Sarcoid heart disease

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Sarcoid of the heart has not been commonly reported in the United Kingdom. The author's personal experience suggested that it was not rare, and an inquiry among colleagues revealed a total of 50 cases, 20 of which were fatal and had necropsy confirmation. The diagnosis had frequently not been made in life.

The clinical features of these cases are analysed and it is suggested that sarcoid infiltration of the myocardium should be considered in any unusual form of heart disease, particularly where disturbance of rhythm is prominent. Treatment with steroids should be tried in the active phase, but the degree of success will depend on the degree of the myocardial involvement. Treatment of rhythm disturbances should be carried out as necessary.

In 1929, Bernstein, Konzlemann, and Sidlick first described sarcoid lesions of the heart and in 1937 Gentzen reported the first death attributable to myocardial sarcoidosis. Since then many reports have appeared, most of them of small numbers of patients with a review of the published reports.

Many of the earlier case reports were of American Negroes, and in 1951 Yesner and Silver reported the first death in a white patient from congestive cardiac failure. In 1951, Adickes, Zimmerman, and Cardwell recorded the first case of myocardial sarcoid to be diagnosed in life and subsequently confirmed at necropsy.

In 1960, Porter added a case of his own and made a valuable review suggesting that the diagnosis should be considered in the differential diagnosis of complete heart block of unknown cause in adults. He collected from the available published reports 53 probable cases of whom 33 died as a result of myocardial involvement.

In 1962, Forbes and Usher reported the first fatal case in the United Kingdom and collected 24 fatal cases from those already published since 1941. This remained the only necropsy report until Ghosh *et al.* reported 6 new cases in 1972.

Scadding (1967) made an exhaustive review of the world reports of myocardial sarcoidosis and suggested that the total was less than 60 cases. In many of these sarcoid was not diagnosed in life and, even when sarcoidosis was diagnosed, cardiac involvement was frequently not suspected until necropsy.

In 1968, Bashour *et al.* reported 3 cases and made

a valuable review, classifying the clinical and electrocardiographic features and the location of the pathological lesions. The view that myocardial involvement was likely only when there was a florid picture of general sarcoidosis has tended to persist. In 1971, Gozo *et al.* reported 2 new cases, together with an up-to-date review of the world publications bringing the total up to 70 cases and including a number of Japanese cases. However, they persisted in stating that clinically recognizable involvement of the myocardium was rare.

It is the purpose of the present report to suggest that while cardiac involvement is uncommon, it is far from rare and may frequently be overlooked. It is also suggested that at least in cardiological practice the overt clinical features of the syndrome of sarcoidosis may be inconspicuous.

In the interest of brevity another full review of the published reports will not be made here; it is already fully covered by the papers referred to.

In Cambridge our finding of 6 necropsy cases (Ghosh *et al.*, 1972) suggested that this condition was not rare. Three of these patients had been seen in life by the author who, while aware of the condition, had not diagnosed it. An inquiry was, therefore, instituted starting with 90 personally known chest physicians and cardiologists in the United Kingdom and through their help many other colleagues were involved. The pursuit of positive cases was very time consuming and frequently involved lengthy correspondence and several personal approaches. As most of the cases in the study were reviewed retrospectively, only positive findings can

be recorded. Frequently reports were not as complete as could be wished, but in all cases the criteria of Scadding (1967) for the diagnosis of sarcoidosis were fulfilled. Scadding's definition begins, 'Sarcoidosis is a disease characterized by the presence in all of several affected organs or tissues of epithelioid cell tubercles, without caseation though some fibrinoid necrosis may be present at the centres of a few tubercles, proceeding either to resolution or to conversion of the epithelioid tubercles into avascular acellular hyaline fibrous tissue', and concludes, 'monotonously repetitive noncaseating epithelioid cell tubercles with more or less fibrosis. This histological pattern, then, . . . though we shall be able to demonstrate it completely in only a small proportion of cases, must be our defining characteristic; a clinical diagnosis of sarcoidosis is simply a statement of belief that if we have the opportunity of looking we should find these widespread changes.'

All cases in the present series were carefully scrutinized by the author and many of those submitted were rejected as the evidence of sarcoid was thought to be insufficiently conclusive – yet a number of these patients may nevertheless have had sarcoidosis. Cases with extensive pulmonary involvement and dying from cor pulmonale were excluded. All cases had clinical or pathological evidence of cardiac involvement. In 1972 at the 6th European Congress of Cardiology in Madrid a preliminary report of 51 collected cases was made (Fleming, 1973). This series has now been modified by the addition of a new case and the omission of two previously included. One of these has since died. This patient had heart block and a positive Kveim test, and at necropsy showed a non-specific fibrotic change which was not diagnostic of sarcoidosis. The other was a woman who was found to have sarcoid granuloma in left atrial biopsy taken at the time of mitral valvotomy for rheumatic mitral stenosis and who was also found to have a positive Kveim reaction. This case was thought to be too atypical to include in this analysis.

The purpose of this paper is to report an analysis of 50 cases of sarcoid heart disease in the United Kingdom. Of these, 6 from East Anglia have previously been published (Ghosh *et al.*, 1972). The rest were reported to me by colleagues and, apart from the patient mentioned by Raftery, Oakley, and Goodwin (1966) about whom further information including necropsy findings is now available, have not previously been published.

Questionnaires seeking details of cases were sent to 90 colleagues personally known to me. All but one of these eventually replied and many produced cases by discussing the subject with colleagues. A number recollected cases but could not find the details and

some volunteered that they had never thought of the diagnosis.

The questionnaire was of little use in producing the required details, which had to be sought by persistent personal inquiry.

It is known that various colleagues, e.g. Mikhail, Mitchell, and Ball (1972) have their own series of cases, which are not included in this study.

Location of patients

Eighteen were from East Anglia and were all seen by the author. Of the other 32 cases, 13 were single cases from a centre and the remainder numbered from 2 to 6 from a centre. Many large centres approached in the inquiry produced only a single case or none at all. There is no reason to believe that sarcoidosis in general is more common in East Anglia (Research Committee of the British Thoracic and Tuberculosis Association, 1969) and it is suggested that the diagnosis may be overlooked elsewhere.

All but three of the cases were diagnosed after 1960.

The age and sex, and race composition of the series were as follows: Age range: 23 to 77 years (mean 42.2); men 27, women 23; white 47, West Indian 3.

There is no definite difference in the sex ratio and the age range is wide. It is noticeable that the great majority of cases were European.

In 14 cases the diagnosis of sarcoidosis was only made at necropsy and had not been suspected in life.

The mode of cardiac presentation is shown in Table 1.

TABLE 1 *Mode of cardiac presentation*

<i>Presentation</i>	<i>No.</i>
Heart block of any degree	24
Ventricular ectopics or ventricular tachycardia	20
Tachydysrhythmias	16
Sudden death	12
Congestive heart failure	10
T wave changes suggesting cardiomyopathy	10
Simulating myocardial infarction	5
Tachy- plus bradycardia	5
Valve involvement	3

The salient feature of this Table is the high incidence of heart block and of tachydysrhythmias which were often resistant to treatment. The degree of block was frequently variable and ranged from bundle-branch block through to complete block.

Records are not complete enough to make a profitable detailed analysis of these dysrhythmias. Sometimes the block disappeared completely, with or without treatment with steroids, and some cases were paced. Some patients alternated between complete block and varying tachydysrhythmias. Ventricular ectopic beats, frequently multifocal in origin, and ventricular tachycardia were common. Sudden death was presumably due to block or ventricular fibrillation.

Other cases presented as intractable heart failure with T wave changes. Five cases presented with convincing evidence of myocardial infarction which was subsequently found to be due to massive involvement of the myocardium with sarcoid granuloma, the coronary arteries being normal.

Valve involvement was uncommon and was an incidental finding in 2 cases. Only in the case of Raftery *et al.* (1966) was it haemodynamically important.

Involvement of organs other than the heart

These are detailed in Table 2.

TABLE 2 *Involvement of organs other than the heart*

<i>Other organs</i>	<i>No.</i>
Evidence of involvement of other organs	49*
Lymph nodes	39
Lungs	32
Liver (often microscopical)	11
Eye	10
Spleen	8
Bone marrow	5
Skin	5
Neuropathy	3
Parotid	3
Pituitary	1
Uterus	1
Kveim positive (total tested unknown)	20

* Caused by one case of incomplete necropsy – evidence in heart indisputable.

This Table includes all the data – clinical, biopsy, and necropsy. As mentioned, reports were often incomplete, so only positive findings are recorded. Therefore, the reported figures are probably an underestimate. For instance, even at necropsy liver involvement was frequently microscopical and must have been overlooked unless specifically sought. This Table supports the claim that the diagnosis of sarcoidosis with general involvement was justified in this series. However, in a number of cases there was massive involvement of the heart and inconspicuous involvement of other organs which could not have been clinically evident.

There were 20 fatal cases, 11 men (age range 33–60 years, mean 44.4) and 9 women (age range 36–77 years, mean 52.5): only one woman was coloured. Eleven died suddenly (age range 33–66, mean 44.4) and 4 of congestive heart failure (age range 45–56, mean 49.0). Three died after valve replacement, and 2 as the result of a road accident.

The cases of road traffic accident will be discussed later.

It will be remembered that in 14 of these cases the diagnosis of sarcoidosis was not suspected in life.

A summary of the necropsy findings is given in Table 3.

TABLE 3 *Summary of necropsy findings*

<i>Organs containing sarcoid granulomata at necropsy</i>	<i>No.</i>
Total	20
Heart	20
Lungs	19
Lymph nodes	19
Liver	7
Spleen	7
Eye	occasionally
Bone marrow	
Nerve	
Uterus	

Again these are positive findings only and reports were frequently far from complete. The involvement of organs other than the heart was frequently inconspicuous. The liver was reported as being involved in fewer than a third of cases and frequently this was microscopically only.

Even at necropsy the diagnosis will be overlooked unless it is carefully borne in mind. In minor involvement of the heart it is the ventricular septum that is most frequently involved and histological sections should always be taken from this area.

Treatment

It was positively reported that 20 cases had been treated with corticosteroids, 2 had been paced, and a wide variety of antiarrhythmic drugs had been used. However, it was not felt that a detailed analysis of the treatment used could be profitably made.

There follow some illustrative cases. From the many bizarre clinical stories it has been difficult to make a representative selection. These are divided into proved and presumed cases of sarcoid infiltration of the heart.

Proved cases

Case 1 (Previously briefly reported by Ghosh *et al.*, 1972). An 8-year history of alternating tachycardia and

heart block. Well and in sinus rhythm shortly before death – not diagnosed in life.

This woman of 59 suddenly collapsed and died. The diagnosis of sarcoid involvement of the heart was first made at necropsy.

She had been seen by the author 8 years previously with supraventricular tachycardia (Fig. 1A) after uterine curettage. When the heart rate was controlled by digoxin she was found to have left bundle-branch block (Fig. 1B) which was followed 6 years later by complete block (Fig. 1C). At that time she was treated with long-acting isoprenaline, but this had to be stopped because of multiple ventricular premature systoles and bouts of tachycardia. She reverted spontaneously to sinus rhythm and remained well for nearly 6 years on no treatment. She had a tendency to multifocal ventricular ectopic beats and the left bundle-branch block persisted (Fig. 1D). A few months before her death she was seen and was in sinus rhythm and well. The PR interval was 0.24 sec and the left bundle-branch block had gone (Fig. 1E).

Necropsy showed the heart to be covered by numerous small greyish-white nodules, mainly in the lateral and posterior wall of the left ventricle but also extending into the ventricular septum (see Ghosh *et al.*, 1972). Histologically these were typical sarcoid granulomata. Microscopical lesions were also present in the right ventricle and the left atrium and also in the lungs and the liver.

Case 2 Widespread sarcoid not diagnosed in life, cardiomyopathy with fatal ventricular dysrhythmia.

This patient of 49 had a long-standing history of asthma. In 1967 uterine curettings were said to show tuberculous granulomata. She subsequently had a hysterectomy and, though the granulomatous condition was confirmed, no acid-fast bacilli were seen. In 1968 she was admitted as an emergency because of dyspnoea and epigastric pain. She was found to be in gross congestive cardiac failure with hepatomegaly. She also had an active iritis which was under treatment at an Eye Hospital. An electrocardiogram showed multiple ventricular ectopic beats and was said to have been suggestive of myocardial infarction. There was a Q wave in lead I and elevated ST segments with T wave inversion from V2 to V6. Later the electrocardiogram showed numerous multifocal ventricular ectopic beats leading to ventricular tachycardia and fibrillation. Resuscitation was only temporarily successful.

At necropsy her heart weighed 350 g. The valves were normal, but in the myocardium there were a number of whitish confluent areas of infiltration.

Microscopical examination showed that the lesions in the heart consisted of extensive areas of fibrosis with scattered relatively numerous giant cells and lymphocytic foci (Fig. 2). The abdominal lymph nodes were largely replaced by non-caseating granulomata which were free of acid-fast bacilli. Asteroid bodies were seen in a number of giant cells. Similar sarcoid deposits were found in the lungs and in the spleen.

Case 3 Presentation with Adams-Stokes attacks and complete heart block.

This 51-year-old woman in 1960 gave a year's history of syncopal attacks. At hospital her pulse rate was found to be 24 a minute and the electrocardiogram confirmed the presence of complete heart block. Subsequent electrocardiograms showed variable PR intervals with occasional ventricular ectopic beats and left bundle-branch block pattern. Chest x-rays showed appearances suggestive of pulmonary fibrosis. She had no specific treatment, she failed to do well, and subsequently died in an Adams-Stokes attack.

FIG. 1A-E Electrocardiograms of Case 1 over 7-year period (see text).

The heart at necropsy weighed 350 g, and the most striking feature was the presence of fibrotic changes in the region of the ventricular septum. All valves were normal and the coronary arteries were normal. Histologically the heart showed that there were sarcoid lesions in the pericardium, the myocardium, and the ventricular septum. Similar lesions were also found in the lungs, the spleen, liver, lymph nodes, and bone marrow.

Case 4 Young man presenting as myocardial infarction and subsequently dying suddenly.

This 32-year-old man was a well-known athlete who gave a history of occasional dizzy turns for the previous two years. In October 1970, after a strenuous football match, he felt weak and unwell. The following day he

FIG. 2 Photomicrograph ($\times 35$.) of myocardial involvement in Case 2. This shows extensive infiltration of myocardium with granulomatous tissue containing many giant cells.

developed chest pain, sweated, and felt dizzy, and was admitted to hospital where he was found to have a tachycardia with a rate of 250 a minute. With treatment this reverted to sinus rhythm. The differential diagnosis was thought to lie between massive pulmonary embolism and myocardial infarction. His electrocardiogram showed little change throughout his hospital stay and was similar to the one of 10 November 1970 in Fig. 3. He had a prolonged PR interval with dropped beats. There was left axis deviation, partial right bundle-branch block, and evidence of inferior infarction. He made steady progress, though first-degree heart block persisted. This was variable, sometimes with a PR interval as long as 0.3 sec, and sometimes there was a Wenckebach phenomenon with dropped beats. The basic ventricular complexes showed little further change. He was treated with anticoagulants and further investigations were negative. He returned to work, gradually increasing his activities, and in March 1971 he was well and returning to cricket. The PR interval remained prolonged. On 24 March 1971 he collapsed and died at work.

The chest x-ray had shown some cardiomegaly, but normal lung fields and no suggestion of hilar lymphadenopathy.

At necropsy the heart was massively enlarged and

weighed 830 g. The right and left ventricles were both quite solid with sarcoid tissue. The left ventricle was 2.5 cm in thickness (Fig. 4) and an enormous mass of tissue occupied the ventricular septum. Both atria were involved, particularly the right atrium which was solid with sarcoid tissue and measured 1.4 cm in thickness. The valves themselves were normal and coronary arteries were free from disease.

The lungs contained miliary nodules and the hilar glands were enlarged.

Histology showed that the myocardium was largely replaced by massive involvement with typical sarcoid granulomatous disease (Fig. 5, 6, and 7). Sarcoid granulomata were also found in the lungs, the hilar nodes but not in the liver, spleen, or other organs.

Case 5 Presenting with a toxic illness and tachycardia – ? myocarditis ? myocardial infarction.

This man, aged 31 at the time of his death, was admitted to hospital in June 1971 and was subsequently seen by the author. He presented with a 3-week influenza-like history with malaise, fever, and aches in the limbs. This cleared and he returned to work but developed a cough with clear sputum, which persisted. He was admitted to hospital after the development of severe

FIG. 3 Case 4. Electrocardiogram showing persistent appearances resembling myocardial infarction.

FIG. 4 Opened left ventricle of heart of Case 4 showing massive involvement with granulomatous tissue. The heart weighed 830 g.

central chest pain radiating down both arms and associated with dizziness and sweating. Shortly after the onset of pain he developed rapid regular palpitation.

The electrocardiogram showed sinus rhythm with grossly abnormal deep symmetrical T wave inversion and ST elevation in the anterior chest leads, particularly in V1 to V3. Apart from rhythm changes the basic appearance of the electrocardiogram (Fig. 8) changed little throughout the rest of his life. He was treated in the coronary care unit and the following day he developed a tachycardia lasting for one hour. He had a rate of 200 a minute and was treated by intravenous practolol with reversion to sinus rhythm.

The chest x-ray showed no gross cardiomegaly, but in the lung fields there were patchy changes in both the right upper and mid-zones. His serum enzymes remained normal, the erythrocyte sedimentation rate was 23 mm in 1 hour. Numerous investigations for virus and other infections were negative. The provisional diagnosis was one of myocardial infarction and he was treated accordingly, and with anticoagulants. His fasting lipids and triglycerides were normal.

The patient recovered from this extremely severe illness, but the chest x-ray and the electrocardiographic appearances changed little.

He had to be readmitted on 18 August 1971 because 2 days previously he had again developed chest pain radiating up into the neck and down both arms. It had recurred on several occasions lasting up to 3 hours. Each bout of pain had been accompanied by rapid regular palpitation. The electrocardiographic appearances were basically unchanged, but he had a number of multifocal ventricular premature systoles. Again, shortly after admission, he developed a tachycardia of 200 a minute similar to the previous occasion. This was unresponsive

FIG. 5 *Case 4. Relatively localized tubercle in myocardium. ($\times 80$.)*

FIG. 6 *Case 4. Diffuse involvement of myocardium. ($\times 35$.) Granulomatous tissue, giant cells, and fibrosis.*

FIG. 7 Case 4. Giant cell ($\times 200$.) in Fig. 6.

FIG. 8 Case 5. Electrocardiogram suggesting myocardial infarction.

to a large number of drugs and was reverted to sinus rhythm by DC shock.

He made slow but steady progress. A Kveim test, which had been started previously, was biopsied and found to be positive. As a result of this a diagnosis of pulmonary and cardiac sarcoidosis was reached. He was started on treatment with prednisone 20 mg daily in November 1971, together with practolol. He improved symptomatically, but there was little change in either his chest x-ray or his electrocardiogram. The prednisone was gradually reduced early in 1972. He remained fairly well, and had no particular complaint when he was seen at outpatients a fortnight before his death. He collapsed suddenly while dressing at home.

At necropsy the heart (Fig. 9) was extensively involved with sarcoid granulomatous tissue. This infiltrated the wall of the left ventricle and down into the interventricular septum. It also characteristically extended on to the epicardial surface. The right ventricle was normal in thickness, but anteriorly was fully involved by sarcoid. The involvement of the ventricular septum was similar. The coronary arteries were entirely free from atheroma and the valves were normal.

FIG. 9 *Case 5. Left ventricle opened to show massive, full thickness involvement of the myocardium and the septum. The pericardium is also involved.*

Histologically the tissue in the heart was classical sarcoidosis with asteroid bodies in the giant cells. There was also involvement around the bronchi, the lung, mediastinal lymph nodes, the liver, and the spleen.

Case 6 Mitral valve involvement.

This 26-year-old Jamaican woman with florid sarcoidosis with uveitis, bilateral hilar lymphadenopathy, and a positive Kveim test, presented at the Royal Postgraduate Medical School with acute subvalvar mitral incompetence. She had a mitral valve replacement and was referred to by Raftery *et al.* in their report of 1966 and by Scadding (1967). Histology of the valve showed replacement by fibrous tissue; there were granulomata in the valve that were reminiscent of Aschoff's nodules. The appearances were thought to have been modified by steroid treatment.

In 1971 she died suddenly while at home in the United States. At necropsy the heart weighed 450 g and was involved in a granulomatous process, with the free wall of the left ventricle and the interventricular septum being particularly affected. The atrial walls also showed some granulomata. Histological examination of the areas in the heart showed typical sarcoid granulomata with giant cells. The lungs, liver, spleen, and mediastinal nodes were also involved.

There was no positive history of dysrhythmia and no specific studies of the conducting system were made.

Case 7 Microscopical involvement of the ventricular septum.

This 34-year-old man had no previous medical history. He was found dead close to his car in the early hours of the morning after a motor accident with some unusual features. He had a traumatic amputation of the leg.

At necropsy all the organs, including the heart, appeared to be macroscopically normal.

The pathologist carried out a detailed histological examination chiefly with the object of excluding fat embolism. This, however, disclosed classical lesions of sarcoidosis involving the heart, the lungs, the liver, and the spleen. In particular, the foci in the heart were present in both the myocardium and the pericardium (Fig. 10) and were especially numerous in the region of the interventricular septum (Fig. 11). It is possible that cardiac dysrhythmia precipitated syncope and contributed to the accident.

Presumed cases of sarcoid involvement of the heart

Case 8 Example of cardiomyopathy with left ventricular failure and frequent ectopic beats apparently benefiting from steroid treatment.

This man of 50 was first seen by the author in 1971 when he complained of palpitations, dyspnoea, and a vague discomfort in the chest on exertion.

In 1959 he had had erythema nodosum and a chest x-ray at the time showed enlargement of the hilar glands, which was thought to be consistent with sarcoidosis. Subsequently this glandular enlargement had disappeared and the chest film had become normal.

On examination the only abnormality was an irregu-

FIG. 10 Case 7. Tubercle in pericardium. ($\times 80$.)

larity of the rhythm and a loud third heart sound. The liver and spleen were not palpable.

The electrocardiogram showed sinus rhythm with tall P waves and frequent multifocal ventricular premature systoles (Fig. 12A). There were also minor T wave changes in the left ventricular leads. Chest x-ray showed moderate cardiac enlargement. A diagnosis of sarcoid cardiomyopathy was made.

Liver biopsy showed a granulomatous lesion consistent with sarcoidosis, and the Kveim test was positive. He was treated with diuretics, practolol 300 mg b.d., and he was given prednisone 10 mg b.d. for 3 months.

On this treatment he immediately felt very much better, he lost his symptoms, and his electrocardiogram improved (Fig. 12B).

He has since continued on a smaller dose of practolol and remains entirely well in sinus rhythm without ectopic beats and with normal ventricular complexes. The heart size is now nearly normal.

Case 9 Long-standing cardiomyopathy.

In 1964, at the age of 39, this patient developed atrial fibrillation, which was resistant to DC version. Subsequently she suffered a cerebral embolus. A year later chest x-rays showed enlargement of the hilar glands and a gland biopsy showed sarcoid granulomata. Because of

her heart condition she was treated with warfarin and steroids. Subsequently she went into congestive cardiac failure and has continued to need treatment for this. In 1967 she developed a cutaneous lesion of the toe and on biopsy the appearances were characteristic of sarcoidosis. In 1971 she remained well, though her heart had progressively increased in size over the years and antifailure treatment had to be continued. The electrocardiogram showed T wave inversion in the left ventricular leads.

Case 10 Known case of pulmonary sarcoid. Cardiomyopathy fully investigated by left heart studies and coronary arteriography – apparently benefiting from steroid treatment.

This patient of 46 was well and had a normal chest x-ray until 1964 when he developed a diffuse pulmonary mottling and a diagnosis of sarcoidosis was made and confirmed by scalene node biopsy. Thereafter he remained well, with partial resolution of the pulmonary shadows. In 1968 his electrocardiogram was normal. In 1972 he noticed rapidly increasing dyspnoea and became orthopnoeic. He was found to be in congestive cardiac failure and was treated with digoxin and diuretics. He had a gallop rhythm and an electrocardiogram showed sinus rhythm with left bundle-branch block. He was extensively investigated at the Brompton Hospital

FIG. 11 *Case 7. Tubercle in ventricular septum. ($\times 200$.)*

and the left ventricular failure was confirmed by left heart studies and echocardiograms. A left ventricular end-diastolic pressure of 20 mmHg was recorded. Full coronary arteriography was carried out and there was no evidence of coronary heart disease.

Prednisolone, 5 mg four times a day, was added to his treatment. After one week his effort dyspnoea was much improved and the gallop rhythm had disappeared. He was considered to have sarcoid myocardiopathy. At the end of 1972 his symptomatic improvement was maintained.

Case 11 Example of transient cardiomyopathy treated with steroids.

In 1967 this man of 30 developed erythema nodosum and was found to have hilar gland enlargement. On full investigation it was found that the electrocardiogram showed T wave inversion in leads V₄ to V₆ and aVL. A conjunctival biopsy showed sarcoid granulomata and a muscle biopsy showed similar appearances.

He was in mild heart failure and this was thought to be due to myocardial sarcoid involvement. As this did not remit he was treated with prednisone, 20 mg three times daily. He then rapidly improved and his electrocardiogram and his heart size returned to normal. The prednisone was tailed off about a year later and since then he has kept well with a normal chest x-ray and electrocardiogram.

Case 12 An example of a case with complete heart block apparently spontaneously remitting.

This patient of 63 first came under medical attention in 1964 because of recurrent Adams-Stokes attacks and the finding of complete heart block. She was treated with isoprenaline up to 16 tablets daily and remained free from attacks on this treatment. In August 1965 she developed typical erythema nodosum and her Mantoux test was negative. A Kveim test was carried out and this gave a strongly positive reaction. The erythema nodosum subsided spontaneously and her disease was regarded as sarcoidosis with cardiac involvement. She has subsequently remained well and in due course reverted to sinus rhythm, which she has maintained without further treatment. The electrocardiogram still shows left bundle-branch block.

She apparently had activity of her sarcoidosis at the time of development of her relatively transient heart block.

Discussion

Incidence

From this study no attempt can be made to assess the frequency of sarcoid heart disease except to suggest that it is much more frequent than has been regarded hitherto. The present collection of cases is much the largest that has been reported. Previously

A

B

FIG. 12A and B Case 8. *Electrocardiogram before and after corticosteroid treatment.*

the biggest series was that of 5 cases in coloured patients reported by Longcope and Fisher in 1941, in surveying a series of 316 cases of sarcoidosis. However, there have been increasing numbers of case reports over the years, and in 1960 Kirchheiner suggested that myocardial involvement was by no means rare and Porter in 1960 also drew attention to the increase in frequency. However, in 1971 Gozo *et al.* were still describing clinically recognizable sarcoid involvement of the heart as rare.

The fact that so many of the well-verified cases in the present series have been located through a relatively small number of sources suggests that there may be many more cases which are not yet diagnosed. As Scadding (1967) says, the frequency of cardiac involvement in sarcoidosis is unknown.

In the first 275 cases of his series of sarcoid, only 2 had clinical features suggestive of sarcoid granulomata in the myocardium and in both of these the evidence was no more than circumstantial.

Mikhail *et al.* (1972) studied a series of 147 histologically confirmed cases of sarcoidosis by electrocardiography and in 11 of them they found an abnormal electrocardiogram pattern where the changes coincided with the resolution of sarcoidosis. They suggested that these changes were highly suggestive of myocardial involvement by sarcoidosis. All but one of these patients was symptom free and a considerable number of them were coloured. This report again suggests that the harder one looks for myocardial involvement the more it is to be found.

My relatively superficial inquiries at our local

chest, skin, and eye clinic where patients with sarcoidosis are seen did not produce any cases not already known to me. No routine cardiological survey was made of these clinics. The majority of the patients in this report presented originally with cardiac symptoms or signs.

Age

The reported age range is wide – the youngest being a Negro girl aged 6 at the time of death (Taussig and Oppenheimer, 1936) and the oldest being a man of 74 years (Güthert and Hübner, 1944). The average age of 71 cases calculated by Gozo *et al.* 1971 was 40 years. The age range in the present series is not out of keeping with this.

Sex

The sex incidence reported varies in different series, but overall there is no definite male or female preponderance – neither is there in this series.

Race

As mentioned, many of the early reports were of coloured people, and recent reports such as Mikhail *et al.* (1972) have a high coloured content. In their review of 68 reported cases where race was mentioned, Gozo *et al.* (1971) found that 26 were Caucasian, 27 were Negroes, and 15 were Japanese.

The fact that only 3 of the present 50 cases were not white is, therefore, notable.

Treatment

Heart failure and tachycardia should be treated by the appropriate drugs, and in this series the wide variety of treatment that would be expected was used. Practolol has appeared to be particularly useful in controlling paroxysms of tachycardia.

Heart block has been treated with long-acting isoprenaline (Fleming, 1965) and by pacing in 2 cases. Pacing in sarcoid of the heart was first described by Phinney in 1961. Block may be transient as noted in Case 12 reported here and mentioned by Moyer and Ackerman (1950) and Duvernoy and Garcia (1971), who describe a 34-year-old man who went into sinus rhythm with first-degree heart block after being paced for 3½ years.

The frequent involvement of the ventricular septum with progression to more complete degrees of heart block indicates that pacing is imperative in all patients with more than partial block and these must be kept under careful observation.

Corticosteroids Treatment with steroids in patients with sarcoidosis is usually avoided unless strictly necessary (Scadding, 1972). The variable natural history of the disease makes any beneficial

effects from steroids almost impossible to assess and, as Scadding (1972) says, there is no objective evidence of benefit in myocardial sarcoid. However, there is suggestive evidence in some cases. Case 8 in this report appeared to show rapid benefit from steroids given for only 3 months and this benefit has been sustained in the 18 months since they were stopped. Case 11 and others not detailed here have also appeared to benefit. Other cases are reviewed by Gozo *et al.* (1971).

Obviously a great deal would depend on the nature and the extent of the pathology. In a patient such as Case 7 where there was microscopical involvement of the interventricular septum, it is conceivable that steroids could assist complete resolution, but in others such as Cases 4 and 5 with gross replacement of the full thickness of the ventricular myocardium it could only be hoped that further destruction might be arrested.

However, the prognosis of sarcoid involvement of the myocardium is so bad that it is suggested that wherever it is even suspected of being in an active phase steroids should not be withheld. There can be no rules about the mode of administration of the drug or the duration of the treatment. Each case must be treated on its merits.

Prognosis

The outlook is obviously precarious in all cases with myocardial involvement. The high incidence of sudden death in this series is reflected in other reports. More surprising, perhaps, are the number of cases similar to Cases 4 and 5 who have managed to lead a normal life with massive, almost total, involvement of the myocardium in an active granulomatous process which must have been going on for a long time.

Diagnosis

It is realized that all non-caseating granulomata are not sarcoidosis, and in making the diagnosis in this series the strict criteria of Scadding (1967) were applied. Many cases that were submitted were excluded on the grounds of inadequate proof of the diagnosis. In the positive cases the diagnosis was always supported by clinical or histological proof of sarcoidosis elsewhere. The only exception was a necropsy case where the evidence in the heart was conclusive but, unfortunately, no other microscopical examination was made. The shortcomings of the Kveim test (Lancet, 1971) are appreciated, but it is felt with a good reagent this test can be useful in adding weight to a clinical diagnosis. Where lymph nodes can be biopsied these will give the best possible confirmation. The liver was infrequently

affected, and it is evident from this study that a negative liver biopsy would not preclude the diagnosis of sarcoidosis. The data in the series as a whole were too incomplete to allow a useful analysis of the biochemical and other aspects of sarcoidosis to be made. However, it should again be stressed that in this series the florid clinical manifestations of sarcoidosis were frequently absent and the diagnosis must be made in their absence. Forbes and Usher (1962) make this point and in their case the myocardium was massively involved, but the only other manifestation of sarcoid was some enlargement of the mediastinal nodes and very sparse microscopical tubercles in the spleen.

The diagnosis should be thought of in any patient with obscure heart disease – heart block in a young person, troublesome tachycardia, variable dysrhythmia, 'cardiomyopathy', myocardial infarction with unusual features, and, rarely, valve involvement or pericarditis.

Clinical features

The features demonstrated in this report have already been described and summarized by the various reviews referred to above.

Lack of complete data in all cases made a more detailed analysis of the dysrhythmias impossible, but it is not surprising that the collected reports (Bashour *et al.*, 1968; Gozo *et al.*, 1971) show that any and every form of dysrhythmia can occur.

When it is understood that any part of the myocardium and the conduction tissue can be involved, this is not surprising – nor is the variable type of dysrhythmia. Sudden death is very common. It is of interest to speculate on whether a sudden rhythm change had any bearing on the death in a road traffic accident in two of the presently reported cases.

Congestive cardiac failure and T wave changes are understandably frequent with diffuse myocardial involvement.

Valve involvement is uncommon, and Case 6 is the only one in this series where this was haemodynamically significant. This case has already been referred to by Raftery *et al.* (1966) and by Scadding (1967; p. 296).

In our other 2 cases the aortic valve was resected for other pathology and the discovery of sarcoid granulomata was an incidental finding, and yet at necropsy microscopical involvement of the myocardium and of other organs was evident.

Powell-Jackson, Roberts, and Scott (1971) have reported a clinical case of mitral incompetence appearing during a phase of active sarcoidosis and thought to be due to that disease.

Roberts and Cohen (1972) record the case of a 26-year-old woman symptom free until 10 days before death when she went into left ventricular failure with mitral incompetence. She developed ventricular fibrillation and heart block, was paced, but died in asystole. At necropsy all 4 cardiac chambers were massively involved with sarcoid with complete replacement of the papillary muscles. Sarcoid tissue was also present in lymph nodes, lung, liver, and spleen.

Pericardial involvement is relatively common at necropsy – showing as epicardial granulomata (see Fig. 9 and 10). Shiff, Blatt, and Colp (1969) report the case of a 31-year-old Negro woman with recurrent pericarditis with effusion. Biopsy at thoracotomy proved this to be due to sarcoid involvement of the pericardium. However, clinical pericarditis is uncommon. One of Gozo *et al.*'s (1971) cases was a 27-year-old Negro woman with a haemorrhagic pericardial effusion. The heart was extensively involved (weight 746 g) with sarcoid granulomata extending through the pericardium.

Presenting like myocardial infarction. Case 4 and 5 are examples of this presentation simulating myocardial infarction. In these there was transmural involvement of the left ventricle giving the electrocardiographic appearances of transmural infarction. Such cases are described in other reports (Gold and Cantor, 1959; Hines and Sancetta, 1963; Duvernoy and Garcia, 1971). These last describe an interesting case of a 30-year-old Negro woman who had a 2½-year downhill course with heart failure and recurrent ventricular arrhythmia. She was studied by left ventricular cineangiography and shown to have two ventricular aneurysms which at necropsy were shown to be due to fibrosis and granulomatous replacement of the left ventricular wall.

Pathological features

It is not proposed to embark on a detailed description of this which is already well described by Porter (1960), Hudson (1965), Scadding (1967), and Ghosh *et al.* (1972).

Suffice it to point out that the heart may be involved anywhere to any degree from microscopical tubercles as in Case 7 to massive replacement of the myocardium as in Case 4. It is perhaps worth repeating the frequency with which the ventricular septum is involved – a point also made by Bashour *et al.* (1968) who found that in a total of 45 reported deaths due to myocardial sarcoid this area was recorded as being involved in 20.

This study has only been made possible by the co-operation of a multitude of colleagues. Frequently a number of colleagues have been involved in supplying the details

of a single case. Rather than make an attempt, which would inevitably be incomplete, to thank all those concerned a general acknowledgment is made herewith.

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Addendum

Since this paper was completed, one of the cases included in it has been reported in detail by Fawcett and Goldberg (*British Heart Journal*, in the press).

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