BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 14 1961

CLINICAL ASPECTS OF CARDIOMYOPATHY

BY

J. F. GOODWIN, M.D., F.R.C.P.
Senior Lecturer in Medicine and Physician

H. GORDON,* M.D., M.R.C.P.
Voluntary Research Assistant, Department of Medicine

A. HOLLMAN, M.D., M.R.C.P.
Assistant Lecturer in Medicine

AND

M. B. BISHOP, M.B., Ch.B., D.C.P.
Nuffield Research Assistant, Department of Surgery

From the Departments of Medicine and Surgery, Postgraduate Medical School and Hammersmith Hospital, London

[WITH SPECIAL PLATE]

The term "cardiomyopathy" has come into use to describe disorders of the heart not due primarily to rheumatic, hypertensive, coronary-artery, thyroid, or congenital disease. It is often assumed that cardiomyopathies are rare diseases; but, while this is true of some, recent work has tended to suggest that a number of cardiomyopathies may be commoner than previously thought. Nevertheless, despite increased awareness of the condition, we remain extremely ignorant of the causation of most of the cardiomyopathies.

No definition of the cardiomyopathies is entirely satisfactory, but the following is proposed as being generally useful. "Cardiomyopathy—a subacute or chronic disorder of heart muscle of unknown or obscure aetiology, often with associated endocardial, and sometimes with pericardial, involvement, but not atherosclerotic in origin."

Cardiomyopathy may be classified in many ways. The object of the present communication is to suggest a general classification for cardiomyopathy and to emphasize especially the methods of clinical presentation of this condition, basing conclusions on data derived from patients studied personally. So far as is possible the pathology has been correlated with the clinical presentation, with electrocardiography and radiology, and with the results of special investigations, such as angiocardiography and cardiac catheterization. No attempt has been made to give a full classification of all causes of cardiomyopathy.

Patients Studied

Sixty-six patients have been studied at Hammersmith Hospital, some of them in conjunction with our colleague, Dr. Donald Teare, of St. George's Hospital. Necropsy data have been available for most of these patients, but in some cases the clinical studies have been retrospective. Table I shows the pathological classification in the 66 cases studied, but does not necessarily indicate the relative frequency of the various types in the general population. There were 20 patients in whom cardiomyopathy was associated with, but not necessarily due to, a generalized disease such as carcinomatosis, a generalized infection, or a hypersensitivity state. Twelve patients did not have any associated general disease; in 7 of these there were characteristic pathological appearances such as endomyocardial fibrosis or endocardial fibroelastosis; in the other 5 the myocardial changes were non-specific. In the third group of 7 patients the heart was involved by a generalized disease such as amyloidosis, diffuse sclerosis (scleroderma), haemochromatosis, or leukaemia. Finally, there were 27 patients in whom a pathological or clinical diagnosis of asymmetrical hypertrophy of the heart had been made (Teare, 1958; Goodwin *et al.*, 1960; Hollman *et al.*, 1960). This condition, the pathology of which will be discussed later, produced evidence of obstruction to inflow or outflow of some part of the heart. The majority of patients showed evidence of obstruction to left ventricular outflow, thus simulating aortic stenosis. A smaller number showed some evidence of obstruction to right ventricular inflow, simulating tricuspid stenosis, and the minority showed evidence of obstruction to right ventricular outflow or left ventricular inflow. On the basis of these findings we suggest that cardiomyopathy may arise in three principal ways: (*a*) in association with

TABLE I.—*Pathological Classification of 66 Cases of Cardiomyopathy*

1. *Associated with general disease*

	No. of Patients
Carcinomatosis	4
Cirrhosis of liver	2
Infection	7
Hypersensitivity	4
Puerperal	1
Aplastic anaemia	1
Migrating thrombophlebitis	1
Total	20

2. *Without associated general disease*

	No. of Patients
Non-specific	5
Endomyocardial fibrosis	2
Familial	1
Endocardial fibroelastosis	1
Localized cardiac damage	3*
Total	12

3. *Cardiac involvement by generalized disease*

	No. of Patients
Amyloid	1
Scleroderma	2
Polyarteritis nodosa	2
Haemochromatosis	1
Leukaemia	1
Total	7

4. *Asymmetrical hypertrophy (obstructive cardiomyopathy)*

	No. of Patients
Right ventricular inflow	9
Right ventricular outflow	3
Left ventricular outflow	14
Left ventricular inflow	1
Total	27

* 2 with cardiac infarct, 1 with anomalous coronary artery.

*Frank Forman Medical Foundation Fellow, University of Capetown.

some generalized disease; (*b*) without generalized disease and without specific pathology; (*c*) of unknown aetiology, but often with characteristic pathology.

TABLE II.—*Clinical Types of Cardiomyopathy*

	No. of Cases
Type 1: Congestive heart failure often with atrio-ventricular valvular incompetence	
Simulating ischaemic heart diseases; "heart failure of uncertain aetiology"	35
Type 2: Obstructive	
Simulating stenotic valvular disease—principally aortic	27
Type 3: Constrictive	
Simulating constrictive pericarditis	4
Total	66

Clinical Presentation (Table II)

Clinically the patients could be divided into three types according to the effect of the cardiac disease upon the function of the heart. There was not a close correlation between the clinical types and the pathological groups except in the case of asymmetrical hypertrophy and obstructive cardiomyopathy. The commonest mode of presentation (which occurred in 35 cases) was that of persistent congestive heart failure with a large heart, gallop rhythm, and often pansystolic murmurs indicating mitral or tricuspid valvular insufficiency.

The second type presented with evidence of obstruction to cardiac flow, usually simulating aortic stenosis. In this group ejection murmurs suggesting obstruction to flow were common, except in those patients with evidence of obstruction to inflow of the right ventricle, in whom diastolic murmurs of tricuspid character were sometimes heard. There were 27 cases of this type, which corresponded to the pathological group described as asymmetrical hypertrophy.

The third and least common type simulated constrictive pericarditis; systolic murmurs were trivial or absent, and the heart was not usually as large as that found in the type with congestive heart failure.

With regard to the first and third types, patients may at some time show both constrictive and congestive types of clinical manifestations, depending on the development of further changes in the heart with progression of the disease. It is considered that the constrictive presentation is due to a tight and rigid myocardium which fails to relax in diastole, thus simulating the tight constriction of the heart in constrictive pericarditis. This type of presentation has been described in patients with myocardial fibrosis (Robin and Burwell, 1957; Nye *et al.*, 1957) and in amyloid disease (Hetzel *et al.*, 1953; Brigden, 1957). Other important factors in this group are probably endocardial sclerosis contributing to the myocardial stiffness, and in some cases involvement of the pericardium also. Intraventricular thrombosis is known to occur in cardiomyopathy, and systemic embolism is not unknown. Thus intramural thrombosis may well organize, giving rise to fibrosis and contributing to rigidity of the heart's action, so that a patient after initially presenting with congestive heart failure might proceed to the constrictive picture with the development and organization of intramural thrombus. For example, endomyocardial fibrosis either may present as congestive heart failure with mitral or tricuspid insufficiency or simulate a pericardial effusion or constrictive pericarditis (Williams and Shaper, cited by Davies, 1960). A constrictive pattern may very occasionally be seen in ischaemic heart disease, but usually yields to that of tricuspid incompetence.

The three clinical types will now be discussed in detail.

Type 1: Congestive Heart Failure Often with Atrio-ventricular Valvular Incompetence

This type was encountered most commonly, but in a number of cases only a retrospective study of the clinical records was possible. Exact clinical details were therefore not always available, but the over-all clinical picture will be made the subject of a more detailed report later. Cases occurred with specific disorders, such as scleroderma, or with non-specific myocardial pathology which in 20 cases was associated with a generalized systemic disease (Table I). The onset in these patients was very variable but usually insidious, and the duration of the disease varied from a few days to several years, usually being in the region of one year. Dyspnoea was almost invariable, being usually confined to effort, but sometimes paroxysmal in nature. Cardiac pain occurred in a small number of cases, and it is thus not surprising that such patients were often regarded as having ischaemic heart disease. On examination there were signs of congestive heart failure with oedema, raised jugular venous pressure, and often tricuspid incompetence shown by a systolic wave with sharp *y* descent in the venous pulse. The heart was usually considerably enlarged, sometimes grossly so, and gallop rhythm was common. Sometimes four heart sounds were heard, but a summation gallop was most common. The heart sounds were often quiet and muffled, and pericardial effusion had occasionally to be considered in the differential diagnosis. Pansystolic murmurs of both tricuspid and mitral incompetence were not uncommon. The murmur of tricuspid incompetence was heard best in the tricuspid area, and usually, though not always, increased on inspiration; that of mitral incompetence was heard at the apex and tended to decrease or not to alter with inspiration.

The arterial pulse was usually small, and atrial fibrillation occurred in about one-third of the cases. Neither these murmurs nor any other physical signs necessarily gave a clue to the aetiology, except in cases where the disease which affected the heart muscle also gave signs elsewhere in the body, such as haemochromatosis.

Radiology of the heart showed considerable or gross cardiac enlargement, sometimes with pleural effusions, and with the pulmonary vascular patterns associated with heart failure and pulmonary hypertension. Calcification within the heart or in the pericardium was not seen. The electrocardiogram commonly showed low voltage, with flat T waves and evidence of biventricular hypertrophy. Bundle-branch block and atrio-ventricular block were not uncommon, and atrial fibrillation occurred in about one-third of the patients. The blood picture showed no specific features, except for an eosinophilia in three cases. The biochemistry was essentially normal.

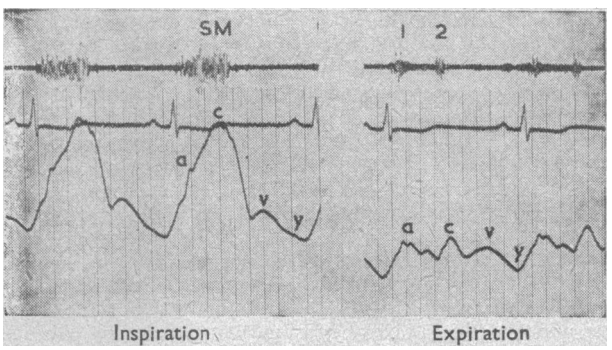
This type will now be illustrated by a case report.

Case 1

A woman aged 72 developed dyspnoea on effort in 1939 which became slowly progressive; she also noted mild Raynaud's phenomenon in the hands. In 1952 she was admitted to Hammersmith Hospital in congestive heart failure, which responded to treatment. At this time angiomata and cyanosis of the face and lips were noted. The arterial oxygen saturation was 95%. Her vital capacity was only 2 litres. In 1953 she lost weight and developed steatorrhoea. Both liver and spleen were enlarged at this time. In 1956 dysphagia for solid foods began, and in 1957

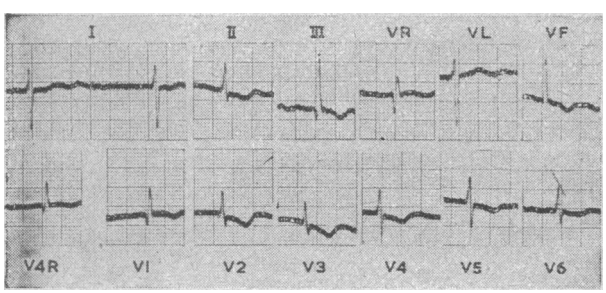
dyspnoea became even more severe and oedema of the abdomen and legs developed. It was elicited that a sister had died of cardiac failure of unknown cause.

Examination showed an elderly, frail lady with tight, shiny skin on the face and fingers and multiple telangiectases on the face. There was marked cyanosis of the face and digits, with moderate dependent oedema. The pulse was 60 to the minute, regular, and of small volume. The blood-pressure was 90/70 mm. Hg. The jugular venous pressure was 15 cm. above the sternal angle, with distended external jugular veins and a dominant *v* wave with sharp *y* descent (Text Fig. 1). The cardiac impulse was diffuse, the apex-beat being localized in the sixth intercostal space, just inside the anterior axillary line. A pansystolic murmur increasing on inspiration was present at the left sternal edge and radiated towards the apex (Text Fig. 1). There was ascites,



TEXT FIG. 1.—Jugular venous pulse, electrocardiogram, and phonocardiogram in Case 1. The pansystolic murmur (SM) and the large systolic (c) wave are seen to be increased on inspiration. (1=first heart sound; 2=second heart sound.)

with enlargement of liver and spleen. Haemoglobin 12 g. per 100 ml.; W.B.C. 4,000 per c.mm. (polymorphs 79%). Blood cholesterol 116 mg. and blood urea 84 mg. per 100 ml. Urine normal. Radiology of the chest showed generalized cardiomegaly with poor pulsation. The right atrium and ventricle and main pulmonary arteries were especially enlarged. The gastro-intestinal tract showed poor oesophageal motility with loss of mucosal pattern, a small sliding hiatus hernia, and diverticulosis of the sigmoid colon. Radiographs of the hands showed osteoarthritis and slight peripheral calcinosis, and a skin biopsy revealed incorporation of sweat-glands in connective tissue. The electrocardiogram (Text Fig. 2) showed Grade III right



TEXT FIG. 2.—Electrocardiogram of Case 1. There is a dominant R wave in leads V4R to V6 with right axis deviation, and an RS pattern in V5, indicating Grade 3 right ventricular hypertrophy. The low voltage and T-wave inversion in the chest leads is consistent with a generalized myocardial disorder.

ventricular hypertrophy with low voltage in the chest leads. The inverted T waves in precordial leads were considered to be due either to right ventricular hypertrophy or to a generalized myocardial disorder.

A diagnosis of generalized scleroderma was made, but the congestive heart failure progressed to a fatal outcome despite treatment.

Pathology (Special Plate, Fig. 1; Table III).—The heart showed right ventricular enlargement with areas of refractile fibrillary replacement fibrosis of the myocardium. The endocardium and pericardium were both normal. The tricuspid valve ring was stretched. The small pulmonary arteries showed some degree of sclerosis.

TABLE III.—*Pathological Details of the Hearts of Cases* 1-3

Case No.	Heart Weight (g.)	Left Ventricle	Right Ventricle	Circumference of Tricuspid Valve Ring (mm.)	Circumference of Mitral Valve Ring (mm.)
1	442	Normal	Hypertrophied (5 mm.)	130	100
2	495	Hypertrophied (21 mm.)	Hypertrophied (7 mm.)	115	85
3	365	Normal	Hypertrophied (6 mm.)	135	85

COMMENT.—In this case severe sclerosis of the myocardium in association with generalized systemic sclerosis and scleroderma led to progressive cardiac failure with cardiac dilatation and tricuspid insufficiency. Mitral insufficiency was not noted. There was no endocardial or pericardial involvement, and the pattern of cardiac constriction did not occur, presumably because fibrotic replacement led to progressive dilatation of the heart and poor contractility. Though the cause of diffuse sclerosis is unknown, the clinical diagnosis was obvious in this patient before death and the method of heart failure was clear. The sclerosis of the small pulmonary arteries caused pulmonary hypertension, which explained the large main pulmonary arteries and the cardiographic signs of right ventricular hypertrophy, and contributed to the tricuspid incompetence and heart failure.

Type 2: Constrictive Cardiomyopathy

The four patients of this type will be illustrated by case reports.

Case 2

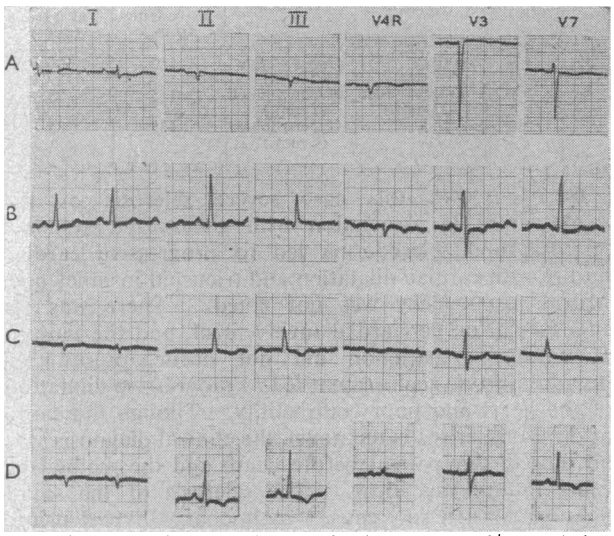
A woman aged 55 complained of angina of effort for one year accompanied by dyspnoea on exertion and oedema of the ankles. For two months she suffered from paroxysmal cardiac dyspnoea, and for two weeks from rapidly increasing dyspnoea on effort and oedema. Further and more protracted episodes of chest pain occurred subsequently. The past and family histories were non-contributory.

On examination there were orthopnoea at rest and extensive oedema with ascites. The pulse was 90 per minute, regular, and of small volume. The blood-pressure was 130/75 mm. Hg., and the jugular venous pressure 16 cm. above the sternal angle with large *a* and *v* waves with sharp *x* and *y* descents. The venous pressure increased on inspiration. A weak cardiac impulse was felt in the mid-clavicular line. The first and second heart sounds were soft, but a loud third heart sound was audible. There was basal congestion of both lungs, with a pleural effusion on the right side. The liver was enlarged four fingerbreadths below the costal margin, with slight presystolic pulsation. The tongue, finger-tips, and skin were all normal, and there was no rash. Haemoglobin 15 g. per 100 ml.; P.C.V. 48%; W.B.C. 9,000 per c.mm. (polymorphs 58%; eosinophils 11%). Biochemical tests showed: serum cholesterol 276 mg. per 100 ml.; serum glutamic oxalacetic transaminase 80 units (normal 16). The serum potassium varied from 3.6 to 6 mEq per litre, the serum sodium was normal, but the serum albumin was 3.4 g. and globulin 4.1 g. per 100 ml. Congo-red test negative; urine normal. Radiology of the chest (Special Plate, Fig. 2) showed generalized cardiac enlargement, a right-sided pleural effusion, and left-sided congestion with horizontal costo-phrenic lines, indicating pulmonary venous hypertension. The electrocardiogram (Text Fig. 3A) showed low voltage in limb leads, the T waves being flat or slightly inverted throughout. The deep

S waves in V5 and V2 suggested biventricular enlargement and possibly anterior infarction.

Cardiac failure persisted, and she died suddenly three months after admission, following an attack of cardiac pain.

Pathology (Special Plate, Fig. 5).—Both ventricles were enlarged (Table III). Extensive deposits of amyloid material were present in the myocardium around small vessels and



TEXT FIG. 3.—Electrocardiogram in four cases of constrictive cardiomyopathy. A. Case 2, showing low voltage, flat T waves, and deep S waves in leads V4R, V3, and V7. B. Case 4, showing ST depression in leads I, V3, and V7, and inverted T wave in V3. C. Case 3, showing low voltage, sinus tachycardia, and long PR interval (0.36 sec.). D. Case 5, showing low voltage and inverted T waves in leads II, III, and V7.

scattered through the interstitial tissue. There were also deposits of amyloid substance on the endocardium and pericardium. There was no evidence of amyloid anywhere else in the body.

COMMENT.—The attacks of cardiac pain and raised transaminase level suggested the presence of ischaemic heart disease with cardiac infarction, but the constrictive pattern in the jugular venous pulse led to the suggestion that the condition might in fact be due to constrictive pericarditis or cardiomyopathy. The lack of great cardiac enlargement, together with the haemodynamic pattern, suggested the possibility of amyloid disease, and this diagnosis was made before death. The extensive involvement of the myocardium, together with that of the endocardium and pericardium, explained the pattern of cardiac constriction. Murmurs were absent and atrio-ventricular valvular incompetence did not occur. The cardiac pain and raised transaminase level may be explained by destruction of the myocardium and replacement with amyloid tissue. Though the amyloid surrounded the blood-vessels, their lumina were in fact clear, and occlusive coronary artery disease was absent.

This case illustrates the usefulness of the haemodynamic pattern in distinguishing amyloid disease of the heart from ischaemic heart disease.

Case 3

A man aged 46 years. In 1950 enlargement of the liver and spleen was detected prior to a haemorrhoidectomy. Symptoms were absent until 1953, when progressive tiredness, dyspnoea on effort, and swelling of the abdomen developed. For a few weeks there was vague tightness across the chest on effort and after meals. The family history was negative.

Examination showed a dark-skinned man with bruises on the skin. Hess's test was positive. There was a generalized slight lymphadenopathy. Ascites and firm, smooth, diffuse enlargement of the liver to the level of the umbilicus were present. The spleen was hard and moderately enlarged. The pulse was regular at 120 per minute and there was pulsus paradoxus. The blood-pressure was 130/95 mm. Hg, and the jugular venous pressure was raised to the angle of the jaw, with large *a* and *v* waves and sharp *x* and *y* descents. The cardiac impulse was impalpable and the heart sounds were faint, with a gallop rhythm due to a third heart sound. The lungs were clear. Haemoglobin 12 g. per 100 ml.; W.B.C. 9,000 per c.mm. (lymphocytes 73%, with atypical forms; polymorphs 25%; eosinophils 1%); platelets 30,000 per c.mm. Urine normal. Biochemistry showed serum albumin 3.1 g., globulin 3.5 g., urea 22 mg., and cholesterol 123 mg. per 100 ml. The electrolytes were normal. Bone-marrow biopsy showed an increased proportion of mature lymphocytes; liver biopsy showed reticulosis with increased lymphocyte production; and lymph-node biopsy showed hyperplasia with pleocytosis and fibrosis, suggestive of a Hodgkin's type of reticulosis. Radiology of the chest (Special Plate, Fig. 3) revealed a high diaphragm. The heart was not obviously enlarged and there was good pulsation; there was no calcification. The electrocardiogram (Text Fig. 3C) showed sinus tachycardia, and first-degree heart-block with a P–R interval of 0.36 sec. Low-voltage complexes in limb leads with flat or inverted T waves throughout suggested generalized myocardial disease. Cardiac catheterization gave the following pressures (mm. Hg): right atrium 14/6, right ventricle 43/7, and pulmonary artery 40/28. Cardiac output was 6.2 litres per minute. A pericardial effusion was excluded by passing the tip of the catheter to the border of the right atrium. A diagnosis of reticulosis with cardiac involvement was made.

Improvement followed treatment for the reticulosis and for heart failure, but atrial fibrillation developed, and he finally succumbed to an intercurrent infection.

Pathology (Special Plate, Figs. 6 and 7).—The right ventricle was enlarged and the tricuspid valve ring stretched (Table III). The myocardium showed a heavy, diffuse infiltration with abnormal lymphocytes, and fibrosis and oedema. The endocardium, and to a lesser extent the pericardium, were heavily infiltrated with lymphocytes.

COMMENT.—This patient suffered from a reticulosis which involved the heart extensively, and the heavy infiltration of all three layers of the heart explained the signs of cardiac constriction. The development of atrial fibrillation must have been related to involvement of the atria, but is a feature which has not been seen in the other three of our patients with the constrictive presentation. The dilatation of the tricuspid valve ring was unexpected and may have been a terminal event.

Case 4

A man aged 30 had for three to four years noticed fatigue, low-grade fever, vertigo, and exertional dyspnoea. In October, 1955, there was sudden weakness of the right leg and left arm, with mild vertigo. At this time the peripheral blood was noted to contain 55% eosinophils. In December, 1956, he suffered an arterial embolism to the left leg, which was followed by intermittent claudication. From January to May, 1957, dyspnoea on exertion increased. Past and family histories were negative.

On examination the arterial pulse was 82 per minute, regular, and of normal volume. The blood-pressure was 160/100 mm. Hg, and the jugular venous pressure 15 cm. above the sternal angle, with marked *a* and *v* waves and sharp *x* and *y* descents. The cardiac impulse was quiet, with a slight right ventricular lift. A late third heart sound was heard along the left sternal edge. Both femoral pulses were weak and the posterior tibial pulses feeble; the left dorsalis pedis pulse was absent. The lungs were clear; the liver palpable, firm, and non-tender. The spleen was also palpable and firm. There was no ascites. The central

nervous system was normal, except for slight increase in knee- and ankle-jerks on the right side. The optic fundi and skin were normal. Haemoglobin 13 g. per 100 ml.; W.B.C. 10,000 per c.mm. (neutrophils 32%; eosinophils 43%); platelets 100,000 per c.mm.; E.S.R. 5 mm. in 1 hour. Blood urea, serum bilirubin, thymol turbidity, zinc sulphate, and acid phosphatase tests all gave normal results, and alkaline phosphatase was 39.5 and 25.5 mg. per 100 ml. respectively on two occasions. Serum cholesterol 240 mg. per 100 ml.; serum albumin 3.9 g. and serum globulin 3.9 g. per 100 ml. Complement-fixation test for toxoplasmosis negative. Urine normal.

Radiology of the chest (Special Plate, Fig. 4) showed considerable cardiomegaly involving mainly the right ventricle. Cardiac pulsation was sluggish, but there was moderate pulsation of the left atrium, which was slightly enlarged. Both pulmonary arteries were somewhat enlarged. The diaphragm and lung fields were normal. The electrocardiogram showed depressed ST segments in leads V3 to V6 and lead 1, with inverted T waves in V1 and V3 suggesting myocardial disease (Text Fig. 3B). Cardiac catheterization pressures (mm. Hg) right atrium, $a=24$, $v=24$, $x=7$, $y=10$. Pressures rose on inspiration. Right ventricle 37/12 and pulmonary artery 34/12 mm. Hg; pulmonary "wedge" pressure (mm. Hg), $a=23$, $v=22$, $x=9$, $y=10$, mean=15. Pressures rose on inspiration. Cardiac output 3.6 litres per minute. There was no intracardiac shunt. A raised pressure was thus demonstrated in both atria, and an early diastolic dip consistent with cardiac constriction was present in the right ventricle. Increase in pressure on inspiration was obtained in both right atrium and pulmonary "wedge" positions. All these findings were consistent with cardiac constriction, but did not indicate where the constriction might lie.

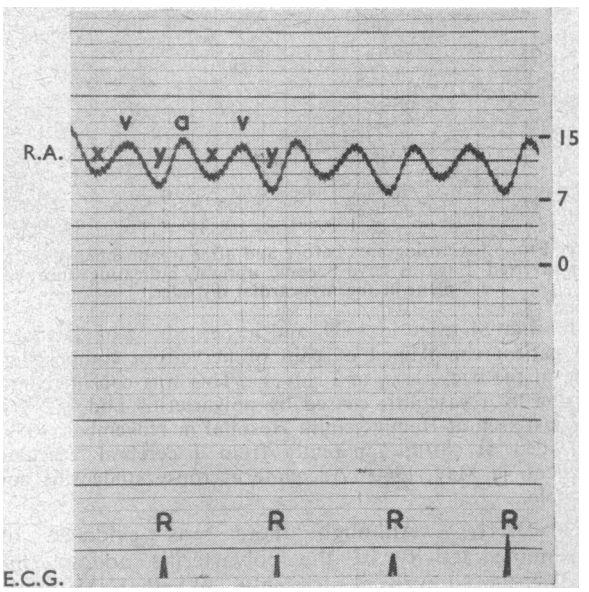
A diagnosis of constrictive cardiomyopathy was made. The eosinophilia, enlarged liver and spleen, and repeated neurological phenomena, together with evidence of peripheral arterial embolism, all suggested that constrictive pericarditis was not the cause. Polyarteritis nodosa was considered because of the eosinophilia, hypertension, and neurological signs, but it was thought that Löffler's "constrictive endomyocarditis" with endocardial thrombosis and subsequent emboli fitted the whole picture better.

Treatment with anticoagulants and steroids was instituted, but the patient has left the country and has not been seen since.

COMMENT.—In this case the evidence of constriction was clear, but the exact cause remains uncertain in the absence of necropsy data or further clinical manifestations of a generalized disease. The eosinophilia and evidence of endocardial thrombosis, however, would harmonize with the so-called Löffler's type of cardiomyopathy. In view of the eosinophilia and evidence of multiple emboli, treatment with steroids and anticoagulants was considered the best method of control.

Case 5

A man aged 52 complained of cough at night with slight exertional dyspnoea and tiredness for three years, increasing over the last year. For six weeks he had noticed swelling of the ankles. On examination in April, 1957, the arterial pulse was normal, without paradox. The jugular venous pressure was 15 cm. above the sternal angle, with marked a and v waves with sharp x and y descents (Text Fig. 4). The cardiac impulse was diffuse and the pulsation quiet. There was a loud late third heart sound heard at the left sternal edge, but no murmurs. The blood-pressure was 130/75 mm. Hg, and there were bilateral pleural effusions and basal rales. The liver was enlarged to the umbilicus, with a firm edge but no pulsation. There was no oedema. Haemoglobin 15 g. per 100 ml.; W.B.C. 12,000–25,000 per c.mm., with the eosinophil count varying from 25 to 50%. The E.S.R., liver function tests, and electrolytes were all normal. No lupus erythematosus cells were found. The Congo-red test and toxoplasma agglutination tests were negative, as were the Wassermann and Kahn reactions. No disorder of blood-clotting was found. The blood urea was 24 mg. per 100 ml., calcium 4.6 mEq per litre, phosphate 3.1 mg. per 100 ml., bilirubin 1.3 per 100 ml., alkaline phosphatase 15.1 units, and acid formal stable phosphatase 4.2 units. The electrocardiogram (Text Fig 3D) showed low voltage and inverted T waves, suggesting a myocardial disorder. Bone-marrow biopsy showed eosinophilic hyperplasia, and liver biopsy showed central lobular congestion



TEXT FIG. 4.—Right atrial pulse (RA) in Case 5, showing equal a and v waves and sharp x and y descents, and elevated right atrial pressure. R=R wave of electrocardiogram. (Figures refer to pressures in mm. Hg.)

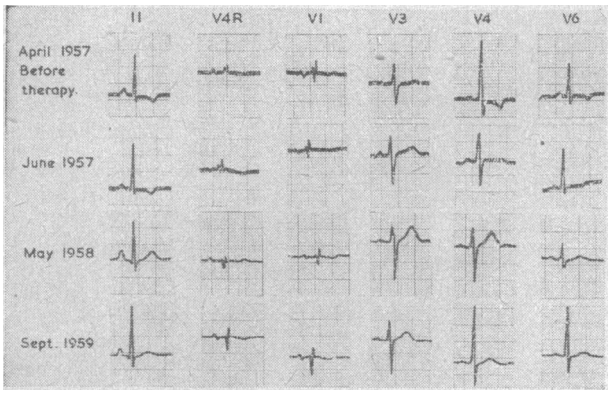
but was otherwise normal. No eosinophilic infiltration was seen. Radiology of the chest (Special Plate, Fig. 8A) showed slight cardiomegaly and bilateral pleural effusions. Cardiac catheterization: right atrial pressure (mm. Hg)—$a=13$, $v=15$, $x=7$, $y=8$; mean=11. The cardiac output was 2.3 litres per minute, and there was no intracardiac shunt (Text Fig. 4). It was not possible to enter the pulmonary artery, and pressures were not obtained from the right ventricle owing to persistent ventricular ectopic beats. The pressure rose in the right atrium on inspiration. The pattern was consistent with cardiac constriction, but did not indicate where the constriction might lie.

A diagnosis of constrictive cardiomyopathy with eosinophilia, possibly due to polyarteritis nodosa, was made. The patient was treated with a low-salt diet, digoxin, and mercurial diuretics, and by aspiration of the pleural effusions. The latter were pale in colour and contained 60% eosinophils. In view of the lack of cardiac enlargement, constrictive pericarditis was seriously considered, but the profuse eosinophilia seemed to make this diagnosis unlikely. Progress was stormy thereafter, for a generalized urticarial haemorrhagic rash appeared, which responded to steroid therapy. Signs of peripheral neuropathy developed, and there was a silent perforation of the small bowel, attributable to prednisolone and requiring surgical intervention. However, the rash cleared after cortisone was substituted for prednisolone.

A final diagnosis of polyarteritis nodosa, accounting for the peripheral neuropathy, rash, and cardiac involvement, was made. It was thought that the polyarteritis was involving the myocardium, producing constrictive cardiomyopathy, rather than involving the coronary arteries and producing ischaemic heart disease.

The patient remained well on digitalis and cortisone. The venous pressure fell to 5 cm. above the sternal angle, but

the constrictive pattern remained. The pleural effusions did not recur and the heart became smaller (Special Plate, Fig. 8B). Later the third heart sound disappeared and the jugular venous pressure fell to 3 cm. above the sternal angle. The cardiogram showed striking improvement (Text Fig 5). The



TEXT FIG. 5.—Cardiograms before and after treatment in Case 5. The inverted T waves have become upright, indicating improvement in the myocardial disorder.

rash recurred twice in 1959, and in September of that year the patient complained of pain of nerve-root compression type in the back, legs, and calves. This was considered to be due to a vasculitis caused by polyarteritis nodosa. He was last seen at Hammersmith Hospital in November, 1959, and died at work, apparently from a cerebral vascular accident, in May, 1960 Adequate necropsy study was not possible.

COMMENT. — Although there was evidence of continuing activity of the polyarteritis nodosa, the cardiac signs improved strikingly. Whether this could be attributed to treatment with steroids is not known, but the improvement is of considerable interest in view of the almost uniformly unsatisfactory nature of treatment for cardiomyopathy. It is interesting to speculate on the exact distribution of the pathological process within the heart, but it may be assumed that the myocardium was heavily involved and possibly the pericardium also.

Type 3: Obstructive Cardiomyopathy

The pathological features of this condition have been described by Teare (1958), and the two main clinical types, involving obstruction to the inflow of the right ventricle and to the outflow of the left ventricle respectively, have subsequently been documented (Goodwin *et al.*, 1960; Hollman *et al.*, 1960). Teare's original study was a pathological one, and illustrated patients who had died suddenly or in congestive heart failure and who at necropsy showed massive irregular asymmetrical hypertrophy of the ventricular septum with irregularly placed and grossly enlarged muscle fibres and bundles with interlacing interstitial fibrosis. One of his cases had been under the care of Hammersmith Hospital with signs suggestive of tricuspid-valve obstruction, and subsequently the patient's family were studied and found to have a high incidence of similar physical signs and other abnormalities suggesting mild tricuspid stenosis (Hollman *et al.*, 1960). It is believed that in these patients the irregular and asymmetrical hypertrophy of the septum was obstructing right ventricular inflow. In one of Teare's cases obstruction to left ventricular inflow by a massive septal hypertrophy simulated mitral stenosis. When the septum obstructs the outflow of the left ventricle the condition simulates aortic stenosis, but has certain important differences. A similar, though not necessarily identical, condition has been described by Brock (1957, 1959), by Bercu *et al.* (1958), by Morrow and Braunwald (1959), by Soulié *et al.* (1959), and by Brent *et al.* (1960).

Table I, section 4, shows the patients with this condition whom we have studied. Nine had evidence of obstruction to right ventricular inflow, and three to right ventricular outflow, two of the latter having signs suggesting that left ventricular outflow was also involved. Fourteen patients had obstruction to left ventricular outflow alone or principally, and one patient had apparent obstruction to left ventricular inflow.

We cannot say for certain without necropsy data whether all these patients have asymmetrical hypertrophy, but there is little doubt that they are suffering from a cardiomyopathy which produces obstruction to the flow of blood within the heart and therefore merits the term "obstructive cardiomyopathy." The majority of these patients have ejection murmurs suggesting aortic or pulmonary valve obstruction, and are sharply to be distinguished from patients with cardiomyopathy with atrio-ventricular valve insufficiency or with cardiac constriction.

Obstructive Cardiomyopathy Involving Right Ventricular Inflow

These patients will not be described in detail, since they have been documented by Hollman *et al.* (1960). They have shown a tendency to sudden death, short ejection murmurs down the left sternal edge, not uncommonly gallop rhythm, and soft early diastolic murmurs, together with a globular heart on fluoroscopy. The cardiogram has not been particularly specific, but most cases showed a *q* wave and inverted T wave in lead III, and in some left precordial leads were abnormal. These cases thus suggested mild tricuspid stenosis or Ebstein's syndrome.

Right Ventricular Outflow Obstruction

There were three cases in this group. In one the diagnosis of corrected transposition of the great vessels and pulmonary stenosis had been made, and at cardiotomy for relief of pulmonary stenosis a massive hypertrophied septum was discovered. The septum was greatly hypertrophied and bulged into the right ventricle in systole. The pulmonary valve was normal. A quantity of muscle was resected from the septum, the gradient was reduced from 110 to 42 mm. Hg, and after the operation the systolic ejection murmur virtually disappeared. Histology of the resected muscle showed hypertrophied muscle fibres. It was thought that this patient, therefore, was an example of asymmetrical hypertrophy, for there was certainly obstruction to right ventricular outflow below the pulmonary valve. The other two cases were of special interest in that they presented features suggesting both aortic and pulmonary stenosis, but being typical of neither. Since it is probable that this combination of physical signs may suggest the diagnosis, these two patients will be considered in detail.

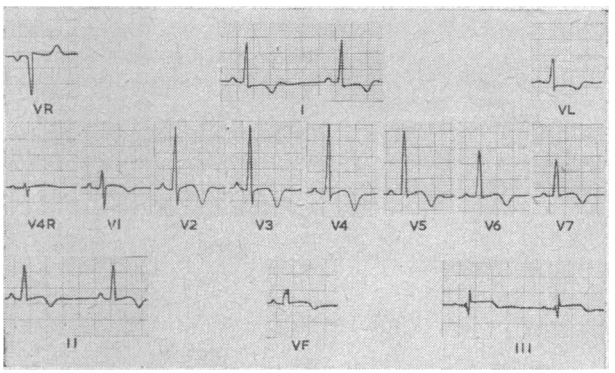
Case 6

A woman aged 37. At the age of 5 years a murmur was heard in the heart at a school medical examination. The patient said she had been breathless on extreme exertion from childhood, and at the present time could not run for a bus without dyspnoea. She had no syncope, but some

tightness across the chest on exertion. There was no past history of rheumatic fever.

Examination revealed a well-developed woman without cyanosis or clubbing of the fingers. The arterial pulse was small and regular, with occasional ectopic beats. The jugular venous pressure was 4 cm. above the sternal angle, with a prominent *a* wave and a sluggish *y* descent. The cardiac impulse consisted of a weak localized apex-beat in the fifth interspace in the mid-clavicular line. There were no thrills and no obvious right ventricular hypertrophy. There was a Grade 3 ejection systolic murmur, which was not quite full length and was loudest at the left sternal edge over the pulmonary artery. There were a faint scratchy diastolic murmur of doubtful aetiology at the left sternal edge and a late fourth heart sound. The pulmonary closure was very faint and delayed, aortic closure being easily heard. A systolic ejection click was heard on some occasions but not others.

Radiology of the chest showed enlargement of the right atrium, left ventricle, and pulmonary artery, and possibly of the right ventricle also. The heart was globular in shape, and the lungs and pulmonary vasculature were normal. The electrocardiogram (Text Fig. 6) was very unusual, with



TEXT FIG. 6.—Electrocardiogram of Case 6. The dominant R waves in leads V2 to V7, and in limb leads, with inverted T waves in all leads except VR, suggest hypertrophy of both ventricles and the septum.

dominant R waves in precordial leads V2–V7, and inversion of T waves from V4R to V7. The T waves were also inverted in leads I, II, III, and VF. The appearances were considered to be consistent with hypertrophy of both ventricles and of the ventricular septum. Cardiac catheterization did not reveal any intracardiac shunts, and the arterial oxygen saturation was 94% at rest and on exercise. There was a pressure gradient of 26 mm. Hg at the level of the pulmonary valve. Angiocardiography showed a very thick left ventricular muscle wall. The aortic sinuses and aorta were normal. There was a persistent deformity and narrowing of the infundibulum of the right ventricle, and the main pulmonary artery was enlarged, but the valve seemed normal. The ventricular septum appeared to be very large, and the infundibular region to narrow during ventricular systole. The left ventricle and ventricular septum were thought to bulge into the right ventricle below the pulmonary valve.

COMMENT.—Though some features, notably the murmur, the dilatation of the pulmonary artery, and the pressure gradient at valve level, suggested conventional pulmonary stenosis, there were many points against it. These were the small jerky pulse, the scratchy diastolic murmur, and the bizarre electrocardiogram, which seemed to be incompatible with simple pulmonary stenosis. The diagnosis was strengthened by the angiographic appearances suggesting a very large septum. However, the presence of the pressure gradient at valve level instead of in the body of the right ventricle, as has been found in other cases, was unusual. The final conclusion was that the patient was suffering from enlargement of the septum due to asymmetrical hypertrophy, which produced obstruction to right ventricular outflow and to some extent left ventricular outflow also.

The next patient is of special interest, since she showed an association of the condition with congenital heart disease and clear evidence of the progressive nature of obstructive cardiomyopathy.

Case 7

A girl aged 15 was first seen at the age of 7 in 1952. Her birth had been normal, but her mother had contracted rubella six weeks before pregnancy started. The patient was well until 8 months of age, and from then on had frequent respiratory infections and bronchitis every winter. Cyanosis had occasionally been seen. At the age of 2½ years a cardiac murmur was heard.

On examination there was no cyanosis or clubbing of the fingers, but the palate was highly arched. There was prominence of the left side of the chest, and a left ventricular type of impulse was noted in the fifth intercostal space 4½ in. (11.4 cm.) from the mid-line. A systolic thrill maximum at the fourth left intercostal space was felt, and there was a loud murmur maximum in the same area with a faint early diastolic murmur at the left sternal edge. The blood-pressure was 105/50 mm. Hg, and the arterial pulse was regular, quick-rising in nature, and of good volume. The jugular venous pressure was normal, as were the femoral pulses. Radiology of the chest revealed enlargement of the right ventricle and pulmonary arteries, with slight hilar pulsation and slight overfilling of the lungs. The electrocardiogram showed right and left ventricular hypertrophy. Cardiac catheterization pressures (mm. Hg): pulmonary artery 57/43, mean 47; right ventricle 57 (systolic). There was a left-to-right shunt at pulmonary-artery level, with a ratio of pulmonary to systemic flow of 1.7 : 1.

A diagnosis of patent ductus arteriosus was made, and a wide, short patent ductus was found and ligated by Mr. L. L. Bromley in 1952. After ligation the thrill disappeared, but in the post-operative period there was a persistent systolic murmur in the left second and third intercostal spaces. This murmur was attributed to aortic stenosis or possibly to residual pulmonary hypertension.

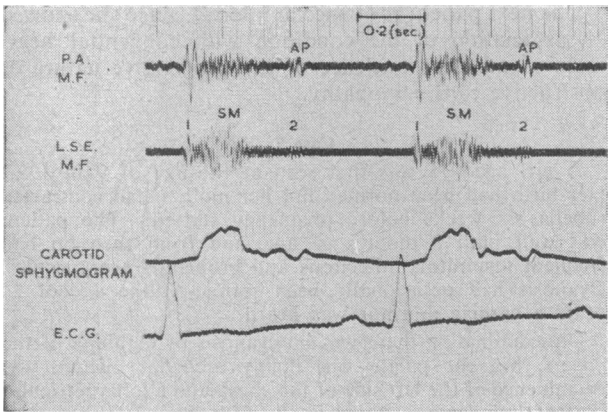
The patient lost all her symptoms, and for the next three years remained perfectly well. When reassessed in 1955 she was found to have a small, quick-rising arterial pulse, the cardiac impulse suggested enlargement of both ventricles, and there was a small *a* wave in the jugular venous pulse. The second heart sound was thought to be normal, but there was a Grade 4 systolic murmur maximal in the third left intercostal space. The electrocardiogram still showed evidence of hypertrophy of both ventricles.

In 1956 a further cardiac catheterization was carried out. No intracardiac shunt was discovered, but there was still evidence of pulmonary hypertension, though less severe than before. The mean right atrial pressure in mm. Hg, was 12, the right ventricle 42/5, and the pulmonary artery 42/16. There was no gradient across the right ventricular outflow tract.

At this point the possibility of mitral insufficiency associated with subaortic stenosis and fibroelastosis was considered.

In May, 1960, she was readmitted for further investigation. Her symptoms had not increased and she was able to undertake fairly heavy exertion without dyspnoea. Examination showed a moon face, but no cyanosis or clubbing of the fingers. The arterial pulse was jerky, of normal volume, and regular. The jugular venous pressure showed a 2-cm. *a* wave, but was otherwise normal. The cardiac impulse showed a marked lift over the right ventricular outflow tract. There was a systolic thrill at the left sternal edge, but not in the aortic area. A Grade 4 harsh ejection systolic murmur was heard at the apex and

the left sternal edge. The second heart sound was split 0.03/second (Text Fig. 7). There was a faint scratchy mid-diastolic murmur increasing on inspiration at the left sternal edge, and probably arising from the tricuspid valve.



TEXT FIG. 7.—Phonocardiogram of Case 7, showing a harsh diminuendo ejection murmur. The second heart sound is split 0.03 per second. SM=systolic murmur; A=aortic-valve closure; P=pulmonary-valve closure; 1=first heart sound; 2=second heart sound; LSE=left sternal edge; MF=medium frequency.

Radiology of the chest showed enlargement of both ventricles and right atrium. The heart was globular in shape and the lung fields normal (Special Plate, Fig. 9). The electrocardiogram showed little change. Cardiac catheterization pressures (mm. Hg): pulmonary artery 42/30; right ventricle 108/0; right atrium $a=20$, $v=12$, mean=10. There was a gradient of 60 mm. Hg low in the body of the right ventricle. The brachial artery pressure was 130/54 mm. Hg. No intracardiac shunt was found. Angiocardiography (Special Plate, Fig. 10) showed narrowing of the outflow tract of the right ventricle below the pulmonary valve, probably due to hypertrophy of the septum, and a massive ventricular muscle wall.

COMMENT.—These three patients illustrate the effect of cardiomyopathy on right ventricular outflow. It seems most unlikely that they are suffering from conventional pulmonary stenosis, and the combination of signs suggesting both aortic and pulmonary stenosis makes the diagnosis of asymmetrical hypertrophy very probable. These patients also illustrate two other important points: the association of the condition with congenital heart disease and the progressive nature of the condition, which has been suspected in our other cases.

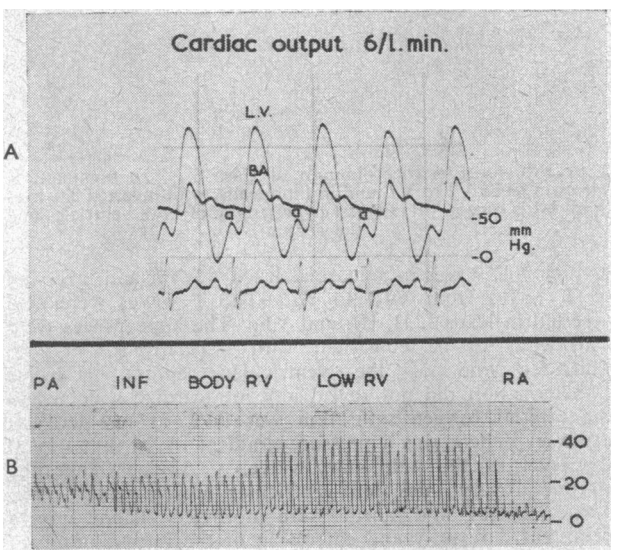
Left Ventricular Inflow Obstruction

Teare (1958) described a patient who clinically suffered from mitral stenosis, but at valvotomy was found to have a muscular mass obstructing left ventricular inflow. At necropsy this patient was found to have asymmetrical hypertrophy of the ventricular septum. We have seen but one case diagnosed clinically and on haemodynamic grounds, and we lack necropsy proof; we therefore cannot comment further on this group.

Left Ventricular Outflow Obstruction

We have described this group under the title of "Obstructive Cardiomyopathy Simulating Aortic Stenosis" (Goodwin *et al.*, 1960). A full description will therefore not be given again, but the salient features will be briefly commented on. These patients presented with a history exactly simulating aortic stenosis, anginal pain, syncope, and dyspnoea on exertion being common. We have seen the condition in childhood and in adult life and in both sexes. Of our 14 patients, 9 were men and 5 women. A familial tendency has also been noted. The physical signs consisted of a normal or jerky arterial pulse, a loud ejection murmur (and often a thrill) maximal at the left sternal edge rather than at the apex or aortic base. There was no calcification of the aortic valve, and dilatation of the ascending aorta was not usually a feature. These were the clinical signs of pure left ventricular outflow obstruction, but there were often some associated signs of obstruction to right-sided inflow or outflow also. Thus a prominent *a* wave in the jugular venous pulse was not uncommon, and we have noted a scratchy tricuspid diastolic murmur. An atrial sound was not uncommon, but an aortic diastolic murmur has never been heard. Reversed splitting of the second heart sound, so common in aortic stenosis, was unusual in this condition. The cardiac impulse tended to be more diffuse and quieter than the thrusting, strong left ventricular impulse found in true aortic-valve stenosis.

Radiology of the chest commonly showed a globular heart with enlargement of the right atrium as well as the left ventricle, but this was not necessarily so, a number of patients having a cardiac silhouette identical with that of true aortic stenosis. The electrocardiogram often showed a deep S wave in lead V5 and T-wave inversion in central precordial leads suggesting enlargement of the septum, right ventricular enlargement as well as left, or necrosis in the region of the septum. Catheterization, commonly revealed a pressure gradient in the outflow tracts of both left and right ventricles (Text Fig. 8).



TEXT FIG. 8.—A. Systolic pressure gradient between left ventricle (LV) and brachial artery (BA) in obstructive cardiomyopathy simulating aortic stenosis. B. Systolic pressure gradient in body of right ventricle in same condition. (The gradients are believed to result from bulging of the hypertrophied septum into both ventricles in systole.) PA=pulmonary artery; RV=right ventricle; INF=infundibulum; RA=right atrium.

That in the right ventricle was usually low in the body and quite unlike that of infundibular stenosis. Angiocardiography from the right side of the heart has revealed a normal aorta and aortic sinuses, but massive enlargement of the ventricular muscle, including the septum. Left ventricular angiography is probably necessary to delineate adequately the septum and outflow tract of the right ventricle, and we plan this in the future.

Results of Operation.—Further information about this group has been obtained at thoracotomy for relief of the outflow-tract obstruction. Three patients have been operated on. In the first (Case 1 (A. Je.), Goodwin *et al.*,

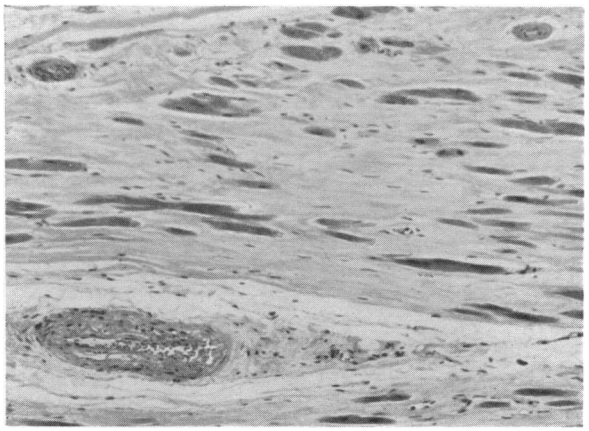


FIG. 1.—Photomicrograph of myocardium in Case 1. Extensive fibrosis can be seen, with strands of surviving muscle cells. (H. and E. ×97.)

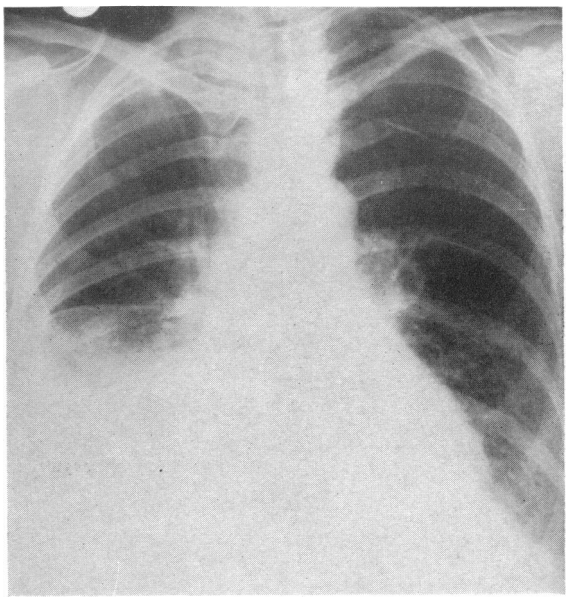


FIG. 2.—Six-foot postero-anterior radiograph of chest in Case 2, showing generalized cardiac enlargement and right pleural effusion.

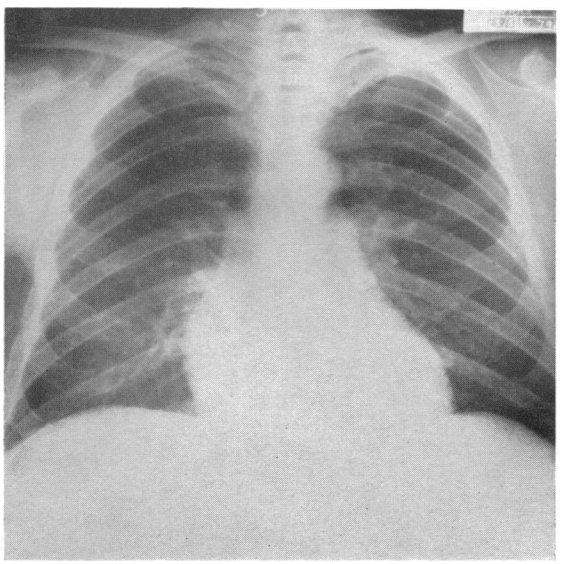


FIG. 3.—Six-foot postero-anterior radiograph of chest in Case 3, showing virtually normal cardiac silhouette.

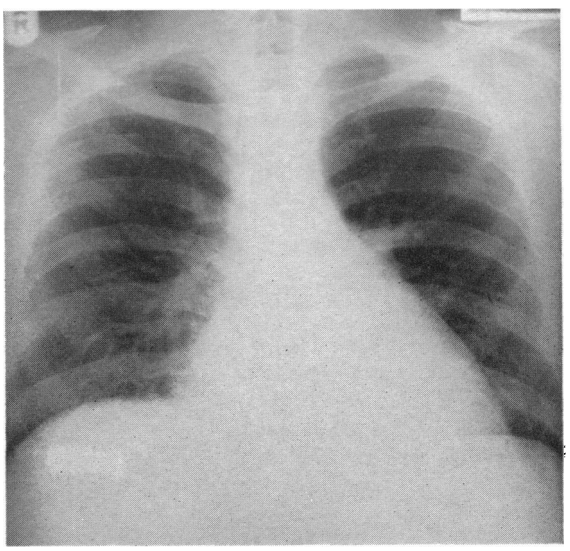


FIG. 4.—Six-foot postero-anterior radiograph of chest in Case 4, showing generalized cardiac enlargement.

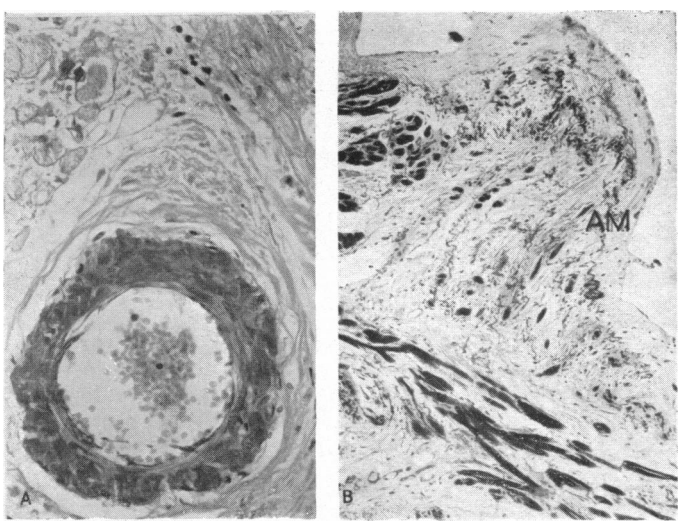


FIG. 5.—Photomicrographs of heart of Case 2. A. Myocardium, showing amyloid material in wall of small coronary artery. (H. and E. ×220.) B. Endocardium, showing extensive amyloid deposit (AM). (H. and E. ×59.)

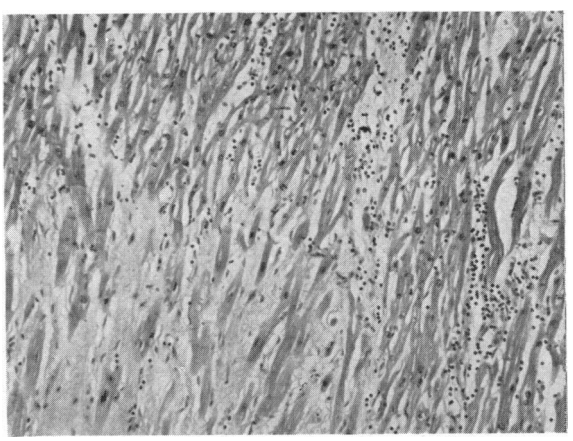


FIG. 6.—Photomicrograph of myocardium of Case 3, showing fibrosis and infiltration with abnormal lymphocytes. (H. and E. ×97.)

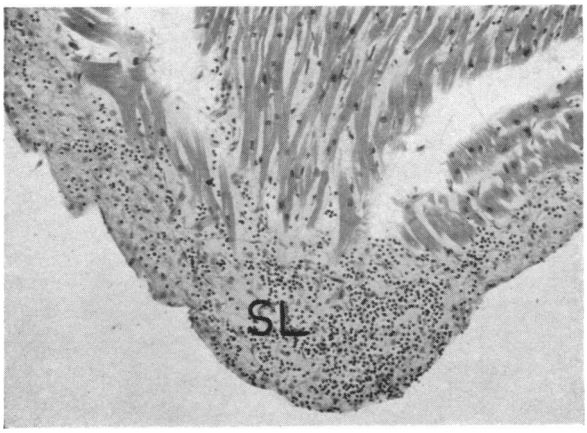


FIG. 7.—Photomicrograph of endocardium of Case 3, showing sclerosis and infiltration with abnormal lymphocytes (SL). (H. and E. ×97.)

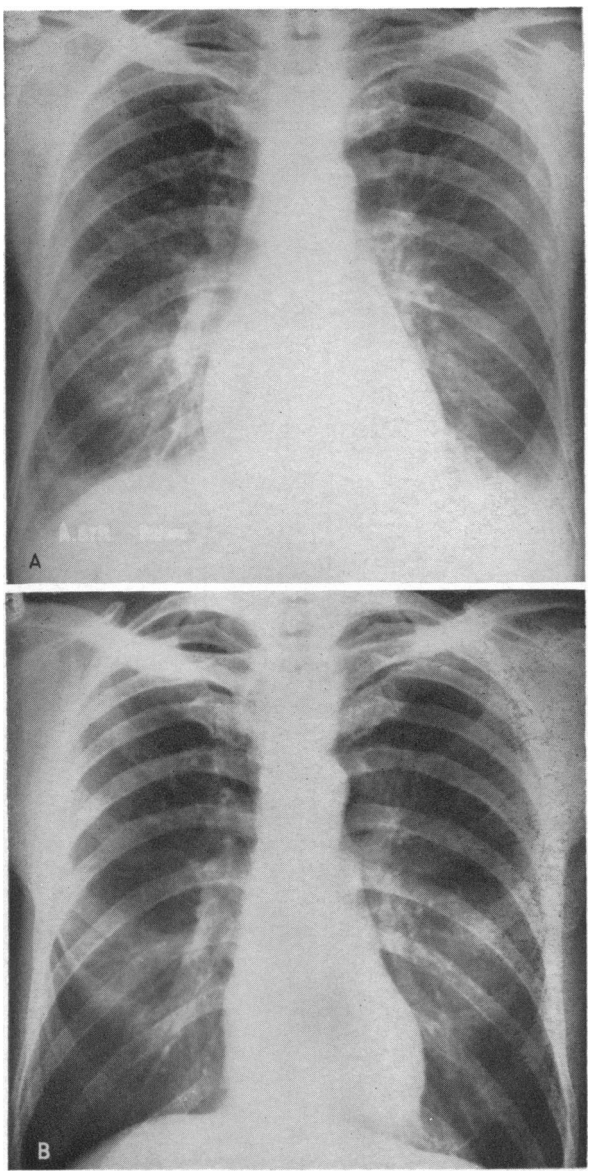


FIG. 8.—Six-foot postero-anterior radiographs of Case 5. A. Before treatment, showing bilateral pleural effusions, prominent pulmonary arteries, and slight cardiomegaly. B. After treatment, showing reduction in heart size and disappearance of pleural effusions.

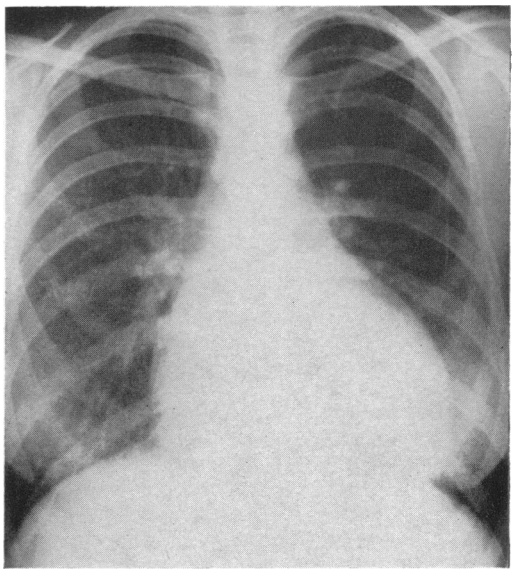


FIG. 9.—Six-foot plain radiograph of chest of Case 7, showing globular heart with enlargement of both ventricles and right atrium.

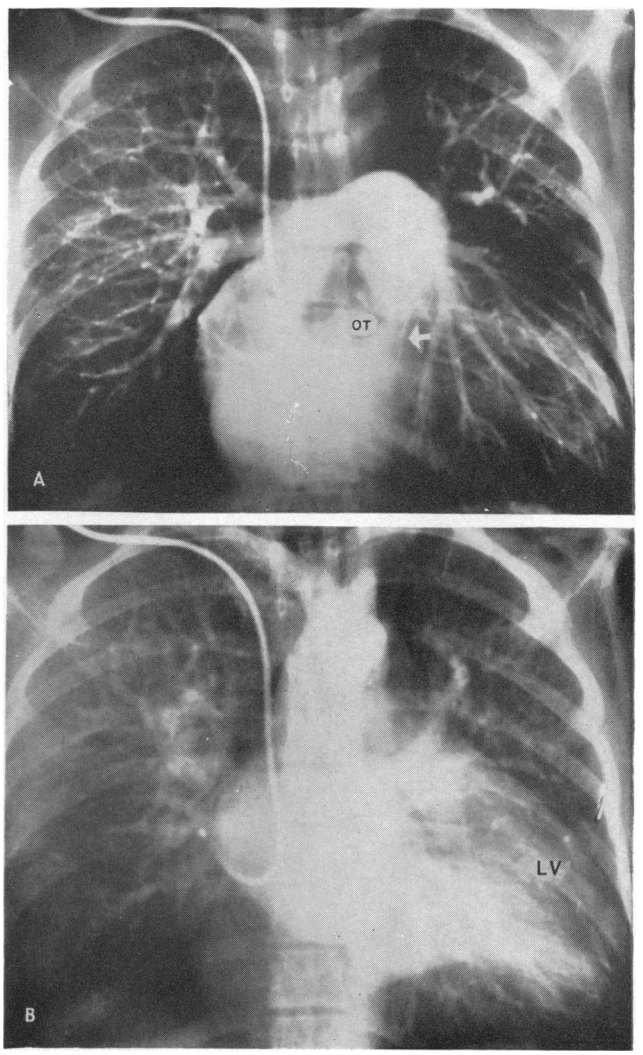


FIG. 10.—Venous angiocardiograms of Case 7. A. Postero-anterior projection, showing narrowing of right ventricular outflow tract (OT) below pulmonary valve. B. Postero-anterior projection, showing massive ventricular muscle wall (LV).

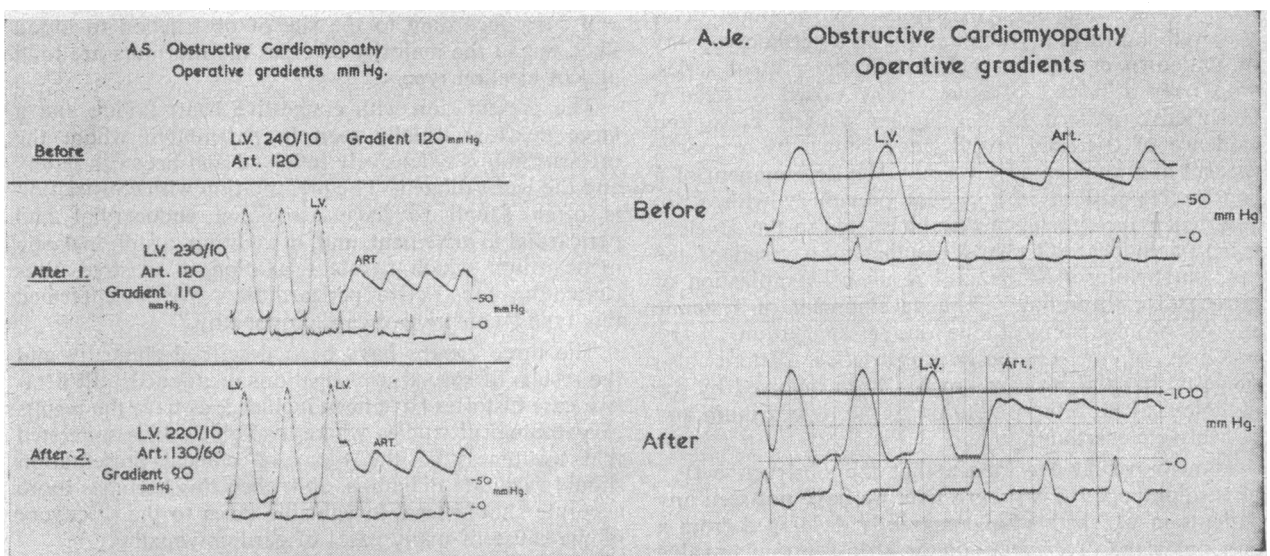
1960), when the left ventricle was explored from the aorta through the aortic valve the septum was found to be enormously enlarged and obstructing outflow. A portion of the septum was removed, and since this the patient has been free from angina, syncope, and dyspnoea. Histologically, the portion of ventricular muscle excised showed large muscle bundles. Though at left ventricular puncture before the operation a gradient between aorta and left ventricle of 60 mm. Hg in systole was discovered, at operation no gradient was found. Following the excision of the ventricular muscle, a small gradient developed, however (Text Fig. 9).

The second patient (A. S.) was found to have a substantial gradient both before operation and in the theatre immediately before the ventricle was explored. On opening the aorta and exploring the ventricle with the heart arrested no definite obstruction to outflow could be discovered. The septum appeared large, however, and a small amount of muscle was removed, but no localized obstruction could be found. Following closure of the aorta and re-starting of the heart the gradient across the outflow tract was only slightly reduced (Text Fig. 9). After the operation the physical signs were unchanged.

The third patient operated on resembled the first in that, though a substantial pre-operative outflow-tract gradient was found at left ventricular puncture, no gradient was found at operation. When the ventricle was explored the ventricular muscle was found to be extremely thick, but again there was apparently no localized hypertrophy of the septum. A small amount of muscle was excised, and after operation the systolic murmur became softer and shorter, but the pulse did not alter appreciably. The histology of the excised muscle in these two patients resembled that in the first.

The capriciousness of the gradients and the difficulty in demonstrating obstruction with the heart arrested are two of the most puzzling features of this condition. They presumably suggest that much of the obstruction is dependent on the way in which the hypertrophied septum functions during systole. We have already suggested (Goodwin *et al.*, 1960) that the character of the pulse might be due to late contraction of the hypertrophied muscle, so that the initial portion of the maximal ejection phase of the left ventricle is rapid. This would explain also the late onset of the systolic murmur. The lability of the gradient is also perhaps mirrored by the lability of the arterial pulse, for we have noted that the jerky nature of the pulse may vary from time to time. If the hypertrophied septum swings across in late systole to block the outflow tract, then it is possible that with the heart arrested no appreciable obstruction might be felt to left ventricular outflow. Some method is required of assessing the obstruction to outflow manually with the heart beating. The function of the septum could also be studied by left ventricular cine-angiography, which we propose to carry out in future.

Thus, while the condition of obstructive cardiomyopathy has clinically recognizable features, and while we believe that many cases are due to asymmetrical hypertrophy as described by Teare (1958), all cases are not necessarily due to this cause. The condition is now being widely described by various authors under different titles. Thus a clinical syndrome which is very similar has been described by Brock (1957, 1959) with the diagnosis of "functional obstruction of the left ventricle," while Bercu *et al.* (1958) used the term "pseudo-aortic stenosis." Morrow and Braunwald (1959) regard the condition as due to "functional aortic stenosis." Under the title of "Une cause d'erreur dans la diagnostique hémodynamique des rétrécissements aortiques," Soulié *et al.* (1959) described two cases in which obstruction to left ventricular outflow appeared to be due to asymmetrical hypertrophy of the septum. Brent *et al.* (1960) have studied members of two families suffering from left ventricular outflow-tract obstruction which they described as "familial muscular subaortic stenosis." Necropsy findings in three cases showed asymmetrical hypertrophy, the massive septum projecting into both ventricles. Brachfeld and Gorlin (1959) have described the syndrome of subaortic stenosis, and their cases in many respects resemble those of asymmetrical hypertrophy. There are, however, almost certainly a number of different conditions which can produce obstruction to left ventricular outflow below the valve. A diaphragm below the valve is well known, and this type of congenital subaortic stenosis may cause great difficulty in differential diagnosis from obstructive



TEXT FIG. 9.—Pressure gradients before and after resection of ventricular septum in two patients with obstructive cardiomyopathy simulating aortic stenosis. In A. Je. a small gradient has developed after resection, but in A.S. the gradient of 120 mm. before resection falls to 90 mm. Hg after resection.

cardiomyopathy. Björk (1960) has described two cases in which a subaortic stenosis was produced by an abnormally placed anterior leaflet of the mitral valve. It is of interest that in his cases the condition was clearly shown by left ventricular angiography. We believe, however, that the majority of cases of left ventricular obstructive cardiomyopathy with the characteristic signs that we have described are due to gross enlargement of the septum. When a gradient is found in the body of the right ventricle, this makes the diagnosis almost certain, for gradients in this situation are not, to our knowledge, found in other conditions. The nearest approach would appear to be the Bernheim syndrome, which possibly has some features in common with obstructive cardiomyopathy.

There is, however, still a great deal to be learned about the condition. Though we are now able to recognize it, we know nothing of its cause, except that there is a familial tendency, that the condition may be associated with congenital heart disease, and that it tends to increase with time. We believe also that there is a functional as well as an anatomical element, in view of the variable gradients and the findings at cardiotomy. It is conceivable that the condition starts as a disorder of function, perhaps as a neuromuscular imbalance of ventricular contraction with asynchrony of the septum and subvalvular regions, and that the gross hypertrophy and fibrosis are secondary phenomena. An infective cause has not been excluded.

Discussion

This study shows that patients with cardiomyopathy as defined by us may present in three major ways: (1) with cardiac dilatation, congestive heart failure, and atrio-ventricular valvular incompetence; (2) with signs of cardiac constriction; and (3) with signs of cardiac obstruction. A clinical differentiation into these three groups has some value, since it may aid diagnosis and occasionally prognosis. The recognition of the obstructive group may give a lead to successful surgical treatment, though it is too early to say whether this will in fact prove generally possible. The distinction between the two former types is not absolute, for patients may vary between the signs of atrio-ventricular valvular incompetence and those of cardiac constriction. This was well shown in a young man with a cardiomyopathy of unknown cause, not included in the present series, who over a period of four weeks varied between a constrictive pattern in the jugular venous pulse and evidence of tricuspid insufficiency shown by a poor *x* descent and augmented *v* wave. The development of a constrictive pattern in a patient previously with atrio-ventricular incompetence may be related to the development of endocardial changes, either as a result of the cardiomyopathy itself or as a result of organization of intracardiac thrombus. The development of systemic emboli would support the latter suggestion. The presence of an obviously constrictive pattern also suggests that the pericardium has been involved by the pathological process in addition to the myocardium and possibly endocardium.

Though we have evidence that the obstructive type of cardiomyopathy is progressive, we have not seen any patients in which this has apparently developed from a previous stage of constriction or atrio-ventricular valve incompetence. We think that this is probably a separate group and that overlap does not occur. The signs in the obstructive group appear to be dependent largely, if not entirely, upon the site of the obstruction, and are therefore remarkably specific. This is another reason for believing that obstruction in many of these patients is due to a specific asymmetrical hypertrophy of the septum, for in this way the simultaneous occurrence of obstruction to both outflow tracts and also to inflow tracts can be adequately explained. The diagnosis of obstructive cardiomyopathy should always be considered in any patient who has murmurs suggesting aortic stenosis but in whom the pulse is atypical. The maximum site of the systolic murmur and thrill down the left sternal edge is also of considerable importance. Patients who appear to have signs of both pulmonary and aortic stenosis should also be strongly suspected of suffering from obstructive cardiomyopathy. Where only right ventricular inflow is involved the signs are likely to be those suggesting tricuspid stenosis of mild degree or Ebstein's syndrome. However, cases with predominant left ventricular outflow obstruction may also show signs suggestive of right ventricular inflow obstruction, and this association may again prove a valuable diagnostic point.

Improved clinical diagnosis and study of all forms of cardiomyopathy should lead to clues as to aetiology in the various groups. Studies of affected families may also prove of considerable value, as may biochemical and other investigations, such as the quest for auto-immune and other antibodies.

Summary

An attempt has been made to classify clinically the cardiomyopathies according to three major clinical presentations: (1) a presentation with congestive heart failure and atrio-ventricular valvular incompetence, usually simulating ischaemic heart disease; (2) a presentation simulating constrictive pericarditis; and (3) a presentation simulating obstruction to one or other inflow or outflow tract, the commonest being the outflow tract of the left ventricle. In the first type systolic murmurs are common, are attributable to atrio-ventricular valve incompetence, and are pan-systolic. In the second type murmurs are equivocal or trivial and may usually be neglected. In the third type the murmurs will vary according to the site of obstruction to blood flow, but in the majority of cases the murmurs are loud and of ejection type.

The presentation with congestive heart failure and a large heart is usually seen in patients in whom the myocardium is extensively involved and becomes flabby and the heart dilated. The presentation with constriction is often found to have associated endocardial and pericardial involvement, and, in addition, a stiff, inelastic myocardium which resists relaxation in diastole, thus simulating constrictive pericarditis. We have termed this type "constrictive cardiomyopathy."

The three groups have been described clinically and the results of special investigations mentioned. Illustrative case histories have been included, as have the results of pathological studies where available. It is suggested that awareness of the types of clinical presentation should facilitate diagnosis, and when this becomes more accurate should lead to valuable clues to the discovery of the cause of many cases of cardiomyopathy.

We are grateful to the physicians of Hammersmith Hospital for permission to study their cases, and the

Department of Medical Illustration and Miss Carole Betts for the figures. Mr. W. P. Cleland kindly provided the operative data. We are also indebted to Professor W. S. Peart for referring Case 4, and Dr. J. Wolstencroft for referring Case 5.

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EXTENT AND PERMANENCE OF DENERVATION PRODUCED BY LUMBAR SYMPATHECTOMY

A QUANTITATIVE INVESTIGATION OF ITS EFFECTS ON SUDOMOTOR ACTIVITY

BY

J. A. GILLESPIE, M.D., Ch.M., F.R.C.S.Ed.

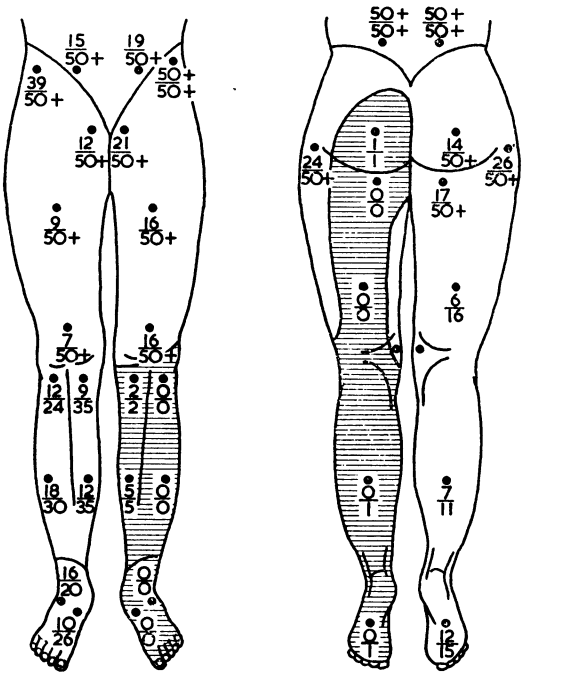
Department of Surgery, University of St. Andrews, Queen's College, Dundee, Scotland; now at St. George's Hospital, London

Is the denervation produced by lumbar sympathectomy permanent? This is a controversial topic of obvious practical importance. This paper presents the results of a quantitative investigation into the early and late effects of operation on sudomotor activity, thermoregulatory sweating being a most sensitive index of recovery of sympathetic function. The very different results obtained in the proximal and distal dermatomes of the limb are illustrated, and their mechanism is discussed.

Sweating was determined by measurement of the electrical conductivity of the skin (Richter, 1929). Dry, non-sweating skin is a poor conductor of electricity, while damp sweating skin is a good conductor. As sweating depends on sympathetic sudomotor activity the skin-conductivity measurements can be used to determine the extent of residual sympathetic activity after operation.

Quantitative Sudomotor Test

Nineteen standard points, sited with due regard to the dermatomes, were marked with ink on each of the lower limbs (Fig. 1). The patient then lay on a couch for 20 minutes with the whole of the lower limbs exposed at a laboratory temperature of 22° C. Thereafter, the electrical conductivity of the skin was measured at each of the marked points, using a commercially made skin-conductivity meter (Light Laboratories). An electrical heat cage was then placed over the trunk and face, and body-heating applied for 20 minutes or longer, till the patient was sweating profusely and his oral temperature had risen by at least 0.3° F. (0.17° C.). It is essential for the test that the stimulus to sudomotor activity is maximal. The skin conductivity was again measured at each of the 19 points. The examining electrode was then moved slowly up the limb from the toes towards the trunk until a sudden increase in conductivity occurred. This point, whose position was always quite precise, was marked, and indicated the junction of



LIMB	TOTAL CONDUCTIVITY IN MICRO-AMPS WITHIN THE SHADED AREA		CONDUCTIVITY [INCREASE IN MICRO-AMPS]
	BEFORE HEATING	AFTER HEATING	
SYMPATHECTOMIZED	8	10	2
NORMAL	133	312+	179+

FIG. 1.—A typical quantitative sudomotor test (see text). The current in microamperes at each of the points within the "denervated" (shaded) area is totalled before and after vigorous body-heating. A similar calculation is made within the corresponding area of the non-sympathectomized limb. The increase in conductivity after heating is a measure of sympathetic sudomotor activity.

normally innervated and denervated skin. By moving the electrode up the limb a number of times the points obtained could be linked up round the limb as a line separating the innervated and denervated parts.

The sudomotor test thus yielded information of two kinds: firstly, on the persisting area of partial or complete sympathetic sudomotor denervation below the line drawn round the limb; and, secondly, on the amount of sweating occurring before and after body-heating at a number of fixed points on the skin within this area. The sum of the readings in microamperes at each of the fixed points below the line of denervation gives a measure of sweating within this area. Comparison of sweating in corresponding areas of the sympathectomized and non-sympathectomized limbs