group (Rs.)				
	0–50	51–100	101–500	500 and over	Total
Idiopathic cardiomegaly	19	10	2	0	31
Ischaemic heart disease	11	12	12	10	45
Rheumatic heart disease	8	9	11	1	29
Hypertensive heart disease	4	4	4	3	15
Cardiomyopathy (other causes)	2	2	2	1	7

TABLE III

CALORIE, PROTEIN, FAT, AND CARBOHYDRATE INTAKE OF PATIENTS SUFFERING FROM CONGESTIVE CARDIAC FAILURE SECONDARY TO IDIOPATHIC CARDIOMEGALY, ISCHAEMIC, RHEUMATIC, AND HYPERTENSIVE CARDIAC DISEASE

IIIA:—Idiopathic Cardiomegaly Compared with Others

	Calories		Fats		Protein		Carbohydrate	
	Idiopathic cardio-megaly	Others	Idiopathic cardio-megaly	Others	Idiopathic cardio-megaly	Others	Idiopathic cardio-megaly	Others
No. of individuals	25	55	25	35	25	55	25	55
Mean	1501	1762	46	55	34	46	224	272
SD	203	234	3	8	7	8	77	48

IIIB:—Mean Values for Ischaemic, Rheumatic, and Hypertensive Heart Disease

	Calories	Fats	Protein	Carbohydrate
Ischaemic	1731	52	45	270
Rheumatic	1764	55	44	276
Hypertension	1816	57	48	271

in 18, 7–10 cm. in 9, and 15 cm. in 1 patient. Splenomegaly was present in 3 and ascites in 10.

Cardiovascular System. There were three clinical types, as judged by the effect of the disease on cardiac function, which appeared to be different stages of the same disease process.

The first type was symptom-free cardiomegaly. These patients were not in heart failure and therefore not included in the present study. Their natural history is being observed and will form the subject of a separate paper. However, two of these patients subsequently developed signs of heart failure presenting the physical signs of type 2.

TABLE IV

FREQUENCY DISTRIBUTION OF SYMPTOMS AND SIGNS

Cardiac symptoms	No. of patients	Symptoms of malnutrition	No. of patients
Dyspnoea	28	Anorexia, nausea	12
Undue fatigue	25	Vague ill health	8
Swelling of ankles	22	Indigestion and flatulence	4
Palpitations	19	Loss of weight	24
Paroxysmal nocturnal dyspnoea	15		
Undue sweating	14		
Angina	8		
Effort syncope	6		
Haemoptysis	3		
Cough	3		
Cardiac signs	**No. of patients**	**Signs of malnutrition**	**No. of patients**
Orthopnoea	14	Generalized oedema	29
Raised jugular venous pressure	28	Mild	10
Jerky pulse	13	Moderate	8
Feeble pulse	15	Severe	10
		Ascites	10
Cardiac impulse		Hepatomegaly	28
Left ventricular	15	3–6 cm.	18
Right ventricular	3	7–10 cm.	9
Feeble	10	15 cm.	1
Auscultation		Underweight	28
Prominent 3rd heart sound	17		
Prominent 4th heart sound	9	Hair changes	8
Summation gallop	2		
Fixed splitting of 2nd sound	1	Skin changes	5
Paradoxical splitting of 2nd sound	2	Angular stomatitis	3
Basal ejection systolic murmur	3	Glossitis	1
Murmur of mitral regurgitation	12	Premature ageing, looking	
Murmur of tricuspid regurgitation	6	older than stated age	28

The second type presented with congestive cardiac failure associated with conspicuous ventricular hypertrophy of either or both ventricles.

The third type presented with congestive cardiac failure and massive cardiac dilatation with atrio-valvular incompetence.

The second and third types will now be discussed in detail.

Type 2: Congestive cardiac failure with evidence of hypertrophy of either or both ventricles. This type occurred in 14 patients (7 male and 7 female). They appeared less ill and had a shorter history than the third type. The average duration of symptoms was 2 years. The jugular venous pressure was raised. A giant 'a' wave measuring between 6 and 15 cm. was present in 6 patients; a less striking but prominent 'a' wave was present in 8 patients. The arterial pulse was brisk or jerky in 7 and felt normal in 7. One patient had a prominent right ventricular cardiac impulse, 8 patients had a prominent left ventricular heave, and in 5 patients the cardiac impulse was both right and left ventricular in type: they were in sinus rhythm and ectopic beats were frequently present. Two patients exhibited paradoxical splitting of the second sound. A third heart sound was audible in 5, a loud fourth heart sound was present in 7, and summation gallop in 2 patients. An ejection systolic murmur was present in 4, heard best between the apex and the lower left sternal border. A late pansystolic murmur (grade 1/4) was heard at the apex in 2. Blood pressure on admission ranged between 150 and 80 mm. Hg systolic and 90 and 60 mm. Hg diastolic. The pressures on admission tended to be slightly raised and fell as the signs and symptoms of heart failure disappeared. In no instance was there sustained hypertension. Pulmonary crepitations were heard in 9 patients. Hepatomegaly with tenderness of the liver and generalized oedema were present in all, and ascites in 4.

Type 3. Congestive cardiac failure with cardiac dilatation and atrio-valvular incompetence, mitral, tricuspid, or both. This type occurred in 14 patients (7 male and 7 female). The average duration of symptoms was 3·7 years. All had signs of congestive cardiac failure. The jugular venous pressure was always raised and above 6 cm., with prominent systolic v waves followed by a steep y descent. The pulse was of small volume, and atrial fibrillation occurred in 8 patients and frequent extrasystoles in 6. The heart was considerably enlarged and the cardiac impulse usually feeble in contrast to the former type. Third sounds were heard in every case, either in the mitral or in the tricuspid areas. Grade 2 to 3 intensity pansystolic murmurs of mitral incompetence were heard; 10 had predominant mitral incompetence, 3 had both mitral and tricuspid incompetence, and 1 had evidence of lone tricuspid incompetence. Crepitations were heard over the lung bases. Massive hepatomegaly and generalized oedema occurred in every patient, 1 had an enlarged spleen and 6 had ascites. The blood pressure varied between 140 and 90 mm. Hg systolic and 80 and 55 mm. Hg diastolic. Signs of pericardial involvement were absent. One patient developed a pulmonary infarct.

Electrocardiograms. The electrocardiograms were abnormal in all patients and are described in Table V.

Radiology of the Heart. There was gross enlargement of the heart; mean cardiothoracic ratio was 0·70 (range 0·53 to 0·80). Considerable fluctuation in size occurred early on. In two patients there was a return to normal size after treatment of the episode of failure. Later, in the course of the disease, enlargement persisted and progressed.

The cardiac silhouette was not characteristic or constant in shape nor was there any clear pattern of chamber enlargement which seemed to affect all chambers. Left ventricular enlargement was common and occurred in 27 patients; gross enlargement occurred in 10. Right ventricular

TABLE V

FREQUENCY DISTRIBUTION OF ELECTROCARDIOGRAPHIC FINDINGS

Abnormal findings	No. of patients
Non sinus arrhythmias	
Atrial fibrillation	8
Paroxysmal atrial tachycardia	1
Extrasystoles (mainly ventricular)	10
Atrioventricular conduction defects	
1st degree heart block	8
Intraventricular conduction defects	
Partial right bundle-branch block	4
Complete right bundle-branch block	1
Complete left bundle-branch block	2
Mean QRS axis	
Normal	17
Horizontal (0–minus 30)	7
Left axis (minus 30 and less)	4
Right axis (105 or greater)	0
Left ventricular hypertrophy Grade 1	3
Grade 2	4
Grade 3	3
Grade 4	1
Right ventricular hypertrophy	1
Biventricular hypertrophy	5
Low voltage complexes with flat or inverted T waves	8

TABLE VI

RESULTS OF LIVER BIOPSY IN PATIENTS SUFFERING FROM CONGESTIVE CARDIAC FAILURE SECONDARY TO IDIOPATHIC CARDIOMEGALY, ALCOHOLIC CARDIOMYOPATHY, ISCHAEMIC, RHEUMATIC, AND HYPERTENSIVE DISEASE, AND A MISCELLANEOUS GROUP

	Idiopathic cardiomegaly	Alcoholic cardiomyopathy	Ischaemic heart disease	Rheumatic heart disease	Hypertension	Miscellaneous
Portal fibrosis						
Grade 1	7	0	5	2	0	0
Grade 2	13	1	0	2	0	0
Grade 3	8	2	0	0	0	0
Total	28	3	5	4	0	0
Percentage	100	100	36	36	0	0
Cardiac cirrhosis	0	0	0	1	0	0
Normal histology	0	0	9	6	5	4
Total	28	3	14	11	5	4

enlargement occurred in 18; gross enlargement in 4. Right atrial enlargement was constant and occurred in all 28; left atrial enlargement in 14. The pulmonary arc was straight in 16 and prominent in 8. The ascending aorta was usually small, with no calcification. The lungs frequently showed pulmonary congestion, pulmonary oedema, and pleural effusions.

Liver Biopsy Studies and Tests of Liver Function. The results of liver biopsy performed in 65 patients suffering from congestive cardiac failure are given in Table VI.

Varying degrees of portal fibrosis were present in all the patients with idiopathic cardiomegaly and alcoholic cardiomyopathy, and in a third of the patients suffering from ischaemic and rheumatic disease.

The degree of fibrosis varied from minimal around the portal tracts, to complete nodular cirrhosis with complete distortion of liver architecture by intralobular strands of fibrous tissue, bile-duct proliferation, and evidence of hypertrophic nodularity. Extreme fibrosis was restricted to patients with idiopathic and alcoholic cardiomyopathy. Cardiac cirrhosis was present in one patient suffering from rheumatic disease.

Serum Proteins. The serum protein levels in patients with idiopathic cardiomegaly and in the controls are given in Table VIIA. The mean total serum protein (6·1g./100 ml.) in idiopathic cardiomegaly was lower than the other heart failure controls (7·1 g./100 ml.). The A/G ratio, 0·77/1 in idiopathic cardiomegaly, was reversed and caused by a distinct fall in serum albumin to 2·7 g./100 ml. and an increase in the serum globulin to 3·4 g./100 ml. The A/G ratio in the controls was 1·04/1 and the respective serum albumin and globulin levels were 3·63 and 3·48 g./100 ml. There was no significant difference in the values obtained in the 3 groups of controls, ischaemic, hypertensive, and rheumatic disease.

The electrophoretic patterns of patients suffering from idiopathic cardiomegaly were compared with the same controls. These figures, along with the values obtained from 50 healthy Ceylonese (Hoover, 1956) and the normal Western figures (Harper, 1963), are given in Table VIIB. Patients with idiopathic cardiomegaly had a lowered serum albumin fraction (39·5%) and much raised gamma-globulin fraction (32·4%). The albumin fraction of the controls and the healthy Ceylonese was slightly lower and the gamma-globulin levels slightly raised when compared with Western figures. The patients with idiopathic cardiomegaly, in common with the control heart failure patients, had a slightly raised beta-globulin.

Repeated electrophoretic pattern determinations on 8 patients suffering from idiopathic cardiomegaly during their stay in hospital while being treated for their heart failure and fed on an adequate diet (200 calories, 70 g. protein, 64 g. fat, and 286 g. carbohydrate) with supplements of calcium caseinate, demonstrated a rise in the serum albumin and a fall in the gamma-globulin levels within 2 weeks (Table VIIC).

Eight patients who returned home to an inadequate diet but continued to take anti-failure treatment registered a further fall in albumin and rise in gamma-globulin.

Other Biochemical Tests. The mean serum cholesterol level in patients with idiopathic cardiomegaly was 154 mg./100 ml., SD ± 38, significantly lower than in patients with ischaemic (265 mg./100 ml., SD ± 70), hypertensive (264 mg./100 ml., SD ± 73), and rheumatic disease (180 mg./100 ml., SD ± 16) at the 5 per cent level of significance.

Similarly, the mean blood urea levels in patients

TABLE VIIA

TOTAL SERUM PROTEIN, A/G RATIO, SERUM ALBUMIN, AND GLOBULIN IN 28 PATIENTS WITH CONGESTIVE CARDIAC FAILURE SECONDARY TO IDIOPATHIC CARDIOMEGALY COMPARED WITH 42 PATIENTS WITH CONGESTIVE CARDIAC FAILURE SECONDARY TO ISCHAEMIC, RHEUMATIC, AND HYPERTENSIVE HEART DISEASE

	Total protein (g./100 ml.)	A/G ratio	Serum albumin (g./100 ml.)	Serum globulin (g./100 ml.)
Idiopathic cardiomegaly				
Mean	6·1	0·77/1	2·7	3·4
Range	4·3–7·6	0·29/1–1·4/1	1·1–3·9	2·5–4·8
Controls*				
Mean	7·1	1·04/1	3·63	3·48
Range	6·6–8·2	0·6/1–1·8/1	2·0–4·7	2·3–4·5

* Controls: ischaemic 18, rheumatic 16, hypertensive 8.

TABLE VIIB

ELECTROPHORETIC PATTERNS OF SERUM PROTEINS IN 28 PATIENTS WITH IDIOPATHIC CARDIOMEGALY COMPARED WITH 42 CONTROLS* WITH HEART FAILURE, NORMAL VALUES FOR CEYLON† AND STANDARD WESTERN FIGURES‡

	Idiopathic cardiomyopathy (28)	Controls (42)	Normal values for Ceylon	Standrad figures for Western norm
Albumin				
Mean	39·5%	51·4%	59·5%	55·2%
Range	(25·4–52·8)	(38·2–60·6)	(50·3–68·7)	
Alpha-1 globulin				
Mean	3·8%	2·3%	2·8%	5·3%
Range	(2·1–7·3)	(2·3–8·8)	(0·73–4·87)	
Alpha-2 globulin				
Mean	10·1%	11·3%	7·7%	8·7%
Range	(5·5–15·0)	(6·4–14·8)	(4·4–10·9)	
Beta-globulin				
Mean	14·2%	15·1%	10·6%	13·4%
Range	(8·7–19·5)	(9·7–20·8)	(8·2–13·0)	
Gamma-globulin				
Mean	32·4%	19·7%	19·2%	11·0%
Range	(18·8–52·1)	(12·5–27·0)	(13·3–25·1)	

* Controls: ischaemic 18, rheumatic 16, hypertensive 8.
† Hoover (1956).
‡ Harper (1963).

TABLE VIIC

MEAN ELECTROPHORETIC PATTERNS OF SERUM PROTEINS IN 8 PATIENTS WITH IDIOPATHIC CARDIOMEGALY BEFORE AND 2–4 WEEKS AFTER TREATMENT WITH HIGH PROTEIN DIET AND ANTI-CONGESTIVE FAILURE MEASURES

	Initial pattern	2–4 weeks later
Albumin	39·7%	46·6%
Alpha-1-globulin	3·1%	4·2%
Alpha-2-globulin	9·5%	10·1%
Beta-globulin	14·3%	14·4%
Gamma-globulin	33·4%	24·7%

suffering from idiopathic cardiomegaly (27 mg./100 ml., SD ± 9) were significantly lower than in ischaemic (34 mg./100 ml., SD ± 10), hypertensive (30 mg./100 ml., SD ± 7), and rheumatic disease (34 mg./100 ml. SD ± 13) at the 5 per cent level of significance.

Blood Studies. Haemoglobin levels and blood picture studies carried out on 20 patients with idiopathic cardiomegaly and 20 controls suffering from heart failure secondary to other causes are given in Table VIII.

The mean haemoglobin of patients with this lesion (10·96 g./100 ml.) was lower than those with ischaemia (11·8 g.), hypertension (11·5 g.), and miscellaneous disorders (12·6 g.), but higher than patients with rheumatic disease (9·2 g.). Anaemia and slightly abnormal blood pictures are not

TABLE VIII

BLOOD PICTURE STUDIES AND HAEMOGLOBIN LEVELS

No. of patients		Haemoglobin (g./100 ml.)		Blood picture			
				Normal	Abnormal		
					Nutritional anaemia and iron deficiency†	Nutritional anaemia	Iron deficiency
Idiopathic cardiomegaly	20	Mean	10·96	8	1	8	3
		Range	(10·8–15·7)				
Ischaemic	5	Mean	11·80	1	3	0	1
		Range	(10·6–12·7)				
Rheumatic	5	Mean	9·2	2	1	1	1
		Range	(3·7–12·6)				
Hypertension	5	Mean	11·5	3	0	1	1
		Range	(9·7–12·2)				
Miscellaneous*	5	Mean	12·6	4	0	0	1
		Range	(10·8–15·8)				

* Virus cardiomyopathy 1; acyanotic congenital heart disease 4.
† Dimorphic picture.

uncommon in patients in the lower income groups in Ceylon.

Pathology. Four necropsies were performed, and the findings are summarized in Table IX. The patients were emaciated. Two showed generalized oedema. One had a pleural effusion and 2 had small pericardial effusions consisting of 100 and 150 ml. clear serous fluid.

Gross Appearance. The average weight of the hearts was 465 g. The hearts were enlarged due to varying degrees of hypertrophy and dilatation of the chambers: the right atrium was dilated in all 4, strikingly so in 2; the right ventricle was dilated in all 4, the wall was thin and flabby in 2, and hypertrophied in 2; the left ventricle was hypertrophied in all 4, strikingly in 2; the tricuspid orifice was dilated in all 4; the mitral orifice dilated in 2. The valve cusps were normal. The coronary arteries were healthy in 3, but there was slight atheroma in 1, a 69-year-old woman. Changes in the endocardium were inconspicuous, there being no endocardial fibrosis. The pericardium was normal. There were no mural thrombi.

The liver was enlarged and firm in consistency in all 4.

TABLE IX

SUMMARY OF PATHOLOGICAL FINDINGS IN 4 PATIENTS WITH IDIOPATHIC CARDIOMYOPATHY

	Case 1	Case 2	Case 3	Case 4
Age (yr.) and sex	50, M	55, M	47, F	69, F
Heart weight (g.)	350	540	410	560
Right atrium	Very dilated	Dilated	Very dilated	Dilated
Left atrium	Slight thickening of endocardium	Normal	Normal	Normal
Right ventricle	Dilated, wall thin and flabby	Dilated, slight hypertrophy	Dilated, wall thin and flabby	Dilated, slight hypertrophy
Left ventricle	Some hypertrophy	Hypertrophied	Slight hypertrophy	Hypertrophy
Tricuspid orifice	Dilated	Dilated	Dilated	Dilated
Tricuspid valve cusps	Normal	Normal	Normal	Normal
Mitral orifice	Dilated	Normal	Normal	Slightly dilated
Mitral valve cusps	Normal	Normal	Normal	Normal
Pulmonary aortic valves	Normal	Normal	Normal	Normal
Coronary arteries	Normal	Normal	Normal	Slight atheroma
Histology				
Right atrium	Normal	Normal	Normal	Slight thickenings of endocardium
Left atrium	Slight thickening of endocardium	Normal	Normal	Interstitial fibrosis
Right ventricle	Oedema and separation of muscle fibres	Normal	Normal	Interstitial fibrosis with fragmenting of muscle fibres
Left ventricle	Some hypertrophy of muscle fibres, no fibrosis	Interstitial fibrosis with hypertrophy of muscle fibres	Normal	Marked interstitial fibrosis with fragmenting of muscle fibres
Liver	Chronic venous congestion and marked fibrosis around portal tracts with bile-duct proliferation	Venous congestion and increased fibrosis around portal tracts	Portal cirrhosis	Portal cirrhosis

Microscopy. There was slight thickening of the endocardium in the left atrium in one and right atrium in another. Myocardial changes were non-specific; both right and left ventricular muscle were normal in 1, hypertrophy with no fibrosis was present in the left ventricle of 1, interstitial fibrosis with muscle hypertrophy occurred in the left ventricle in 1, and interstitial fibrosis and fragmenting of muscle fibres occurred in both right and left ventricles in 1 patient. There was no cellular infiltration present in any. The liver showed fully established portal fibrosis in 2, marked fibrosis round the portal tract with bile-duct proliferation in 1, and increased fibrosis round the portal tracts in 1. There was no deposition of iron pigment, and no evidence of haemochromatosis or cystersiderosis.

The lungs, spleen, and kidneys showed evidence of chronic venous congestion. There was no evidence of infarction.

Course and Prognosis. The course was mainly a chronic one punctuated by frequent relapses and a steady decline in the cardiac state and general health. In proportion to the number of relapses, the heart size failed to revert to normal, and recovery from heart failure became less satisfactory until eventually the syndrome of congestive cardiac failure associated with massive cardiomegaly and generalized anasarca became refractory to all forms of treatment.

Although liver involvement was a constant feature in these patients, as judged by the liver biopsy appearances, no patient suffered from cholaemia or portal hypertension. The clinical picture was dominated by symptoms and signs of bilateral heart failure.

Two patients died of irreversible heart failure and terminal bronchopneumonia. Four patients who appeared to progress satisfactorily died suddenly and unexpectedly. Two of these, who died in hospital, had very low serum potassium levels (2·0 and 1·5 mEq/litre) which may possibly have been a contributory factor.

Treatment. Patients were treated with bed-rest, a nourishing diet (approximately 2000 calories per day containing 70g. protein, 64g. fat, and 286 g. carbohydrate) supplemented with calcium caseinate (Casilan-Glaxo), digitalis therapy, diuretics (thiazides), with supplements of potassium chloride (gr. 10 t.d.s.). Frequent injections of mersalyl and spironolactone were given for intractable oedema.

In view of the successful management of nutritional heart disease amongst the Bantu in South Africa, by Gillanders (1951), with nourishing diets without digitalis and diuretics, a few patients in this series were also treated purely on a dietary régime. They failed to respond. They were then treated with diet and diuretics without digitalis, and here too the response was unsatisfactory. The response of cardiac symptoms and signs to digitalis therapy, however, was dramatic. In view of the poor nutritional background of these patients, notwithstanding their dissimilarity from heart failure caused by beriberi, a few patients were treated with intravenous thiamine (500 mg. daily), but they did not improve.

Response to Treatment. Early on in the course of the disease there was complete recovery with a return of the heart size to normal, in two patients. With each relapse breathlessness and oedema disappeared but the heart remained enlarged and the jugular venous pressure high. Later cardiomegaly persisted, as did the hepatomegaly and generalized oedema, and the heart failure became irreversible and refractory to treatment.

Discussion

It was obvious from the very outset that these patients did not conform to the other established causes of congestive cardiac failure. One striking feature was that they came from the lower income group with a poor nutritional background. It was, therefore, important to establish whether their poverty and malnutrition were the cause or result of their heart disease. For this reason, these patients, all of whom had congestive failure, were compared with patients with heart failure secondary to other common causes, e.g. ischaemic, rheumatic, and hypertensive disease. The latter served as controls, and, unlike patients with idiopathic cardiomegaly, were equally distributed in the different income groups. The association of this anomaly with malnutrition was clearly established. The dietetic histories of these patients compared with the other three groups revealed a significantly lower intake of total calories, protein, fats, and carbohydrates. The total daily calorie intake was low as was the daily protein intake (34 g.), most of which was of vegetable origin.

Clinical proof of malnutrition in older patients is often difficult to establish, and unlike vitamin deficiency diseases there is no therapeutic test which could be applied, such as the dramatic clinical response which follows when an appropriate vitamin is administered. All patients suffering from idiopathic cardiomegaly were underweight, looked considerably older than their stated age, and had generalized oedema and sometimes ascites. They had features associated with malnutrition in Ceylon (Obeyesekere, 1961, 1966). A good index of their response to treatment was a gain in weight following an initial precipitous decline induced by the loss of

oedema fluid. Hepatomegaly was invariable and liver biopsy revealed hepatic fibrosis varying from a minimal fibrosis round the portal tracts to complete nodular cirrhosis. Both the incidence and severity of hepatic fibrosis were significantly greater in patients with idiopathic cardiomegaly than in controls. In earlier studies of malnutrition in Ceylonese adults, similar hepatic changes were described (Obeyesekere, 1966). The exact relation between malnutrition and cirrhosis of the liver is still not understood. It is believed that prolonged protein malnutrition may condition the liver to an increased susceptibility to hepatotoxins which lead to hepatic fibrosis and cirrhosis (*Brit. med. J.*, 1965).

There was strong biochemical evidence in support of malnutrition. Perhaps the most sensitive index of malnutrition is provided by the behaviour of serum proteins. The mean total serum proteins were lower than in the controls, and the A/G ratio was inverted, suggesting that some factor other than congestive cardiac failure was responsible. The electrophoretic pattern of patients suffering from idiopathic cardiomegaly was abnormal, in contrast to the controls suffering from heart failure, and the normal healthy Ceylonese.

The serum albumin was low and gamma-globulin fraction raised. This reverted to normal a few weeks after the patients were fed a well-balanced diet and regressed on their returning home to an inadequate diet. The serum protein pattern in these patients resembled that of infants with protein-calorie malnutrition (Schrimshaw *et al.*, 1956). Other biochemical evidence of malnutrition was the low mean serum cholesterol and blood urea levels. The mean cholesterol level was considerably lower than the mean values for normal Ceylonese men (Obeyesekere, 1964).

A mild degree of anaemia was present: the blood studies were in the main unhelpful.

Wenckebach described beriberi heart disease in 1928 from the East Indies. The patients had predominant right heart failure, with signs of a high cardiac output which responded in dramatic fashion to thiamine therapy. The condition was subsequently described in America and Europe mainly in association with chronic alcoholism. None of the patients in this series suffered from beriberi and the few patients treated with thiamine showed no response. In fact beriberi is extremely uncommon in Ceylon.

There are many obscure cardiomyopathies described from different parts of the vast African continent, about all of which "hangs a vague aura of malnutrition, metabolic defect or intoxication". The subject was reviewed by Davies (1960) with particular reference to morbid anatomy. More recently a study group set up by the World Health Organization discussed diagnostic criteria for tropical cardiomyopathies in living subjects (World Health Organization, 1965). Endomyocardial fibrosis and Chagas' heart disease have fairly well-defined clinical and pathological patterns. A number of less well-defined syndromes—nutritional heart disease (Gillanders, 1951), cardiovascular collagenosis (Becker, Chatgidakis, and van Lingen, 1953), heart muscle disease (Edington and Jackson, 1963), cardiac disorder of unknown aetiology (Stuart and Hayes, 1963), idiopathic cardiomegaly (Reisinger and Blumenthal, 1941)—have been described from different tropical countries. The main finding in this heterogeneous group labelled "cardiomegaly of unknown origin" is cardiac enlargement of unknown aetiology with myocardial failure.

Patients described in this paper gave a long history with an insidious onset. There was no pyrexia, or evidence of infection, parasitic infestation, allergy, leucocytosis, or eosinophilia. The patients presented with chronic heart failure of the hypokinetic type and cardiomegaly without any distinguishing features or with incompetence of one or both A–V valves. There was clinical and biochemical evidence of malnutrition and associated hepatic fibrosis which is known to occur in association with malnutrition in Ceylon. At necropsy, restricted to 4 patients, the hearts were enlarged due to dilatation and hypertrophy of the chambers, there was no endocardial fibrosis and no intramural thrombi, and the valve cusps were healthy. A varying degree of hypertrophy of ventricular muscle was present. Interstitial fibrosis of the ventricles was present in 2. There was no evidence of cellular infiltration. The relationship of idiopathic cardiomegaly encountered in Ceylon to the other types of tropical cardiomyopathies is not entirely clear. Cirrhosis of the liver and defective nutrition were frequently encountered, as was the absence of any known infection or infestation. There was a striking difference in the incidence of embolism which was uncommon in our patients. This raises the important question of whether all these syndromes described from different parts of the world constitute one single disease, with minor differences conditioned by variations in the non-nutritious diets and other environmental factors.

The pathogenesis of idiopathic cardiomegaly is obscure, as is the pathogenesis of all cardiomyopathies. Malnutrition causes widespread metabolic disturbance, alteration in tissue enzyme systems, and considerable changes in endocrine function, which could interfere with cardiac metabolism. In idiopathic cardiomegaly, as in cirrhosis of the liver, the

exact relationship of malnutrition in its aetiology is not understood. There is strong evidence that this condition is in some way associated with poor nutrition. It may even be that prolonged malnutrition predisposes the heart to an abnormal susceptibility to toxic agents which lead to cardiomegaly and subsequent heart failure.

Summary

A syndrome characterized by heart failure, cardiomegaly of unknown aetiology, and hepatomegaly with portal fibrosis was studied in 28 patients suffering from malnutrition. Four cases came to necropsy. Income, diets, liver biopsy, electrophoretic patterns of serum proteins, and other tests on these patients were compared with patients suffering from heart failure secondary to ischaemic, rheumatic, and hypertensive disease.

There were significant differences. Patients with idiopathic cardiomegaly were in the lower income group, while controls were not confined to any particular income level. Their daily calorie, protein, fat, and carbohydrate intake was singificantly lower ($p < 0{\cdot}001$).

Total serum proteins were lower with inversion of the A/G ratio. There was a lowering of the albumin fraction and conspicuous rise in gamma-globulins, resembling patterns of protein calorie malnutrition. This reversed on a nutritious diet and deteriorated on a poor one. All had hepatomegaly and fibrosis round portal tracts; portal cirrhosis occurred in 8. The blood urea and serum cholesterol levels were low. Pathogenesis was obscure but there was a strong association with poor nutrition.

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References

Becker, B. J. P., Chatgidakis, C. B., and van Lingen, B. (1953). Cardiovascular collagenosis with parietal endocardial thrombosis; a clinicopathologic study of 40 cases. *Circulation*, **7**, 345.

Brit. med. J. (1965). Editorial. Natural hepatotoxins. **1**, 1261.

Davies, J. N. P. (1960). Some considerations regarding obscure diseases affecting the mural endocardium. *Amer. Heart J.*, **59**, 600.

Edington, G. M., and Jackson, J. G. (1963). The pathology of heart muscle disease and endomyocardial fibrosis in Nigeria. *J. Path. Bact.*, **86**, 333.

Gillanders, A. D. (1951). Nutritional heart disease. *Brit. Heart J.*, **13**, 177.

Harper, H. A. (1963). *Review of Physiological Chemistry*, 9th ed., p. 133. Lange Medical Publications, Los Altos, California.

Hoover, A. A. (1956). Proceedings of the Twelfth Annual Sessions of the Ceylon Association for the Advancement of Science (Section E), p. 179. Ceylon.

Nicholls, L. (1951). *Tropical Nutrition and Dietetics*, 3rd ed., p. 315. Baillière, Tindall and Cox, London.

Obeyesekere, I. (1961). A malnutrition syndrome in adult females. *Ceylon med. J.*, **6**, 59.

—— (1964). Dietary fat, serum cholesterol, and ischaemic heart disease in Ceylon. *Brit. Heart J.*, **26**, 625.

—— (1966). Malnutrition among Ceylonese adults. *Amer. J. clin. Nutr.*, **18**, 38.

Reisinger, J. A., and Blumenthal, B. (1941). Myocardial degeneration with hypertrophy and failure of unknown cause. *Amer. Heart J.*, **22**, 811.

Scrimshaw, N. S., Behar, M., Arroyave, G., Viteri, F., and Tejada, C. (1956). Characteristics of Kwashiokor (sindrome pluricarencial de la infancia). *Fed. Proc.*, **15**, 977.

Stuart, K. L., and Hayes, J. A. (1963). A cardiac disorder of unknown aetiology in Jamaica. *Quart. J. Med.*, **32**, 99.

Wenckebach, K. F. (1928). St Cyres lecture on heart and circulation in a tropical avitaminosis (beri-beri). *Lancet*, **2**, 265.

World Health Organization (1965). Cardiomyopathies. *Bull. Wld Hlth Org.*, **33**, 257.