ENDOCARDIAL FIBROSIS IN THE SUDAN

BY

W. O'BRIEN, M.D., M.R.C.P.

From the Kitchener School of Medicine, Khartoum, Sudan

Bedford and Konstam (1946) and Davies (1948) described series of cases of heart failure in Africans in which the chief feature at necropsy was endocardial fibrosis. Gillanders's (1951) cases among the Bantus appear to be different. Coming to the Sudan in 1952, I was struck by the number of working-class patients with congestive heart failure in which none of the classical causes of heart failure could be implicated but which corresponded closely to the clinical descriptions of endocardial fibrosis. These patients were for the most part Arabs and not Negroes. Unfortunately it was exceedingly difficult to obtain permission for post-mortem examination. Finally, we obtained permission for two necropsies, and both confirmed the condition of endocardial fibrosis. The following is a clinical description of the condition in 25 patients. In this class of patient rheumatic heart disease and hypertension are common, and yet these cases of endocardial fibrosis with failure outnumbered the total of all other types of heart failure seen by me.

The patients came from all over the Sudan. There were seven peasant farmers, four labourers, four servants (including three cooks), three porters, a cart-driver, a mechanic, a tailor, a shepherd, and three women. Their ages varied from 35 to 80 years, with the major incidence in the fifth decade. Their average age was 54 years.

The diet of each case was carefully recorded, and in only two was it obviously deficient. The only previous illnesses of note were malaria in six cases, syphilis in two, bilharziasis in one, and possibly rheumatic fever in one.

The duration of symptoms varied, but in 18 out of the 25 cases it was under six months. The symptoms started with breathlessness, usually on exertion, but sometimes first noticed on lying down at night. This nocturnal dyspnoea was severe and prevented sleep. Four patients started with pulmonary infarctions. Anginal pain was absent in all cases but one in spite of careful inquiry about such pain. After a variable time there followed swelling of the legs and abdominal distension and discomfort, with or without vomiting.

On examination the patients were of good physique. The pulse was rapid and usually regular, though in five cases there were numerous extrasystoles and in three there was auricular fibrillation. The pulse was of small volume in half the cases and of normal volume in the others. The blood pressure was normal and not particularly low. The jugular venous pressure tended to be very high, and in 10 cases the marked systolic pulsation seen in tricuspid incompetence was present. The liver was usually very large and in three cases was pulsating. Ascites was found in seven patients and oedema of the legs in all.

The apex beat was displaced into the axilla but varied in character, sometimes being difficult to feel and sometimes heaving. The intensity of the heart sounds also varied, but a triple rhythm from addition of the third

heart sound was usual. A presystolic triple rhythm was heard in two cases. Nearly every case had a systolic murmur at the apex, the intensity varying between grades 2 and 4.

General cardiac enlargement with pulmonary congestion was confirmed by radiography. Undue enlargement of the left auricle was not found. The electrocardiographic changes were those of widespread myocardial damage. Right bundle-branch block was present in four, left bundle-branch block in three, inversion of the T wave in standard lead I and in chest leads V_{4-7} in seven patients, and inversion of the T wave in lead I and V_4 in one patient, whilst in two the T wave was inverted in all leads. The haemoglobin was normal in all cases but one. Liver biopsy and histological examination in 11 cases merely showed the changes of passive congestion.

All but five patients were treated with rapid digitalization and mersalyl. Following Gillanders's experience, five cases were given rest only and a full diet, but in all five rapid deterioration necessitated the use of the above drugs. Seven patients died in hospital either in severe heart failure or in sudden peripheral circulatory failure. One patient died after several months in hospital with acute miliary tuberculosis and another from a lung abscess, both conditions having been acquired in the wards. Two patients discharged themselves after treatment had failed to improve their condition; 16 out of 25 patients left the hospital free from congestive failure.

In the following illustrative cases the words "marrissa" and "kisra" recur. Kisra is a sort of pancake made from sorghum, while marrissa is a drink of varying alcoholic content brewed from sorghum grain and said to be particularly rich in vitamin B₁.

Case 1

A labourer aged 45, living in Singa, became ill four months before admission, a number of symptoms appearing at the same time. He became jaundiced, with dark urine and loose green stools, upper abdominal pain, breathlessness particularly at night, abdominal distension, and swelling of the legs. He also developed a cough, which became worse just before his admission, when he began to cough blood-stained sputum. During this illness he had irregular fever. He had never had rheumatic fever, syphilis, or bilharziasis, but had had malaria. His diet was full, consisting of meat five times a week, milk with tea, two eggs a day, fresh vegetables, and kisra. He drank no alcohol.

Examination.—He was of normal build; his pulse was 84 a minute, irregular with extrasystoles, and of small volume; B.P. 100/80; the thyroid was normal and there were no signs of thyrotoxicosis; jugular venous pressure was very high, with marked systolic pulsation; rales were heard at both bases; the liver was enlarged nearly to the umbilicus; ascites and oedema of the legs were present. The apex beat was displaced outwards; the heart sounds were normal apart from a loud third heart sound heard in the apical and tricuspid areas and a widely split second sound in the pulmonary area. A systolic murmur (grade 3) was heard at the apex. X-ray examination showed general cardiac enlargement with an opacity at the right lung base. E.C.G. showed right bundle-branch block. He was treated with digitalis and mersalyl but died after three days.

At necropsy the abdomen was full of straw-coloured fluid and the liver was large and cirrhotic. The lungs were oedematous, and there were several small infarcts and a large one at the right base. The ventricular walls were both hypertrophied and dilated, and a white sheet of fibrous tissue spread from the apex up the ventricular walls, over the papillary muscles, involving the tricuspid valve, which

was very dilated (the whole hand could be passed through). The right auricular appendage was full of ante-mortem clot. All the other valves and the coronary arteries were normal.

Case 2

A camel shepherd aged 40, from Gatana on the White Nile, had been perfectly well until six weeks before admission, when he noticed slight pain in his knees, ankles, and wrists; with this was a slight fever. These symptoms lasted just over a week and then cleared. Three weeks before admission he developed abdominal distension, and ten days later breathlessness on exertion and on lying down. Three days after this his ankles swelled. He had never had rheumatism or syphilis. His diet was probably deficient. He shared 1½ lb. (570 g.) of meat once a month with his family of six. Their camel milk was skimmed to sell the cream. The remainder of the diet consisted of vegetables and kisra. He drank some marrissa once a month.

Examination.—He was a tall spare man; his pulse was 150 a minute, of small volume, and regular; B.P. 110/85; the jugular venous pressure was very high; rales were heard at both bases; the liver was enlarged; ascites and oedema of both legs were present. The apex beat was displaced outwards and was tapping. The heart sounds were normal apart from a third heart sound, and a systolic murmur (grade 3) was heard at the apex. The Kahn test was negative; haemoglobin 15 g.; W.B.C., 4,400, with 8% eosinophils. A week later eosinophils amounted to 18% in approximately the same total count. E.C.G. showed left axis deviation with a biphasic T wave in lead I, and inverted T in lead 6 and biphasic T in V₇. He improved slightly on digitalis and mersalyl, but died suddenly six weeks later after an attack of peripheral circulatory failure.

At necropsy the liver was large and showed the typical nutmeg appearance of passive congestion. The peritoneum was full of fluid. The lungs were oedematous and contained small infarcts. Both ventricles were grossly dilated, the walls being extremely thin. The heart muscle was pale, uniform, and not scarred. The valves except the tricuspid were normal, the latter being dilated and obviously incompetent. On the endocardium were numerous pale firm areas, and the apex of the right ventricle was full of ante-mortem clot. The coronary arteries were normal.

Case 3

A peasant from Merawi aged 55 was a fit man three months before admission, performing the very heavy work entailed in cultivating land which has to be irrigated and worked by hand. He then began to notice increasing breathlessness on exertion, a dry cough, and palpitation. He also had attacks of breathlessness and had to sleep propped up. Two months later his ankles swelled and he developed upper abdominal pain and distension. Previous to this he had had no illness of note. His diet consisted of 1 lb. (450 g.) of meat every four or five days, milk, vegetables, dates, and kisra. He took no alcohol.

Examination.—He was well built; his pulse was 120 a minute, regular, and of normal volume; B.P. 120/90; the thyroid was normal and there were no signs of thyrotoxicosis; the jugular venous pressure was high; the liver was enlarged and tender; and oedema of the legs was present. The apex beat was in the mid-axillary line, the heart sounds were normal except for a loud third heart sound heard in the apical and tricuspid areas. A systolic murmur (grade 3) was heard at the apex. X-ray examination confirmed general cardiac enlargement. The haemoglobin was 91%. E.C.G. showed left bundle-branch block. Liver section and histological examination were normal.

Two days after admission he suddenly lost consciousness, and when he awoke two hours later he had a left hemiplegia, which in turn passed off in 48 hours.

Treatment with digitalis and mersalyl rapidly cleared the venous congestion. He was discharged with a very large heart and a loud third heart sound, but free from failure.

Case 4

A labourer from Merawi aged 48 became breathless on exertion a year before admission. A month before admission he became very breathless in bed and two weeks later his ankles swelled. He had had frequent attacks of malaria in the past but no other illnesses of note. His diet was full, consisting of daily meat, vegetables, milk, and kisra. He had never taken much alcohol and had abstained altogether for five years.

Examination.—He was a tubby little man; his pulse was 140 a minute and regular; B.P. 135/90; the thyroid was normal and there were no signs of thyrotoxicosis; the jugular venous pressure was very high; the liver was enlarged to the umbilicus. The apex beat was felt in the mid-axillary line and was thrusting. The heart sounds were normal except that the second sound in the pulmonary area was widely split. A systolic murmur was heard in the apical and tricuspid areas. X-ray examination showed considerable general cardiac enlargement. The haemoglobin was 101%. E.C.G. showed right bundle-branch block, and liver section revealed only the changes of passive congestion. The Kahn test was negative.

The patient responded well to digitalis and mersalyl, and was discharged free from heart failure.

Case 5

A 35-year-old mechanic from Khartoum developed left pleuritic pain with a dry cough fifteen years before admission. He began to cough up blood, and a week later woke up in the night severely breathless. Three days later his legs swelled and he noticed epigastric pain. He had never had any previous illness of note. His diet was full, with meat daily, and he lived in a well-to-do household.

Examination.—He was of good physique, but in severe congestive heart failure. His B.P. was 120/80; the apex beat was felt in the anterior axillary line, and the heart sounds were normal apart from a presystolic triple rhythm best heard in the tricuspid area. X-ray examination of the chest showed general cardiac enlargement with an opacity in the left mid-zone. The Kahn test was negative; haemoglobin 100%; no eosinophils seen in a count of 8,000 white cells. E.C.G. showed an S wave in lead I, with a diphasic T wave and an inverted T wave in leads II and III. The T waves were also inverted in V₆ and V₇. The S wave in V₁ was markedly notched.

The patient responded well to digitalis and mersalyl, and was discharged a month later free from heart failure.

Case 6

A 65-year-old ex-labourer from Khartoum one year previously suddenly became very breathless on exertion and on lying down. There was swelling of his ankles. He was admitted to hospital and found to be in congestive heart failure. Digitalis and mersalyl were given and he was discharged two months later free from heart failure. In three weeks' time he was readmitted, again in congestive heart failure. This time he had auricular fibrillation and the E.C.G. showed the presence of right bundle-branch block. Once again he responded to the same treatment and was discharged free from heart failure. He remained well for nine months, but after this his breathlessness returned and he was unable to sleep at night. He had had syphilis when 20 years of age but no other illnesses of note. His diet was adequate, with meat, milk, eggs, and fresh vegetables daily in addition to kisra.

Examination.—He was a tall gaunt man who was breathless in bed. His pulse was 50 a minute (he had been on digitalis), irregular from auricular fibrillation; B.P. 145/85 approximately; the jugular venous pressure was very high; the liver was enlarged to the umbilicus and tender; rales were heard at both bases; ascites and oedema of the legs were present. The apex beat was felt between the anterior and mid-axillary lines and was heaving. The second sound

in the pulmonary area was split and there was a systolic murmur (grade 3) at the apex. The Kahn test was negative. X-ray examination showed general cardiac enlargement with no particular enlargement of the left auricle. The liver section showed the changes of passive congestion only. E.C.G. showed auricular fibrillation and right bundle-branch block.

Once again he responded to digitalis and mersalyl, and was discharged free from heart failure.

Case 7

A 42-year-old cook from El Obeid drank a huge quantity of water one evening during Ramadan, when the Muslim takes no fluid from sunrise to sunset. Following this he felt exhausted and generally unwell. Next morning he woke with rapid palpitation of the heart, and this continued on and off for four days. He was admitted to hospital, and after an E.C.G. had been done a diagnosis of paroxysmal ventricular tachycardia was made and the rhythm was restored to normal by quinidine. He was discharged and remained well for five months, when, a month before the present admission, he had a return of the palpitation. There was no breathlessness, but he complained of abdominal distension during the attacks of palpitation.

Examination.—His pulse was 110 a minute, irregular from extrasystoles, and of small volume; the thyroid was normal and there were no signs of thyrotoxicosis; B.P. 130/100; the jugular venous pressure was very high. The apex beat was displaced outwards and the heart sounds were normal apart from a third heart sound heard at the apex and a systolic murmur (grade 3) heard in the same place. E.C.G. showed inversion of the T waves in leads I, V₂, and V₄, with a biphasic T wave in V₆. X-ray examination of the chest confirmed general cardiac enlargement, and liver section showed the changes of passive congestion. He remained in hospital for two weeks without any prolonged attack of palpitation; the pulse rate then rose to 180 a minute and he became very breathless. His hands were cold and he was disorientated. Two days later the pulse rate fell to 48, and then after a few hours he collapsed and died.

Discussion

The aetiology of the condition remains unknown. This series of cases does suggest, however, that certain of the tentative theories put forward previously will not do. Coronary artery disease, at least of the main arteries, is not a factor: the site of the lesion is against it. Anginal pain was strongly denied and atheroma is rare in the Sudanese working-class. During 18 months I have heard only one patient complain of anginal pain, and he had syphilitic aortic incompetence. This is in strong contrast to the middle and wealthier classes of patients, in whom cardiac infarction is common, often at an early age.

Undernutrition and malnutrition were not present in these patients. The Sudan has been prosperous for some time now, and the protein content, including meat protein, is at least adequate. Young children sometimes show nutritional deficiencies and kwashiorkor occurs, but the absence of chronic liver damage in these cases is against any long period of malnutrition. The disease was found, in three cooks. Moreover, Gray (1951) reported the disease in a British Colonial Service doctor and a District Magistrate from Nigeria. Edge (1946) also described what must have been a similar case in a European from West Africa. Alcohol does not appear to have been a factor in these cases.

The disease is not limited to any race and is common in those of Arab stock. Syphilis was not a factor. The uneducated Sudanese is never afraid to admit a history of this condition, and, moreover, the Kahn test was negative in all the cases in which it was done. Eosinophilia was found in only two patients, suggesting that the high incidence in other series is due to parasitic infestation rather than being a mark of the allergic nature of the condition. Again advanced liver disease was found in only one case.

Heart failure due to pulmonary bilharziasis occurs in the Sudan, but is of a different nature from that in these cases. It presents as pure right heart failure, usually with a high cardiac output, and is easily recognized. Again, trypanosomiasis occurs in the Sudan, but it has a limited distribution and few of these patients came from infected areas.

Endocardial fibrosis thus appears as a well-defined clinical and pathological condition occurring commonly in Africa in negroes, Arabs, and Europeans alike. It is probably very widespread, and in the past has been labelled chronic ischaemic heart disease. In the Sudan it appears as heart failure for no apparent cause, occurring in adults associated with embolic incidents and usually responding to digitalis and mercurial diuretics. The cases described above have been in middle-aged and elderly patients, but I have seen unexplained cardiac enlargement associated with electrocardiographic abnormalities in younger patients, including children, which may well be due to the same cause.

ADDENDUM.—Since this article was submitted, the paper by Ball *et al.* (1954) on endomyocardial fibrosis has been published. The cases seem to be similar with the exception that those authors found mitral incompetence a common lesion. All cases of mitral incompetence were excluded from the present series, as, in the absence of necropsy, it was impossible to disprove a rheumatic aetiology. On the other hand there were several such cases, and in view of the Makerere findings they may well have been examples of endocardial fibrosis.

Summary

The clinical features of 25 cases of endocardial fibrosis with congestive heart failure occurring in Arabs in the Sudan are described. No clue to the aetiology of the condition was found.

REFERENCES

- Ball, J. D., Williams, A. W., and Davies, J. W. P. (1954). *Lancet*, 1, 1049.
Bedford, D. E., and Konstam, G. L. S. (1946). *Brit. Heart J.*, 8, 236.
Davies, J. N. P. (1948). *E. Afr. med. J.*, 25, 10.
Edge, J. R. (1946). *Lancet*, 2, 675.
Gillanders, A. D. (1951). *Brit. Heart J.*, 13, 177.
Gray, I. R. (1951). *Ibid.*, 13, 387.

MAXIMUM URINE CONCENTRATION

BY

B. E. MILES, M.D., M.R.C.P.
Consultant Physician, Hereford

A. PATON, M.B., M.R.C.P.

AND

H. E. de WARDENER, M.D., M.R.C.P.
From St. Thomas's Hospital, London, S.E.1

One of the most easily studied functions of the kidney is its capacity to conserve water under conditions of dehydration. In these circumstances water is reabsorbed from the tubular fluid against an osmotic gradient through the influence of endogenous antidiuretic hormones, and the maximum concentration of the solutes is used as an indication of the kidney's capacity to perform osmotic work. Although osmolality is the appropriate property which determines the extent to which the solutes can be concentrated, specific gravity is usually measured for clinical convenience. Specific gravity, however, gives only an approximate indication of the osmolality.

The present paper reports observations on the urines of normal subjects and patients with renal disease, either after 10 to 36 hours' water deprivation or after exogenous "pitressin." The first part of the paper is concerned with the errors which may arise when specific