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Endomyocardial fibrosis in Africa: its diagnosis, distribution and nature

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PAPER

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During recent decades several reports have appeared, mostly in Swiss and American journals, describing rare cases of heart failure caused by fibrosis of the endocardium. That this disease might be something more than a pathological curiosity in tropical medicine was first suggested in a brief report in 1946 by BEDFORD and KONSTAM. They had been impressed by the absence, in a group of African soldiers with heart failure, of valvular or coronary disease, or of hypertension or anaemia. In some of those who came to autopsy they found extensive sub-endocardial fibrosis in the ventricles with adherent organized thrombus. Most of these men came from West Africa, some from East Africa. At about this time independent observations of a similar lesion in African patients were being made in autopsies at Mulago Hospital, Uganda, and were recorded by one of us in 1948 (DAVIES, a, b, c.). Our objects in presenting this paper are :

(i) To draw attention to the high incidence of endomyocardial fibrosis (e.m.f.) in Uganda and to discuss the difficulties of clinical diagnosis in the tropics.
(ii) To review information on the geographical distribution of this disease, with particular reference to Africa.
(iii) To discuss some of the problems of pathogenesis and aetiology.

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CLINICAL AND PATHOLOGICAL DESCRIPTION

Our patients are all Africans, of both sexes and all ages. They come with symptoms of heart failure—dyspnoea, ascites and oedema—of some months' duration. In a study of 20 fatal cases (BALL et al., 1954) we have described in some detail certain characteristic clinical patterns in relation to the different cardiac lesions; these are illustrated in the diagram (Fig. 1). They may occur separately or in any combination (Table I).

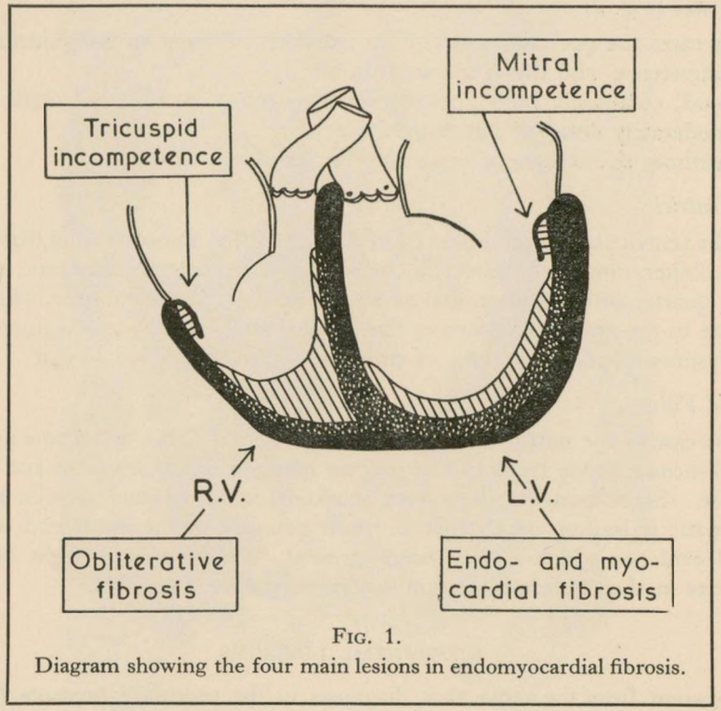

FIG. 1.
Diagram showing the four main lesions in endomyocardial fibrosis.

TABLE I. Main anatomical and clinical subdivisions of e.m.f.

Region	Lesion	Clinical result
1. Left ventricle	Endo- and myocardial fibrosis	Simple bilateral heart failure
2. Right ventricle	Obliterative fibrosis	Pure right heart failure
3. Mitral valve	Adherence of posterior cusp to ventricle	Mitral incompetence
4. Tricuspid valve	Adherence of posterior cusp to ventricle	Tricuspid incompetence

A short description of these different types will serve here to introduce discussion upon diagnosis; this we hope will contribute towards elucidating the world distribution of this disease, particularly in those parts of the tropics and sub-tropics where autopsy data are almost unobtainable.

(i) *Left Ventricle* (*Fig.* 2)

Fibrosis may cover three-quarters or more of the endocardial surface. When the mitral valve is not involved, these patients on examination show only the signs of left or bilateral heart failure. They are dyspnoeic, with pulmonary crepitations, and commonly have signs of pleural effusion; they also have distended jugular veins, enlarged liver, ascites and oedema. There are no murmurs, except perhaps a faint apical systolic.

(ii) *Mitral Valve* (*Fig.* 2)

In other cases the posterior mitral cusp becomes adherent to the ventricle wall. The result is incompetence, and this is apparent in life by :—

(a) A loud, commonly high pitched, apical-systolic murmur and thrill.
(b) A moderately enlarged left auricle which,
(c) Sometimes shows systolic expansion on the X-ray screen.

(iii) *Right Ventricle*

The right ventricular lesion differs from the left in that the advancing fibrosis invariably produces an obliteration of the cavity in the region of the apex by the time it has involved more than a quarter of the endocardial surface (Fig. 3). The symptoms which follow this lesion are due to the rise of pressure in the great veins; hepatic engorgement, ascites and oedema. Dyspnoea and other signs of pulmonary congestion are absent.

(iv) *Tricuspid Valve*

As in the case of the mitral valve, the posterior cusp is liable to become adherent to the ventricle and incompetence results; this process however is less frequent and less severe on the right side. Some patients show very marked jugular venous systolic pulsation, and expansile hepatic pulsation. A systolic murmur maximal at the lower end of the sternum is additional evidence which is sometimes present. Predominantly right heart failure is present here as in the obliterative group described above.

DIFFERENTIAL DIAGNOSIS

It is apparent from the above that diagnosis in the mortuary presents few difficulties provided the prosector is aware of the condition; regarded in the past as burnt-out mural endocarditis, it has been overlooked. Differential diagnosis in life however is not so simple. The main diseases which cause difficulty can be considered in groups (Table II) according to their ability to mimic the physical signs of the different types of e.m.f. (Table I).

TABLE II. Differential diagnosis of endomyocardial fibrosis.

I. Apical systolic murmur	*III. Tricuspid incompetence*
1. Rheumatic mitral valvulitis	1. Rheumatic tricuspid valvulitis
2. Anaemia	2. Bacterial endocarditis
3. Bacterial endocarditis	
4. Large left ventricle	
5. Septal defect	*IV. Large, immobile heart shadow*
	Tuberculous pericarditis
II. Simple heart failure	
1. Beri-beri	
2. "Nutritional heart disease" (Gillanders)	*V. Ascites and oedema*
3. Ischaemic heart disease	1. Constrictive pericarditis
4. Thyrotoxic heart disease	2. Portal cirrhosis

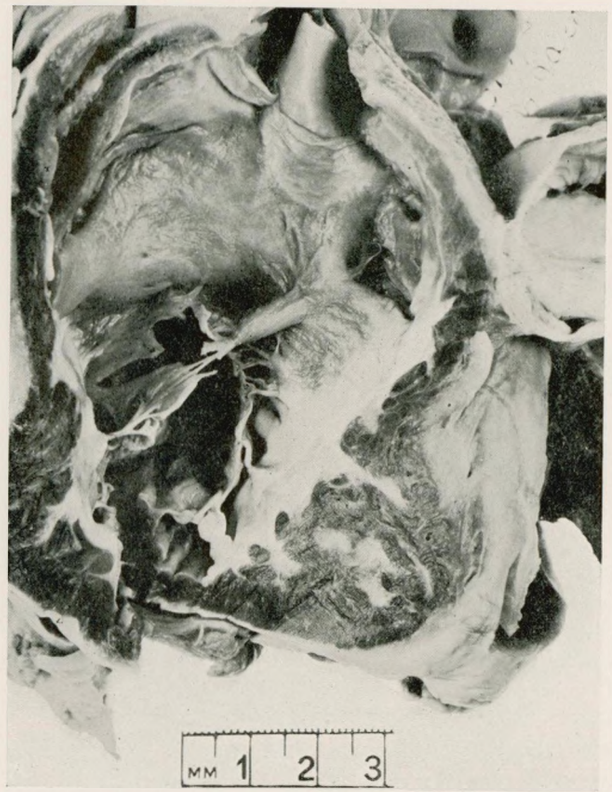

FIG. 2.
Left ventricle, showing at the apex a thick plaque of smooth white fibrous tissue with defined, rolled edges. The fibrous tissue has invaded the papillary muscles, and the posterior mitral cusp is extensively adherent. A bunch of vegetations attached to the anterior cusp, indicate terminal bacterial endocarditis.

Please note: LEGENDS TO FIG. 2
and 3 should be reversed.

(*To face page* 292)

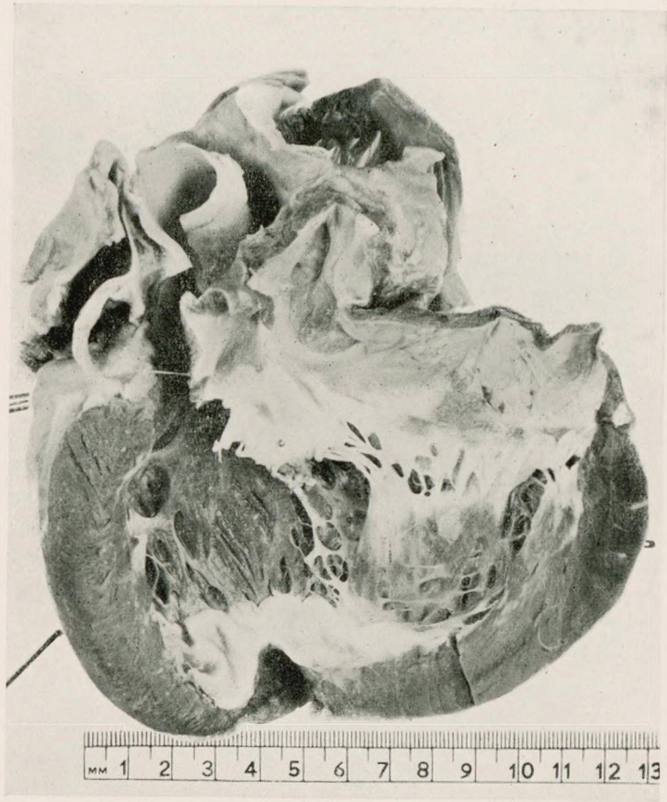

FIG. 3.

Right ventricle, showing advanced obliterative fibrosis. The tricuspid valve (a little torn), seen on the left of the picture, shows great thickening of some of its chordae. The greatly thickened endocardium is seen in section, with strands of white fibrous tissue penetrating deeply towards the apex.

(i) *Other causes of a loud apical systolic murmur*

One of the most important in this group is rheumatic mitral disease. This can generally be distinguished by the diastolic murmur produced by coincident stenosis. In the rare case where this is absent, the distinction may be quite impossible. It may be impossible where mitral stenosis is associated with e.m.f., an unusual combination we have seen on two occasions. Severe anaemia may cause a loud systolic murmur and the signs of heart failure, but these signs disappear as the anaemia responds to treatment.

Bacterial endocarditis of the mitral valve can pose a very difficult problem. It can produce a loud apical systolic murmur, and the accompanying signs—fever, bacteriaemia, emboli—are of no value, as e.m.f. itself is sometimes complicated by bacterial endocarditis. Furthermore, although we have never observed embolism in uncomplicated cases of e.m.f., other writers (SMITH and FURTH, 1943; GRAY, 1951) describing endocardial fibrosis with mural thrombus have commented on the frequency of embolic incidents in their patients in the absence of any infection. Loud apical systolic murmurs are commonly heard with the large left ventricle which develops in hypertension and aortic valve disease. As these are absent in e.m.f. the distinction here is a simple one.

In atrial septal defect, the murmur is usually loudest at the base, and the great dilatation and pulsation of the pulmonary vessels seen on fluoroscopy are distinctive.

The X-ray outline, particularly the large left auricle seen in the right oblique, is of value except in distinguishing from mitral stenosis which also produces enlargement, usually greater than in mitral incompetence. Systolic expansion of the auricle is suggestive when it occurs, but it is commonly slight and sometimes absent.

(ii) *Other causes of simple bilateral heart failure*

By " simple " we mean heart failure without any evidence of valvular disease, ischaemia, anaemia, hypertension etc. to cause failure. E.M.F. of the ventricles which has not involved the valves can present in this way. Such cases have to be distinguished from beri-beri, " nutritional heart disease " (GILLANDERS, 1951), thyrotoxic heart failure and syphilitic coronary stenosis.

In areas where it is a practical problem, beri-beri is simple to exclude by its rapid response to thiamine. GILLANDERS has described a form of heart failure seen in Africans in Johannesburg in which facial oedema was present in addition to other signs of advanced congestive failure, and feeble pulsation of the enlarged heart on screening, resembling pericardial effusion. Chronic liver disease was present in all cases. He was able to demonstrate reversible diminution in the size of the heart and symptoms of failure, by general improvement (particularly as to protein) in the diet, although thiamine, brewers' yeast and vitamin E separately were without effect.

In thyrotoxicosis non-cardiac signs are usually evident, but when these are not apparent, the distinction from e.m.f. may be difficult, although increased heart action and a wide pulse-pressure are not characteristic of e.m.f. In Uganda this problem seldom arises, owing to the extreme rarity of hyperthyroidism in the indigenous population.

An exceedingly common cause of heart failure in many parts of the tropics is syphilitic aortitis. Where coronary stenosis has occurred without aortic incompetence or aneursysm, there is little that is characteristic about the heart failure; a clear history of anginal pain is not always obtained. Widening of the aortic shadow on X-ray examination, in the absence

of hypertension, may be the only distinctive sign. In Uganda positive serological tests are too common to be of much help, nor does a negative test exclude late aortic syphilis.

(iii) *From other causes of tricuspid incompetence*

Apart from bacterial endocarditis, rheumatic valvulitis is the only other common cause of organic tricuspid incompetence. Since this is usually associated with mitral stenosis the distinction is not difficult.

(iv) *From other causes of a large immobile heart shadow*

The heart in e.m.f. often resembles a large pericardial effusion when viewed on the X-ray screen. The enlarged globular shadow with greatly diminished pulsation is common to both conditions. In the case of e.m.f. the lack of pulsation is presumably due to the poor contractility of the myocardium, and to the relatively smaller emptying required of a much dilated ventricle. The distinction is made more difficult by the fact that a hydropericardium is not uncommonly associated with e.m.f. When serious doubt arises the exploring needle is the only reliable arbiter.

(v) *From other causes of recurrent ascites and oedema*

Right heart failure caused by extensive endocardial fibrosis may be imitated very closely by constrictive pericarditis, and by cirrhosis with portal hypertension (Fig. 4). Whether

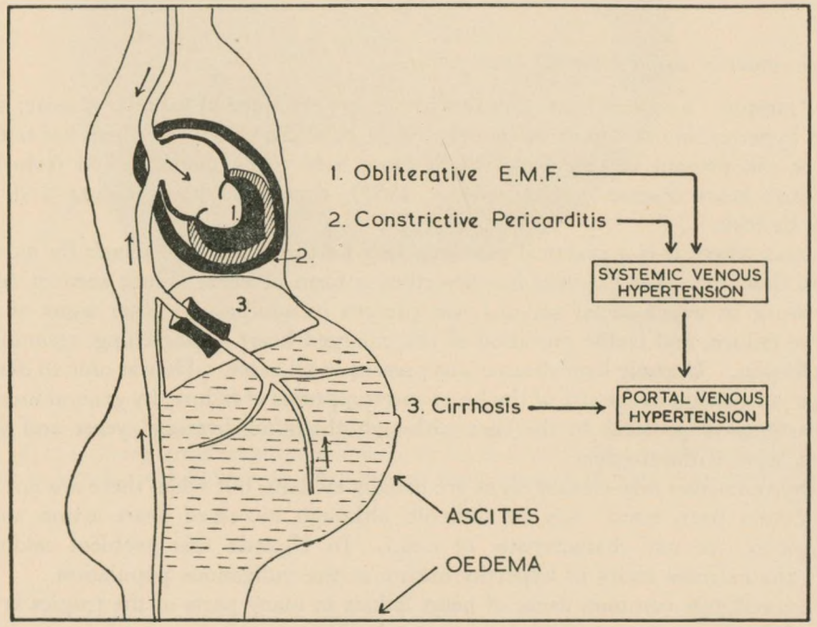

FIG. 4.
Diagram of right heart and great veins, showing three points at which deposits of fibrous tissue may impede venous return.

the rigid fibrous tissue which impedes diastolic filling of the heart is inside or outside, the results are very similar. These include not only isolated right heart failure, but also a very loud 3rd heart sound associated with a palpable shock, absence of murmurs and auricular fibrillation. A small heart shadow on X-ray examination favours pericarditis but there are many exceptions to this rule. Certain distinction is only possible radiologically when pericardial calcification is seen. The distinction is of more than academic importance in view of the good prospect for surgical relief of a constricting pericardium; it is therefore justifiable to advise exploratory thoracotomy in certain cases.

The differentiation from portal hypertension due to cirrhosis is usually apparent because the heart in e.m.f. is commonly dilated, the pulse rapid, and the jugular veins visibly engorged. All these criteria can fail however; one patient seen recently had carried his label of " portal cirrhosis " while under careful observation for a number of years, during which time he was repeatedly tapped for his ascites. When he eventually died, fibrosis was found in the endocardium of the right ventricle, and none in the liver. Among the difficult cases are those in persons with a poorly developed external jugular vein. Here the distinction is made by direct recording of venous pressure by running fine polythene tubing up from an arm vein, and attaching this to a saline-filled U-tube. One patient who appeared to have normal jugular veins, was found to have a pressure of 27 cm. of water.

Proof of hepatic cirrhosis by liver biopsy does not exclude e.m.f. for in a proportion of cases both occur together.

HEART DISEASE IN UGANDA

Some idea of the place of e.m.f. as a cause of heart disease in Uganda may be gained from Table III, recording the figures for all autopsies on patients dying of heart failure in a 3-year period at Mulago Hospital, and from Table IV giving the diagnosis of in-patients with cardiovascular disorders in the medical wards of the same hospital during one year. This hospital is at Kampala, in the central province of the Uganda Protectorate, on the north shore of Lake Victoria. While we cannot assume that the Mulago figures are representative

TABLE III. Autopsy diagnosis in 231 cases of heart failure in 1,773 autopsies at Mulago Hospital, 1951-53.

Diagnosis	Incidence	Percentage of 231 cases
Congenital	2	0.9
Rheumatic	20	8.7
Bacterial endocarditis	11	4.7
Pericarditis, pyogenic	5	2.2
Percarditis, tuberculous	12	5.2
Percarditis, doubtful	3	1.3
Syphilitic aortitis	34	14.7
Endomyocardial fibrosis	33	14.3
Hypertension, renal	37	16.0
Hypertension, essential	6	2.6
Atheromatosis	6	2.6
Coronary thrombosis	0	0
Pulmonary heart disease	12	5.2
Heart failure of anaemia	12	5.2
Miscellaneous diagnoses	4	1.7
Cause not determined	34	14.7

TABLE IV. Cardiac disorders in 167 medical in-patients, Mulago Hospital, 1953.

Diagnosis	Incidence in 167 patients	
	Total	Percentage
Congenital	7	4.2
Rheumatic	15	9.0
Bacterial endocarditis	11	6.6
Pyogenic pericarditis	3	1.8
Tuberculous pericarditis	2	1.2
Syphilitic aortitis	29	17.3
Endomyocardial fibrosis	35	21.0
Hypertension (inc. renal)	32	19.0
Aortic atheroma	8	4.8
Coronary thrombosis	0	0
Pulmonary heart disease	5	3.0
Thyrotoxic heart disease	1	0.6
Heart failure of anaemia	4	2.4
Incomplete diagnosis	21	12.5

A double aetiology was present in six of these patients, as follows :
Endomyocardial fibrosis with rheumatic carditis
,, ,, ,, bacterial endocarditis
,, ,, ,, renal hypertension
Syphilitic aortitis with bacterial endocarditis
,, ,, ,, rheumatic carditis
Pulmonary heart disease with severe anaemia

of the situation in outlying districts of Uganda (for which no data are available), the hospital draws many of its patients from these districts, and we have no reason to believe that the general picture would differ very greatly there.

It will be seen that the prevalence and types of cardiovascular disease as seen in hospital are by no means the same in East Africa as in Europe and North America. With regard to hypertension, it is important to point out that in the majority of our patients this is attributable to renal disorder (WILLIAMS, 1944; DAVIES, 1948b, 1949; RAPER, 1951). Thus while chronic renal disease, syphilitic aortitis and endomyocardial fibrosis between them account for the greater part of the cardiovascular disorders met with in Africans at Kampala, rheumatism is relatively less important than in the northern hemisphere, and coronary and thyrotoxic heart disease are virtually absent. Other local variations in the incidence pattern no doubt occur between one part of the tropics and another. These differences are especially relevant to problems of differential diagnosis, often peculiar to particular regions. They also have to be taken into account in any discussion of the incidence of e.m.f. in countries where vital statistics are lacking and where figures relating the frequency of one kind of heart disease to another are all that we have.

GEOGRAPHICAL DISTRIBUTION

Our knowledge of the world distribution of e.m.f. is fragmentary: present information suggests that it may be widely, though perhaps unevenly, distributed in Africa.

Uganda

Our own cases include patients from all parts of the Uganda Protectorate and some

from neighbouring territories. Analysis by tribes shows a preponderance of Baganda among those diagnosed clinically, and a preponderance of the Ruanda-Urundi group among those coming to postmortem. The former is not unexpected since Kampala is in the Buganda Province. Clinical diagnosis, however, is not always certain, and the postmortem figures therefore assume particular importance. In 2,568 autopsies where the tribal origin was known, there were 24 cases of e.m.f. in 804 patients of the Ruanda-Urundi group (3.0 per cent.) compared with 22 cases in 1,764 autopsies in all other tribes recorded (1.2 per cent.) in the same period. The Ruanda-Urundi tribesmen migrate to the Kampala district from the south-west to find work, usually in the menial grades and poorly paid. Their nutrition and housing are correspondingly inadequate; they lack malaria premunity and fall ready victims to illness from many causes. Their stay in Uganda varies from a few months to a few years.

However the preponderance in the postmortem figures does not necessarily mean that these folk are more prone to e.m.f. than others, since they are more likely to stay on in hospital when seriously ill, and more likely to come to autopsy, than patients who have settled homes and families in the neighbourhood.

We have no information about the occurrence of e.m.f. in the Ruanda-Urundi country, and none from hospitals in the outlying districts of Uganda. We can be fairly sure on clinical grounds that cases are seen at Jinja and Masaka, 50 miles east and 80 miles west of Kampala respectively, but so far postmortem material has not been obtained in Uganda outside Kampala.

Sudan, East and South Africa

To the north, we have no information from the Southern Sudan, but we have learned (KIRK, 1954) that one or two cases confirmed at autopsy have occurred recently at Khartoum. To the immediate east and south of Uganda, no reports of e.m.f. have appeared from Kenya and Tanganyika. Lack of information from the large areas very poorly served medically is not surprising; but that this disease has not been observed in Nairobi, where a large general hospital and pathology department draw their patients and material from all over Kenya may be more significant. We have been unable to find any record of e.m.f. further south in Nyasaland. In Southern Rhodesia a number of cases have occurred at Salisbury (GELFAND, 1954). From discussion and correspondence with colleagues in Johannesburg (BECKER, 1954; HIGGINSON, 1954) we can be fairly certain that the advanced stage of e.m.f. is rarely seen, if it occurs at all there. A few of the cases which BECKER et al. (1953) describe as " cardiovascular collagenosis " have some resemblance to e.m.f., but the majority seem to show quite a different picture. Some of the cases of " nutritional heart disease " which occur in Johannesburg (GILLANDERS, 1951) and Cape Town (THOMSON, 1954) show a degree of endocardial fibrosis which is less than that seen in our cases and more clearly related to the overlying mural thrombosis.

West Africa

No reports are known to us of any cases resembling e.m.f. in Belgian Congo. There is more evidence from West Africa. Most of the patients of BEDFORD and KONSTAM (1946) were natives of this region, though they were not resident there at the time of diagnosis. The three cases reported by EDGE (1946) and GRAY (1951) in Europeans were all in patients with recent residence in West Africa, two of them resident several years in Nigeria, though

it is not certain that they contracted their disease there. Isolated cases have occurred in the Gold Coast (HUGHES, 1953) and in the Gambia (MCFADZEAN, 1952).

United States

Several cases are recorded in the American literature which appear from their descriptions to differ in no way from the e.m.f. which we see in Uganda. Among these are five cases described by SMITH and FURTH (1943); in these, endocardial fibrosis was generally greater in the left ventricle than the right, and was associated with mural thrombus and emboli. TORESON's (1944) patient was a poorly developed girl of 15, who had suffered for years from bronchiectasis; the myocardial changes were more acute than we usually see in our patients, but were concentrated in the inner third of the heart wall and associated with diffuse endocardial thickening. DAMMIN and his colleagues (1951) refer in a brief report to a syndrome of heart enlargement with intractable congestive failure in the absence of a recognized cause, in which they include by implication those of SMITH and FURTH, and of DAVIES (1948a) together with 14 cases of their own. Sub-endocardial and myocardial fibrosis are mentioned in connection with the latter, of which nine came to autopsy; but without further details it is not possible to pursue a comparison with e.m.f.

In the case described by FIENBERG and HOLZMAN (1951) the endocardial fibrosis was extensive in both ventricles, with obliterative changes in the right, and involved both mitral and tricuspid valves. MCKUSICK and COCHRAN (1952) employ the term " constrictive endocarditis " in describing a case with endocardial fibrosis of both ventricles involving the papillary muscles but sparing the valve cusps. These latter two descriptions in particular tally very closely with what we see at Kampala.

There are other reports in which there are points of close resemblance to the condition under discussion, but which differ in important respects such as the extent of myocardial fibrosis or the presence of coronary disease; or which we cannot include for lack of corroborative detail.

United Kingdom

Three British cases have already been quoted in connection with the subjects' residence in West Africa. LENNOX (1948) described what he believed to be the earliest stage of Löffler's parietal endocarditis (see later) with only histological changes in a macroscopically normal endocardium, in a woman who died in status asthmaticus. In a case recently reported by HUGHES and SMITH (1953) there was extensive endocardial fibrosis associated with heparin resistance; but there was myocardial infarction due to coronary disease in this case.

Continent of Europe

It is from the Continent that the largest number of reports closely resembling endomyocardial fibrosis has come. Under the descriptive name " endocarditis parietalis fibroplastica," two cases are described by LÖFFLER (1936), and one case each by MUMME (1940), ROULET (1944), and BERBLINGER (1948). EGGER (1944) describes a similar case with obliterative changes in the right ventricle as " endocarditis obliterans." A possible earlier example with much sub-endocardial infiltration without fibrosis, is described by BÜCHLER (1941-42). These seven cases are reported from Switzerland. FOSSEL (1942) describes two cases of chronic parietal endocarditis from Vienna, and LANDAU and others (1927) record two cases from Paris.

The Far East and the Pacific

It would be particularly valuable to know whether e.m.f. occurs anywhere in these vast regions. We have no information of any reports from Asia.

In the United States literature already quoted, one report (FIENBERG and HOLZMAN, 1951) concerns a soldier who had served in the Solomon Islands a year or two before developing heart failure from e.m.f. of obliterative type.

PATHOGENESIS AND AETIOLOGY

The fibrosis and deformities in e.m.f. seem to be the end-results of a process of whose cause and development we are largely ignorant. Until we can see and study its mode of onset, it is unlikely that we shall be able to establish what are the aetiological factors. Meanwhile, until we are in a position to recognize the disease in its earliest stages, there is a place for speculation.

It is well to consider first whether, in e.m.f., we are dealing with a pathological entity or with an end-result common to several different causes. It cannot be assumed that all the examples of parietal endocardial fibrosis or obliterative endocarditis recorded in the literature, or even all our own cases, have the same pathology. There is more than one way in which endocardial fibrosis and thrombosis could be produced, and clues which may seem to point toward different origins need not necessarily be exclusive. On the other hand, it is difficult to believe that the relatively common occurrence in at least one part of Africa of a strikingly consistent heart lesion, so rarely encountered in the northern hemisphere, does not point to some special aetiological factor or combination of factors operating here.

What are the factors which initiate the fibrosis in e.m.f.? The observed frequency of parietal (non-valvular) endocardial thrombus in these hearts is a striking feature. Is e.m.f. always accompanied by parietal thrombus at some stage ?

A short-acting agent injuring the parietal endocardium could initiate formation of diffuse or local fibrin thrombus, leading to organization and subsequent fibrosis. This would become sub-endocardial, by the extension of new endothelium over the organizing thrombus, as has been shown by DUGUID (1952) to occur in the walls of atheromatous vessels, and by MAGAREY (1951) upon the mitral cusps and chordae in rheumatic carditis. Upon such a surface, especially between trabeculae and behind cusps, a vicious cycle of thrombosis→ fibrosis→ thrombosis could well take place. This is the basis upon which LENNOX (1948) includes his case, assuming endocardial injury initially by an allergen. In this connection we thought it worth while to follow up the observation by HUGHES and SMITH (1953) of heparin resistance in a patient with coronary disease in whom severe endocardial fibrosis was found postmortem; but in four of our patients the coagulation time was normally prolonged after heparin. There is undoubtedly strong evidence from study of the histology and gross anatomy that some of the thick fibrous plaques, especially at the right ventricular apex in the obliterative type, and in the left ventricle behind the posterior mitral cusp, represent organized thrombus.

On the other hand there is the evidence of inner-layer muscle injury. Degeneration and necrosis of muscle fibres may be seen, and extensive fibrosis is common, affecting chiefly the sub-endocardial muscle, sparing almost entirely the outer layers. A toxin injurious to cardiac muscle or a sustained hypoxia or depletion of some nutrient essential for this tissue would exert its most harmful effect upon the inner layers of the myocardium, where tension within the muscle during systole, and the ischaemic effect of this, are greatest. This greater

susceptibility of the inner layer of muscle to chemical injury is the basis of the negative ST deviation in the cardiogram, characteristic of digitalis poisoning and of the muscle hypoxia of severe anaemia and diffuse coronary insufficiency (HOLZMAN, 1952). We have not obtained electrocardiographic evidence of such injury in our patients—this would not be expected in the later stages for reasons discussed elsewhere (BALL et al., 1954). But the extent of fibrosis in the inner one-third of the heart wall in some subjects of e.m.f. might be taken to support such a mode of pathogenesis. If this were the site of the initial lesion, a reaction in the overlying connective tissue and endothelium sufficient to promote mural thrombus might be expected. Replacement fibrosis in the inner layer of muscle, as well as the organization of endocardial thrombus, would thus both contribute to the familiar end-picture of endomyocardial fibrosis.

These two possibilities are not mutually exclusive. Sub-endocardial muscle injury could lead to endocardial thrombosis-fibrosis. So also might the latter, by obstruction of arterio-luminal and Thebesian collaterals from the cavity, impede the circulation in the sub-endocardial muscle and impair its nutrition. Such a sequence is considered by GRAY (1951) and by SMITH and FURTH (1943) in connection with the cases they report, and is the mechanism by which heart failure is believed to intervene in congenital endocardial fibroelastosis (WEINBERG and HIMELFARB, 1943).

It would seem therefore that, with only the evidence of advanced disease to go on, the search for aetiological agents remains wide open. For either of the modes of injury we have discussed (affecting primarily either the endocardium or the muscle), would be capable of setting up a train of events resulting finally in gross fibrosis both of endocardium and sub-endocardial muscle, in association with parietal thrombus.

With these general considerations in mind, there are a number of agents which deserve attention. Among those that have been discussed in the literature are infection, allergy, malnutrition and toxic agents.

Infection

GRAY (1951) after considering all these, suggested that the cause might lie in an unrecognized parasitic, bacterial, or virus agent, and that only from study in Africa of cases in the early stages was the causative organism likely to be identified. While we have no evidence pointing to an infective origin, the existence of viruses capable of causing myocardial injury is now proved, notably the virus of encephalomyocarditis, first isolated in 1944 and 1945 in Florida from captive chimpanzees and gibbons which had died suddenly (HELWIG and SCHMIDT, 1945; SCHMIDT, 1948). In experimental animal infections with EMC virus, lesions were almost confined to the central nervous system and the heart. Diffuse interstitial myocarditis was observed, with foci of necrosis and infiltration, proceeding to fibrous replacement and even calcification in those recovered from paralysis. There was no localization of the lesion in the sub-endocardium. Sera obtained from soldiers recovered from a mild 3-day fever in Manila during 1945-46 contained neutralizing antibody against EMC virus (SMADEL and WARREN, 1947). No cardiac signs and no sequelae were observed in the human cases. In Europe, epidemic myocarditis in infants in the Munich area has been ascribed by STOEBER (1952) to virus infection. It is now known that Mengo encephalomyelitis virus isolated by DICK and others (1948) in the Mengo district of Uganda is closely related to EMC virus (WARREN et al., 1949). Sera from our patients are being examined at the Virus Research Institute, Entebbe, but work on these lines has not proceeded far. PEARCE (1950) has reviewed evidence showing that the ability to produce lesions in the rabbit heart is a property of several viruses, and that an important experimental factor in inducing cardiac localization of virus is a decrease in the amount of oxygen supplied to the heart (PEARCE and LANGE, 1947). Under the conditions of the experiments, the endocardium was more often affected than the pericardium, and the muscle more frequently than either; and in the case of the left ventricle, especially the inner part of the muscle and the large papillary muscles.

Thus although we have no positive evidence as yet to incriminate a virus infection, and although the end picture of endomyocardial fibrosis does not at first sight suggest such an aetiology, it is evident that the possibility of virus infection (by itself or with some other contributing factor) initiating a fibrosis-thrombosis or thrombosis-fibrosis cycle involving the inner layers of the heart wall cannot be dismissed. If such a possibility is to be entertained, the search for the early lesion may have to be made among the minor pyrexial illnesses of obscure aetiology, rather than among persons with manifest heart lesions.

Allergy

The papers of LÖFFLER, MUMME and ROULET, from Switzerland, all describing advanced chronic " endocarditis parietalis fibroplastica " such as we see in Uganda, emphasized the common finding of a high eosinophilia; in the similar cases of EGGER and BERBLINGER eosinophilia was also observed, though to a less striking degree. In a case reported by BÜCHLER, in which the cardiac lesions at autopsy were more acute, eosinophilia, associated with splenomegaly and repeated attacks of a severe urticarial eruption, had been consistently high for a period of 6 years until heart failure developed rapidly a few weeks before death. In all these reports (totalling seven cases) an allergic origin for the endocardial lesion was assumed, supported by the eosinophilia and by the clinical evidence of extra-cardiac allergic features in several cases. We have already referred to the report by LENNOX (1948) of a woman who died of status asthmaticus, in whom the endocardium of the left ventricle showed extensive cellular infiltration, with fibrin on the surface of some lesions, but without extensive thrombosis. These changes were best seen in the depth of the crypts between the columnae carneae, sparing the valves. He suggested that mural thrombus on the basis of such lesions, followed by organization, would produce the end-result of Löffler's "endocarditis parietalis fibroplastica"; and that his case represented the earliest stage of this process.

In all the three British cases to which we have referred (EDGE, 1946; Gray, 1951), eosinophilia was recorded. All three patients had lived in West Africa and in two of them infestation by *Loa loa* (which does not occur in Uganda) had been present. The third case was ascribed by the author to arsphenamine sensitivity, but the grounds for this are not altogether convincing. Eosinophilic myocarditis in association with undoubted arsenical dermatitis has been described (BROWN and MACNAMARA, 1940), but this was a massive cellular infiltration throughout the myocardium, rapidly fatal.

An obvious difficulty in following up this approach is the much commoner finding of eosinophilia, attributable to a number of causes, in the tropics. So far eosinophilia has not been a pronounced feature in our cases; it has been present in some, absent in others, but has not been looked for consistently. However, its absence in the later stages of e.m.f. does not exclude an eosinophilic reaction as having been present at the beginning. Eosinophilia was not recorded in the cases of SMITH and FURTH nor of TORESON. In FIENBERG

and HOLZMAN's case one differential count of 35 per cent. eosinophils was recorded among other counts without eosinophilia. McKUSICK and COCHRAN do not mention it.

Rheumatic heart disease and Cardio-vascular collagenosis

In some ways advanced e.m.f. is strikingly similar to chronic rheumatic carditis. In some cases of rheumatic mitral disease the chordae and papillary muscles are affected very much as in e.m.f., and we have seen two cases of e.m.f. in which mitral stenosis has occurred. In general, however, the distribution and end-results of the fibrosis are different in the two diseases, involving in e.m.f. the apex and walls of the ventricle rather than the cusps, and causing incompetence rather than stenosis. When the mitral valve is involved, it is by adherence of the chordae and the ventricular surface of the cusp to the ventricle—not by inflammation at the free margins and auricular surface of the cusps and their fusion at the commissures. It is in the relentless progress of the deformity, continuing in the rheumatic heart long after episodes of acute carditis have ceased, that the resemblance between e.m.f. and rheumatism lies, rather than in its location and effects. In his studies of the mitral valve, MAGAREY (1949; 1951) ascribes this process to continuing fibrin deposition and organization, a mechanism which we have suggested is also concerned in the production of endocardial fibrosis in e.m.f. It is not possible, for want of material, to compare an earlier stage of e.m.f. with acute rheumatism.

The conception of " cardiovascular collagenosis " advanced by BECKER and others (1953) may have some bearing on our problem. Mural thrombosis in the heart was the finding on which they based their study, and it is not surprising therefore, that some of the cases they included resembled e.m.f. The process as they describe it is primarily a collagen disorder, with endocardial thrombosis as a secondary feature. The implications of BECKER's work are discussed elsewhere (DAVIES and BALL, to be published).

Toxin or Depletion

Several authors (GRAY; SMITH and FURTH; BECKER et al.) have considered the possibility of a chemical injury of the myocardium, by toxin or deprivation, and we have mentioned the anatomical factors of blood supply which might determine that the brunt of such damage fell upon the sub-endocardial layer of muscle.

As already indicated a large proportion of our patients are poor, and it is not unlikely that some of them have spent long periods in a state of suboptimal nutrition, particularly as to first class protein. GILLANDERS (1951) and HIGGINSON and others (1952), working in South Africa, have ascribed obscure heart enlargement and failure in some of their African patients to malnutrition, and in some cases were able to reverse the failure by improvement in the diet. No specific nutrient was incriminated, but the suggestion of a protein deficiency was made, and a constant association with hepatic cirrhosis noted; it was suggested that the nutrition of the heart muscle may be dependent in a special degree upon healthy liver function. Chronic liver disease has been present in some of our patients, and the serum albumin is sometimes low, but neither of these is a constant finding in e.m.f. Malnutrition was not a feature in the patients of GRAY or EDGE from West Africa; there was, however, evidence of malnutrition in the histories of some of the cases reported from the U.S.A. (SMITH and FURTH, 1943). The description by BRINKMAN and PRIOR (1950) of " chronic beri-beri heart " in a New Zealander closely resembles endomyocardial fibrosis. This patient developed dyspnoea after 4 years' privation as a prisoner of war in Italy and Germany.

Vitamin B deficiency is considered in several accounts of e.m.f., only to be dismissed. There is nothing similar in the pathology of the two conditions. In Uganda clinical manifestations of thiamine deficiency are exceptionally rare.

It has been shown by FOLLIS and others (1942) that in animals kept on a potassium deficient diet for 8 days or longer there occurred necrosis of muscle fibres in the myocardium, followed by infiltration with leucocytes and healing with proliferation of connective tissue. This did not occur in control animals with adequate potassium. Necrosis in cardiac muscle has also been observed in rabbits on vitamin E deficient diets (BRAGDON and LEVINE, 1949). In cattle kept on E-deficient rations, GULLICKSON and CALVERLEY (1946) reported cardiographic evidence of progressive impairment of myocardial function, and atrophy and scarring of muscle; more recently these observations have been extended in lambs (BACIGALUPO and others, 1953). In both these deficiencies other tissues, notably skeletal muscle, are known to be injured, and in neither is there a sub-endocardial localization. It is difficult to believe that either could of itself lead to e.m.f. We have no clinical evidence of vitamin E deficiency in this country. Short periods of potassium lack, due to dysentery, tissue trauma, etc., have no doubt been experienced by some of our patients, but this is not a risk peculiar to this part of the world. Without far more detailed medical histories than we have been able to obtain from any of our patients, we can do no more than detail these possible nutritional factors.

One form of depletion which is common among the poorer folk everywhere in the tropics is anaemia, often of a severity seldom matched in temperate climates today. Undoubtedly the heart muscle, among other tissues, is adversely affected by the sustained hypoxia, and the electrocardiogram suggests that it is inner layer muscle that suffers most. We have not found anaemia in e.m.f. more frequent or more severe than in patients otherwise affected, but here again we are hampered by the lack of reliable medical histories, and we cannot exclude past anaemia as a factor in the early stage of the disease. The pathology of severe Addisonian anaemia, however, gives no grounds for supposing that any permanent change results from prolonged hypoxia, given recovery to a reasonable haemoglobin level.

Intravenous drugs of a variety and toxicity hardly known in temperate climates have been in common use in tropical Africa for many years. If any such substance in sufficient concentration were capable of damaging the endocardium, the right heart would be most liable to initial injury by the intravenous route. If myocardium rather than endocardium were susceptible, the injury would be diffuse in either or both ventricles, though liable to affect most severely fibres in the inner layer of muscle. The medical histories of our patients, however, as far as they go, contain nothing distinctive or consistent with regard to intravenous medication or other chemotherapy.

DISCUSSION

It seems hardly probable that this comparatively high incidence of e.m.f. is peculiar to one small area in the middle of Africa. The evidence for its occurrence in other parts of the continent is as yet meagre, but there is little doubt that at Kampala it occurred and was overlooked until a few years ago. With the increase in hospital beds there has been a steady rise in the number of autopsies performed by the pathology staff at Mulago. Once the disease is recognized, familiarity sharpens observation, and examples of e.m.f. have turned up with increasing frequency. Thus the paucity of records from other parts of the

continent (where so often autopsy study is nearly impossible) should occasion no surprise, and should not be accepted too readily as indicating its absence.

Advance in our knowledge of this disease may be expected from two directions, study of its distribution and of the early lesion.

We need much more information about distribution—geographical, climatic, racial, and in relation to hazards of malnutrition, occupation and exposure to infection. As such knowledge accumulates, the field of speculation as regards aetiology will be narrowed progressively, by exclusion. The characteristic appearances of the lesion of established e.m.f. and the clinical manifestations we have described will suffice for mapping distribution in this way. To study the early lesion is a different matter. It is very probable that e.m.f. is never fatal at this stage. It is likely that the earliest changes are not macroscopically very obvious. Thus the discovery of very early cases at autopsy will be fortuitous, and until we can determine what clinical manifestations (cardiac or other), if any, they produce, the accumulation of material which will throw light on the onset of this disease is likely to be a slow process. Nor must we forget that whatever may be true of gross endomyocardial fibrosis sufficient to cause heart failure, there is nothing specific about minor degrees of endocardial fibrosis or of parietal thrombus; and to distinguish between what is, and what is not, the precursor of e.m.f. proper will present a considerable problem.

Summary

(1) The pathological and clinical features of endomyocardial fibrosis (e.m.f.) are briefly described, and differential diagnosis is discussed.

(2) Attention is drawn to the comparatively high incidence of this disease among Africans at Kampala. Its incidence in other parts of Africa, and its world distribution, are discussed on the basis of reports of similar cases in the literature and information from other sources.

(3) The cause is not known, nor are the pathology nor the clinical manifestations of the earliest lesion. Possible modes of pathogenesis are discussed and possible aetiological factors considered.

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DISCUSSION

Dr. D. Evan Bedford : Dr. BALL has described a form of heart disease which is prevalent in Uganda and the basis of which is an extensive sub-endocardial fibrosis often complicated by mural thrombosis in the ventricles. The coronary vessels are intact but the valves may be secondarily involved in the fibrosis. This disease is very similar to that described by KONSTAM and myself (1946) in West and East African troops, in the Middle East, and is probably allied to that described by GILLANDERS in South Africa.

A rather similar form of heart disease has long been recognized as occurring in Europe and America, though it is extremely rare in comparison with Africa. In 1901, JOSSERAND and GALLAVARDIN of Lyons described a condition of rapidly progressive heart failure in young subjects due to primitive subacute myocarditis. The valves and coronary vessels were intact, but there was extensive myocardial fibrosis, mainly of the endocardial aspect, and thrombus formation in the ventricles. Later GALLAVARDIN and GRAVIER (1928) attributed the condition to tuberculosis. They did not find any specific tuberculous lesions in the heart, but regarded the fibrosis as due to the toxic effect of tuberculous lesions in the mediastinal glands or the lungs.

This view has recently been revived, or at least reviewed, by PERRIN, FROMENT and LENÈGRE (1953) who found tuberculous lesions of the lungs or mediastinum in six of 30 collected cases. LENÈGRE and GERBAUX (1952) have also described endocardial fibrosis with intraventricular thrombus formation in association with massive thrombosis of the pulmonary artery or its main branches and cardiac enlargement.

In America endocardial fibrosis in young subjects has been described under such titles as isolated myocarditis, idiopathic myocarditis, cardiac hypertrophy of unknown origin in young subjects, parietal endocardial sclerosis, etc., and the subject is well reviewed by SMITH and FURTH (1943). Mural thrombosis is common in these cases.

Another rather similar form of heart failure associated with myocardial fibrosis and mural thrombosis has been described as occurring in pregnancy and the puerperium (GOULEY, MCMILLAN and BELLET, 1937).

Cardiac enlargement and myocardial fibrosis associated with hypoplasia of the aorta is another rare cause of unexplained heart failure in young adults and I mention it especially because aortic hypoplasia was present in many of our African cases of endomyocardial fibrosis, and, indeed, it is extremely common in Africans quite apart from heart failure. Cardiac enlargement and failure associated with aortic hypoplasia was described long ago in Germany (FRAENTZEL, 1889; APELT, 1905) and more recently by DELCOURT, DENOLIN and LEQUIME (1948). It is discussed by Maude ABBOTT (1927), and by CABOT (1926) as a cause of cardiac hypertrophy. Hypoplasia of the aorta has also been regarded as due to endocrine disorders and as associated with status thymolymphaticus and sudden death (COOKE and CLOAKE, 1943).

During the recent war, I encountered many cases of unexplained heart failure mainly in West African troops in the Middle East, and KONSTAM and I (1946) described briefly the clinical finding in 40 cases, in 17 of which a postmortem was obtained.

The main clinical features were the rapid onset of congestive heart failure, often starting as left heart failure and pulmonary oedema, and quickly progressing to right heart failure with swollen liver and dropsy. The heart was grossly enlarged, sometimes simulating a pericardial effusion, and on radioscopy pulsation was diminished. The rhythm remained normal, apart from extrasystoles, and fibrillation was not observed. There was a gallop rhythm, a very small pulse, and usually pulsus alternans. The blood-pressure was low.

Radiographs showed an extremely small aorta in many cases, and in several this was confirmed at necropsy. These patients often responded moderately to treatment with digitalis and mercurial diuretics, and the heart became smaller, but they never recovered completely and failure recurred if they left hospital. In all cases the coronaries were intact and the valves were normal except in two cases with old rheumatic valve lesions. We found no evidence of malnutrition, avitaminosis, or polyneuritis in our patients, and their diet was not only adequate but was far better than that which they were accustomed to before they joined the forces. There was no response to vitamin B therapy, nor to diet.

Pathologically, there was gross dilatation with some hypertrophy of the heart; the left ventricle was both hypertrophied and dilated, and the right dilated without much hypertrophy. In some cases there was extensive endocardial fibrosis, often with mural thrombosis which was partly organized. Microscopically, there was sub-endocardial necrosis and fibrosis but little inflammatory reaction.

All our patients had served for some time before their heart failure appeared, all were well fed, and investigation in hospital failed to show any cause for the cardiac enlargement. While sporadic cases of very similar endomyocardial fibrosis had long been described, here for the first time the condition was encountered in a whole series of Africans by the same observers, and a sufficient number of cases was investigated to identify this form of heart disease as a clinical and pathological entity in Africa.

Shortly afterwards, DAVIES published an account of this form of heart disease in Uganda and named it endomyocardial fibrosis. GILLANDERS (1951) has described a form of nutritional heart disease occurring in Bantu which presents clinical features very similar to those of endomyocardial fibrosis, but with little or no myocardial fibrosis at necropsy. In a later paper, some degree of fibrosis and mural thrombosis was reported in these Bantu cases, which I believe are related to the heart disease described by DAVIES and BALL, and by KONSTAM and myself. In many ways our cases are intermediate between those occurring in Uganda and those in South Africa, but in the latter there was cirrhosis of the liver of nutritional origin.

When we come to consider the aetiology, there is much to be said in favour of a nutritional origin. Nutritional disease (kwashiorkor) is prevalent in Uganda, and in the Bantu cirrhosis of the liver was found. It is a fair assumption that our patients had suffered from malnutrition in the past. DAVIES (1948) states that every African goes through a kwashiorkor phase in childhood but that the body adjusts itself biochemically as the process continues.

In our cases there was certainly no immediate relation between malnutrition and heart failure, but if there had been malnutrition in childhood, heart failure might still be an end-result. In this respect, the aortic hypoplasia is significant. Why is the African aorta so small ? Surely it has never developed during the growth period, when malnutrition and presumably low blood-pressure were present. It may be that the myocardium, like the aorta, develops defectively and that it gives way under strain in later life. In our cases Army life certainly represented unaccustomed physical strain and might have caused dilatation of a defective heart muscle.

I do not believe that, in our cases, there was usually sufficient fibrosis to explain cardiac dilatation and failure and, indeed, the reverse may be true. Dilatation of the ventricles, by stretching the myocardium, may injure it and fibrosis may be the consequence of this on the lines of Eyster's " injury theory " of cardiac hypertrophy.

One serious objection to the nutritional theory is the undoubted occurrence of endomyocardial fibrosis with heart failure in Europeans who have lived in West Africa and in whom previous malnutrition is unlikely. Before the war, I had seen a few cases of unexplained failure in Europeans returning from Africa, and GRAY (1951) has described the postmortem findings in two such cases, one of which I saw during life and diagnosed as endomyocardial fibrosis on clinical grounds. While I think that the evidence in favour of a nutritional origin of this disease is strong, I do not regard it yet as conclusive, and further investigation in Africa is required to settle the problem.

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Dr. A. J. Hawe : In Accra some varieties of cardiac disease are easily recognized. Those most commonly seen are aortic incompetence, aneurism of aortic arch or innominate vessel and hypertensive failure. Acute infective endocarditis and tuberculous pericarditis are less common conditions. But rheumatic heart disease, as judged by the rarity of mitral stenosis is a rare condition. So also is coronary occlusion. Apart from states such as congenital heart disease, which does not appear to occur with the same frequency in Africans as in Europeans, there remain two groups where the aetiology has not yet been satisfactorily explained.

In the first of these groups patients are seen with recurring attacks of congestive failure. Young and middle-aged adults of both sexes are especially affected. There is evidence of mitral incompetence and a marked tendency to alternation. Enlargement of the liver with ascites and oedema is the rule. These patients are assisted by rest in bed, digitalis preparations, and mercurial diuretics. They do not succumb in hospital and the chance of postmortem examination has been rare. Electrocardiography shows low voltage curves. There is little evidence that these patients are suffering from malnutrition since they are commonly seen in a class where this is unlikely. There is no evidence that their clinical state is relieved by diet or thiamin. Neuritis is not a feature.

The second group of cardiac failures is frequent in children of both sexes between the ages of 5 and 15 years. These present themselves with gross ascites and enlarged livers which frequently extend a hand's breadth below the costal margin. There is jugular engorgement and periods of distress occur. Examination reveals an area of increased cardiac dullness, and X-ray examination shows the picture of an effusion. In those cases where paracentesis has been performed the fluid was straw-coloured and contained lymphocytes. No tubercle bacilli have been found and animal inoculation has proved negative. The majority give normal retention figures after the injection of bromsulphthalien. A distinguishing feature is the long duration of the illness; some of the cases have been observed over periods of 4 to 6 years. During the intervals of remission, these young patients experience remarkably little distress.

Following a personal visit by Professor DAVIES to West Africa some years ago, we had high hopes that these problem heart conditions would prove to be cases of sub-endocardial fibrosis. So far, however, the condition of sub-endocardial fibrosis has not been seen at autopsies done in Accra.

Dr. I. R. Gray : Endomyocardial fibrosis may be encountered in this country. Three proved cases have been reported in Europeans who had spent many years in Nigeria. In addition I have come across one further case in a European who has so far survived the illness, and have seen another case in a Negro who died in this country, in which autopsy was not obtained. The fact that this condition occurs in Europeans in whom there is no history of malnutrition or alcoholism suggests that dietary deficiency is unlikely to be the cause. The high incidence in Africa as opposed to other parts of the World suggests an infective or parasitic origin. The resemblance of the pathological lesion to certain of the collagen diseases need only indicate that hypersensitivity to an antigen is part of the process.

I would like to draw attention to two other clinical features of the disease as encountered in my patients: A high eosinophilia was found in two of them. One of these presented with neurological signs which were found at autopsy to be due to multiple cerebral emboli. Cases of endomyocardial fibrosis are recorded in the literature as frequently showing peripheral emboli.

Dr. E. A. Beet : For the past 3 years I have been studying heart disease among Africans in Northern Nigeria. During this time I have collected notes on 255 patients, all of whom were admitted to hospital under my care.

The common causes of heart disease in Northern Nigeria are syphilitic aortitis, hypertension (the majority being of renal origin), rheumatic heart disease, and heart failure of obscure origin. Incidences are as follows,

Syphilitic aortitis	23 per cent.	
Hypertension	21 ,,	
Rheumatic heart disease	18 ,,	
Failure of obscure origin	10 ,,	(15 per cent. of patients in failure)

Having listened to Dr. BALL's interesting address, and having examined the fine specimens he has shown us tonight, I have little doubt that most, if not all, of the patients in the group of heart failure of obscure origin were in fact suffering from endomyocardial fibrosis.

Owing to the lack of laboratory facilities, and to the fact that most of my subjects were Hausa and Fulani, who are of the Muslim faith and therefore averse to postmortems, I have been unable to have an autopsy in all my fatal cases. However I have managed to perform postmortems myself on 46 of the 74 fatalities; among these I came across one definite case of e.m.f. involving the right ventricle. This autopsy incidence for e.m.f. is unquestionably too low as I was primarily interested in rheumatic heart disease and, therefore, the subjects

selected for autopsy were chosen from this view point and are not representative of the group as a whole. In addition I have little doubt that I missed cases of e.m.f. where the typical changes were less obvious.

From the point of view of diagnosis the position would appear to be a little different in Northern Nigeria from that in Uganda and Accra, owing to the greater incidence of rheumatic heart disease in Northern Nigeria. This condition is commonly encountered there as can be seen by the figures I have given. I have the impression that, although rheumatic heart disease may be uncommon along the coast in West Africa, it is frequently met with in the dryer, more open, savannah country of the hinterland. Owing to the frequency with which one meets mitral stenosis in Northern Nigeria, one is apt to classify cases of pure mitral regurgitation as being of rheumatic origin, whereas actually some may be due to e.m.f. After hearing Dr. BALL's able description of e.m.f. I think I have been guilty of this error; however the number of cases concerned would be too small to affect the figure I have given as the incidence for rheumatic heart disease to any appreciable extent.

I would like to ask Dr. BALL if any of his cases have presented with embolic phenomena, owing to the liability of thrombus formation on the plaques in the ventricles these should occur commonly. I have considered that cases of heart disease which present with emboli are probably due to bacterial endocarditis, perhaps this is incorrect.

I would also like to ask if he has any information on the incidence of keloid in his e.m.f. cases. It appears to me that the liability of the African to produce fibrous tissue in excess as a result of injury may be one of the reasons for the excessive fibrous tissue found in the endocardium in e.m.f. Perhaps this might be one of the reasons why e.m.f. is so much more uncommon in Europeans than in Africans, although it definitely does occur. Is it not possible that in the African, owing to this peculiarity of excessive fibrous tissue production, e.m.f. manifests itself so much more frequently as a result of the mechanical effects produced by the fibrous plaques, whereas, in those people who do not react in this way, the disease would be less obvious and less disabling ?

As an aid to diagnosis I think that the presence of a pronounced eosinophilia is suggestive. I have the impression that my patients with heart failure of obscure origin showed this more frequently than did those suffering from other diseases.

With regard to aetiology, I find it difficult to accept malnutrition as an important factor, at any rate at the time that the disease brings the patient to hospital; although it is possible that in early childhood, when kwashiorkor is so common, irreversible changes may take place which, in the course of time, produce the full blown picture of e.m.f. My patients with heart failure of obscure origin were not more malnourished than those suffering from other conditions; any improvement taking place while in hospital could be accounted for by bed rest and therapy directed against heart failure, rather than from an improved diet. From GILLANDER's account of his cases I am of the opinion that the condition I see in Nigeria differs from that which he describes.

Dr. Ball (in reply) : I was interested in Dr. HAWE's references to the electrocardiograms in his patients. We find a low voltage to be one of the commonest abnormalities in the E.C.G.'s of our patients with e.m.f. in Uganda. Auricular fibrillation on the other hand is rare; we have only seen it once in a proved case and once in a suspect.

Dr. HAWE referred to cases of hydropericardium. We also see this condition occasionally. One patient whom we were able to observe for some time had over two litres of clear, straw-coloured fluid in his pericardium; this was one of the results of his right heart failure which was caused by obliterative endocardial fibrosis of the right ventricle.

Questions were asked about the incidence of embolism. This seems to depend in some way on the race of the patient. In our African patients we do not see infarcts in spite of the high incidence of mural thrombus, unless the lesion becomes terminally infected by bacterial endocarditis. In the reports of patients in U.S.A. however, and in the European patients from West Africa, embolism has been a common finding.

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