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SOUTH AFRICAN ENDOMYOCARDIOPATHY AND ENDOMYOCARDIAL FIBROSIS: A CRITICAL REVIEW

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SUMMARY

A summary of the investigations made on South African endomyocardiopathy and Endomyocardial fibrosis is reported and a general survey of the literature of these cardiopathies is made. It is concluded that, considering the present data, these cardiopathies are two different diseases.

INTRODUCTION

Africa has been the source of many papers on exotic cardiopathies, cardiac aneurysms [4, 91, 112, 140], post-operative intra-cardiac thrombosis [106], filarial cardiopathy [113, 126] — but none have aroused more interest than the condition termed herein South African Endomyocardiopathy and Endomyocardial Fibrosis. In the last fifteen years many papers on these forms of heart disease have originated from Africa as well as case reports of similar perhaps identical conditions in other parts of the world. In 1960 Davies [48] reviewed these diseases and this work is written to bring the information up to date and in and attempt to understand the conditions which exist in the African and South American continents after a personal examination of material in several African centres.

With every disease there comes a time when careful reassessment is needed before progress can be expected and this is especially so in those morbid entities where the etiology, pathogenesis and geographic distribution are unknown and about which information may be difficult to obtain because it often appears in journals of limited circulation, terminology is confused or misleading, and case reports often contrive to confuse and not to clarify the situation. The nature of the entities described is often difficult to distinguish even by experts in this field. Williams [182] wrote in 1954: "... there is a curious tendency, all too evident in the literature and in discussion on this subject (Endomyocardial Fibrosis), to gather together uncritically into one group, and to quote as examples of a particular pathology, descriptions and case-reports which have nothing really in common, except their extreme obscurity...". Thirteen years later his words are as true as ever.

SOUTH AFRICAN ENDOMYOCARDIOPATHY

It was not without some hesitation that the term "South African Endomyocardiopathy" (SAEMC) [18] was chosen to describe the disease now to be discussed. A survey of the literature indicated that many synonyms have been used: Nutritional Heart Disease [77], Chronic Malnutrition Heart [89], Cardiovascular Collagenosis with Parietal Endocardial Thrombosis [20], Becker's Disease [48], Cryptogenic Heart Disease [90], Cryptogenic Heart Disease of the African [149], Primary Mural Endocardial Disease [33], Primary Myocardial Disease [115], Idiopathic Mural Endocardial Disease [18], Idiopathic Cardiac Hypertrophy [11, 26], Idiopathic Cardiomegaly [107], Heart Muscle Di-

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sease [59], Acute Reversible Heart Failure in Africans [85]. BECKER et al. [20] and CHATGIDAKIS & BARLOW [33] mentioned still more terms in their papers: Endocardial Fibrosis [45, 83], Endomyocardial Fibrosis [16], Diffuse Endomyocardial Sclerosis [111], Congenital Endocardial Fibro-elastosis [99], Adult Endocardial Fibro-elastosis [94], Chronic Fibroplastic Myocarditis [176], Constrictive Endocarditis [121], Parietal Endocarditis [105], Fibroplastic Parietal Endocarditis [109], Fibrosis of the Endocardium and Myocardium with Mural Thrombosis [161], Endocarditis Obliterans [60], Primary Subacute Myocarditis [175], Myocarditis Perniciosa [25] and some forms of the "Pregnancy Heart" [81, 122].

The great number of names listed above shows that there is still much to learn about SAEMC, and that this term may include diseases of widely differing etiology which are clinically and haemodynamically indistinguishable at present. Different names have been used in different publications by some Authors to describe the same disease. Care is necessary in naming these entities because the specific etiology is obscure and labels implying etiology are unsatisfactory, while names which are too broad in scope, e.g. cryptogenic heart disease, while perhaps in a sense correct are so indefinite and cover such a variety of lesions as to prove a barrier to further progress. Premature identification is as dangerous as undue separation. Cases accepted by one Author may be unacceptable to others. Just as etiology implying names are unsatisfactory, so are names which indicate pathogenesis where the pathogenetic mechanisms remains obscure.

The names listed above can be divided in four groups:

1) Endomyocardial Fibrosis and its synonyms (endocardial fibrosis, endomyocardial sclerosis). They were considered synonymous with SAEMC by Becker's group probably because they [18, 33] and other Authors [59] considered Endomyocardial Fibrosis the final stage of SAEMC; later, however, Becker himself [19] and other South African workers [28] considered both to be different diseases. This is the overwhelming opinion of those who work in Africa.

2) Fibroplastic Parietal Endocarditis and its synonyms (parietal endocarditis, endocarditis obliterans, myocarditis perniciosa). LÖFFLER [109] described two cases of "Endocarditis Parietalis Fibroplastica mit Bluteosinophilia" and since then other similar cases has been reported in the literature. WEISS-CARMINE [108] and BRINK & WEBER [29] published detailed reviews of this condition. Although cases have been published in Africa [18, 29, 179], BECKER [18] and BRINK & WEBER [29] thought that it would be better to regard it as a distinct desease although its cardiac manifestations are very similar to SAEMC.

3) Pregnancy or Peri-partum Cardiopathy. Since the paper of GOULEY et al. [81] in which seven cases were described further examples have been reported. MEADOWS [122] thought that its relationship to pregnancy was not fortuitous because it occurred in 1 of every 1,300 deliveries. BENCHIMOL et al. [23], from a study of 18 cases, concluded that Peri-partum Cardiopathy "is not a specific or characteristic clinical syndrome, but is rather the result of multiple factors leading to cardiac failure". They classified this cardiopathy in five groups according to the etiology: 1) Cases that are undoubtedly related to toxaemia of pregnancy; 2) Cases that are probably related to toxaemia of pregnancy; 3) Cases that are due to non-specific myocarditis; 4) Cases with pre-existing hypertensive heart disease and; 5) Specific myocarditis, difficult to identify clinically, and usually requiring pathological data for a correct diagnosis. Of these groups, only the third may be directly related to SAEMC. There are only 2 reported cases in this category and in both the diagnosis of malnutrition heart were suggested initially but was subsequently discarded at least as the sole causal factor. Peri-partum cardiopathy has been reported in South Africa by SEFTEL & SUSSER [150] and BECKER [18]. The last cited Author observed seven cases and from the morbid anatomical point of view they "could not be distinguished from similar cases not associated with pregnancy". To re-inforce the relationship between SAEMC and Peri-partum Cardiopathy it should be added that COSNETT [41] found SAEMC frequently in Zulu women of the child-bearing age which generally developed within six months of delivery. On the other hand because: 1) most cases of Peri-partum Cardiopathy recover completely [26, 122], whereas SAEMC seems to be a fatal disease, 2) SAEMC occurs in men and in women

and 3) because of the peculiar geographical incidence of SAEMC, the identity of these two cardiopathies is doubtful; however they may have a pathogenic relationship.

4) Others. The other synonyms are difficult to judge. Perhaps Congenital Endocardial Fibro-elastosis should be excluded. GOWING [82] in a survey of the literature reported 76 cases of Congenital Endocardial Fibro-elastosis showing that the age of death ranged from stillbirth to six and a half years and 80% of them died in the first year of life. Although this condition resembles Adult Fibro-elastosis it is generally agreed that the two conditions are not related [82, 168, 171]. KELLY & ANDERSEN [99] stated that Congenital Endocardial Fibro-elastosis is familial and possibly due to a metabolic defect leading to myocardial weakness with secondary endocardial changes. This entity has been reported in South Africa [11, 18] and it seems to occur with the same frequency as in other countries [18]. In SAEMC there is no evidence of a genetic transmission [89], its age incidence is different and it is considered a primary endocardial disease [18, 33]. Therefore it is probably preferable to consider SAEMC and Congenital Endocardial Fibro-elastosis as separate entities.

In this article the term SAEMC [18] is used because "endomyocardiopathy" allows many pathogenetic interpretations and there is no doubt that there are pathological changes both in the endocardium and myocardium. The prefix "South African" gives to the name a more concrete character appointing the geographic area from whence comes the bulk of informations about this disease. Therefore it seems that South African Endomyocardiopathy is non-comital regarding the pathogenetic interpretation and still indicates "a morbid entity" (despite the doubts of some workers even in South Africa [80, 104].

Geographical, Racial, Sex and Age Incidence

Reports of cases similar or identical to SAEMC have come from all over the world [15, 40, 54, 55, 60, 61, 67, 69, 80, 86, 107, 108, 115, 120, 146, 167] but the disease is more common in South Africa [8, 18, 77, 123, 148, 169, 179]. HIGGINSON et al. [90] in 537 cases of death from heart failure found 80 cases, and COSNETT [41] found 138 cases of SAEMC in 1,000 consecutive cases of "heart diseases in Africans", in South Africa.

All Authors agree that although it occurs in the Caucasian it is commoner in the African, particularly in the Bantu. From the work of SCHRIRE [148] and COSNETT [41] it seems that the higher incidence in the African is real and can not be explained by the differences of demographic incidence of the races. Cosnett stated that SAEMC is from 16 to 32 times more common in the Zulu than in Indians leaving in the same area.

There is no difference in sex incidence in BECKER'S [18] and LAUCKNER et al. [103] experiences but other workers state that the corrected sex ratio showed a male preponderance [90,123].

All ages are affected. The youngest patient was 15 months old [11] and the oldest 71 [18]. The great majority of the patients are found in the age group 30-50 years.

Etiology

The etiology of SAEMC in unknown. Many possible causes have been suggested, genetic or developmental [145], infective [67], chronic malnutrition [77, 89] and an auto-immune disease with the endocardium as the target organ [20].

EDINGTON & JACKSON [59] wrote that "glycogen storage disease, amyloidosis, thyroid disease, alcohol and the collagen diseases can be excluded as aetiological agents in Ibadan (Nigeria), nor is there evidence of a myocarditis of viral origin. Neither did coronary artery disease appear to be an aetiological agent. Rheumatic disease played no part in the pathological process". SAEMC is not related to bacterial endocarditis or the carcinoid syndrome. Chagasic cardiopathy can be excluded. It is also unlikely that Fiedler's or isolated myocarditis is related to SAEMC because the commonest pathological findings in Fiedler's myocarditis cellular infiltration, necrosis of the myocardium and fibrous scarring of the myocardium with little or no cellular infiltration, are not significant features in SAEMC [89].

Attempts to detect cardiac antibodies in the serum of patients with SAEMC have been unsuccessfull [123].

It is known that certain plants may cause both human and animal diseases. Leaves of plants from the genus Senecie used to brew "bush teas" produce hepatic veno-occlusive disease [92] and cases of this disease have been described in South Africa [165]. In the same region of Africa the *Pachystigma pygmaeum* (Rubiaceae family) is responsable for a heart disease in sheep called GOUSIEKTE [178]. CONNOR [39] called attention to the resemblance between the myocardial degeneration in Gousiekte and the myocitolysis in Endomyocardial Fibrosis. These facts may suggest the possibility that, somehow, plant toxins may cause SAEMC (or Endomyocardial Fibrosis) but, as yet, there is no clear evidence of this.

Malnutrition has been suggested as a possible cause of almost every obscure diseases occuring in Africa. It must be remembered that the "effect of undernutrition on cardiovascular function is surprisingly slight" [93]. Two dietary deficiences are known to have serious cardiovascular consequences, iron and thiamine. Iron deficency has not been reported in cases of SAEMC and it must be strongly stressed that this disease should not be confused with beri-beri heart disease. GILLANDERS [77], who used Nutritional Heart Disease to describe the features of SAEMC, stated that the disease which he described was not the same as the beri-beri heart disease reported by WENCKEBACH [181] and BRINKMAN & PRIOR [31]. At the recently convened Second Scientific Meeting of the Associations of Physicians of South Africa [123] the relationship between beri-beri and SAEMC was questioned and it was pointed out that, although beri-beri does occur in the Baragwanath Hospital (Johannesburg), it is much rarer than SAEMC. There are obvious clinical differences. Beri-beri patients have a hyperkinetic circulation, which the SAEMC cases do not, and the response to thiamine in beri-beri is dramatic whereas this vitamin does not improve patients with SAEMC. Whether malnutrition plays any complementary role in SAEMC is unknown.

A paper on the geographical distribution of SAEMC within Africa and in particular South Africa is still lacking. Epidemiological surveys are very difficult to organise in that continent but it would be a worthwhile project which might bring us nearer to understanding the etiology of SAEMC.

Clinical Aspects

The commonest initial manifestation is dyspnea, followed in the average case three weeks later by edema [20]. Paroxysmal nocturnal dyspnea is not common [77]. Hemoptysis and coughing may be the first signs but generally tend to occur later. Pyrexia is common and varies from an occasional spike of fever to more prolonged episodes which last from a few days to weeks.

Generalized cardiomegaly is a constant finding. Tachycardia from 100 to 150 was noted in 81% of cases reported by BECKER et al. [20]. Gallop rhythm is obten present and functional murmurs can be heard. Rarely diastolic and systolic murmurs suggesting organic valve disease may be found [101]. The circulation dynamically is hypokinetic or normokinetic [89, 123, 149] and there is no significant alteration of the systolic and diastolic pressures. A raised jugular venous pressure was present in 84%, a large liver in 60% and serous cavity effusions in 40% of the patients studied by BECKER et al [20]. Signs and symptoms of embolism or pulmonary infarction are common.

On radiological examination generalized enlargement of the cardiac silhouette is observed and the slight movement of the heart borders in some cases is a characteristic feature [20]. Slight enlargement of the main pulmonary artery segment is common [123]. GILLANDERS [77] reported congestive changes in the lung fields in 90% of his cases. Pleural effusions are very frequent.

The ECG pattern of SAEMC is not distinctive [18], although the electrocardiogram is abnormal in every case [26]. These findings must be interpreted with caution because by "western standards" the majority of healthy Africans have abnormal electrocardiograms [84]. The main differences found by GRUSIN [84] are two: 1) peculiarities in the S-T segment and T and P waves; 2) serial ECG tracings show several striking, unexplained modifications. In SAEMC chiefly the RS-T segments and T waves are altered. In the 17 patients observed by BECKER et al. [20] only one showed RS-T segment elevation in the standard leads, all others showed depression of RST or flat or inverted T waves. In their opinion subendocardial damage in some and digitalis administration in others may account for the

depression of RS-T segments. GILLANDERS [77], also pointed out how often successive SR-T and T wave changes occur. Inconsistent findings are ventricular extrasystoles, bigeminal rhythm, supraventricular tachycardia, block patterns and abnormalities of the P wave [20]. SCHAMROTH & BLUMSOHN [147] found significant left axis deviation in 46% of SAEMC and 23% had slight left axis deviation. These Authors observed that "in the absence of coronary heart disease and advanced hypertension the presence of left axis deviation is a pointer to a cardiomyopathy" and thus it may help in the differential diagnosis of SAEMC from pericardial effusion, myxedema, or mitral regurgitation.

BRINK & LEWIS [27] studied the coronary blood flow, energetics and myocardial metabolism of SAEMC. In contrast with the findings in idiopathic cardiomyopathy, alcoholic cardiopathy, hypertensive and valvular heart disease the oxygen extraction by heart muscle is not increased either at rest or during exercise. At rest, there is no evidence of anaerobic metabolism but exercise tends to produce this mechanism of energy supply. Myocardial performance is reduced and the efficiency ratios remain normal unless in cases with very bad prognosis. Apparently there is no uncoupling of oxidative phosphorylation to explain the metabolic upset of the heart.

The prognosis of SAEMC is bad. A minority of cases run a rapidly progressive course but the majority pursue a subacute, relapsing or chronic course [149]. The average duration of the disease is approximately six months and the extremes consist of cases of fulminating cardiac failure surviving for one to two days and chronic patients suffering from recurrent attacks who may survive for five years after the onset of the first symptoms [20, 26]. Finally it must be added that KEELEY [98] described a case of SAEMC who became clinically and radiologically normal and did not relapse at all during six years. KEELEY [98] observed that many cases who improve are discharged from hospital and are not followed up; he suggested that a revision of the prognosis of this disease must be done.

As can be deduced from its prognosis SAEMC has no adequate treatment. The patients may improve with digitalis and diuretics but they do relapse and deteriorate with very few exceptions. Steroids have been tried but without success [26, 123]. Anticoagulants may be helpful in preventing thrombosis [26]. GILLANDERS [77] in his publication states that of 30 patients 8 died, 9 made a complete recovery and 13 a partial one when adequately nourished. All these 22 patients were eventually discharged from the hospital. Only 12 of these surviving cases were followed up and all of them had relapsed or deteriorated. HIGGINSON et al. [89] stated that clinical recovery accrues from a good general diet but not from thiamin. They also observed that some patients who are apparently going well die suddenly and unexpectedly and that SAEMC has an inevitably fatal outcome.

Pathology

At post-mortem the main changes are found in the heart. A small excess (50-100 ml) of pale straw-colored fluid is common in the pericardial sac. The average weight of the heart is between 400 and 600 gm but hearts weighing more than 600 g are not uncommon. Dilatation is to be found in all hearts but there is a controversy about hypertrophy. HIGGINSON et al. [90] state that in all of their 80 cases the heart was hypertrophied whereas BECKER et al. [20] found that usually there was no hypertrophy. This discrepancy may be, perhaps only a matter of differing criteria for a diagnosis of hypertrophy since both groups agree on the weight of the hearts. So, it is possible that HIGGINSON et al. [90] use criteria based on the weight of the organ whereas Becker and his associates [20] use the thickness of the walls of the heart chambers for assessment. A slight preponderance of the hypertrophy and dilatation in the right side of the heart was observed by some Authors [90] and EDINGTON & JACKSON [59] stated that the muscle wall is especially thickened in the pulmonary outflow path.

In most hearts mural thrombi are present, and in some series they have been found in 100% of the cases [20]. They can be found in all chambers but less frequently in the right ventricle. They may either be recent superimposed on an apparently intact endocardium and myocardium, or they may be well organized thrombi forming a fibrous layer which sometimes extends into the myocardium [20]. In rare cases fibrosis of the

subendocardial region may resemble that seen in Endomyocardial Fibrosis. There is no significant change in the cardiac valves and coronary vessels.

Of the extracardiac findings edema, ascites, pleural effusions and chronic venous visceral congestion are prominent. Infarcts in organs other than the heart were registered by some Authors in 35% of the cases [90] and by others in 78% [20].

There is no agreement about the microscopical aspects of SAEMC. It is very difficult to explain this discrepance particularly as the different Authors consider that they are describing the same morbid condition [59, 162]. All that can be done is to give the various descriptions of the microscopical aspects of SAEMC.

HIGGINSON et al. [90] stated that the endocardium is usually normal. Sometimes mild nonspecific diffuse or focal thickening is observed and small foci of lymphocytes, macrophages and plasma cells are noted in the endocardium. The most significant endocardial lesions are noted in relation to thrombus formation. These thrombi are most frequent between the interstices of the trabeculae carnae and cases were observed where they arose or extended into the Thebesian veins. The thrombi showed all stages of development. Marked elastic tissue formation was not a feature. Calcification was not seen. In the myocardium, hypertrophy of muscle fibers, discrete edema and small foci of fibrous scarring which occasionally are associated with scanty lymphocytic infiltration may be seen. The papillary muscles and trabeculae carnae may be covered by organized thrombi and the muscle fibres are often degenerated, showing a "moth-eaten" appearance. Occasionally similar changes are noted in the absence of thrombi.

BECKER [18] wrote that the predominant histological features are to be found in the membrane propria of the mural endocardium and he summarized his findings in the acute cases (acute cardiac failure lasting from 1-2 days to 31 weeks) in the following way: a) acute serous (or mucinous) mural endocarditis (focal or diffuse) either virtually acellular or of all degrees leading up to an acute neutrophilic infiltration, b) fibrin deposits on the surface-focal or diffuse, c) haemorrhagic lesions, d) gradual infiltration and incorporation of fibrin in the endocardium and formation of fibrino-fibrous polypi on the surface of endocardium and in Thebesian veins, e) more extensive mural thrombi organized by granulation tissue, f) degenerative changes in the inner third of the myocardium underlying the acute mural endocarditis, g) vascular ectasia in the subendocardium and the inner myocardium, h) similar fibrin thrombi in lung vessels.

In the more chronic cases BECKER [18] describes fibrosis of the parietal endocardium and the immediately subjacent myocardium usually accompanied by elastic tissue hyperplasia. Interstitial fibrosis and edema of the myocardium were often marked, mainly in the inflow tract and the apex of the left ventricle. Presence of fibrino-fibrous polypi or cushions in the lumen of the Thebesian veins may be seen.

EDINGTON & JACKSON [59] were impressed by the degeneration of the myofibrils and therefore they called this morbid condition "heart muscle disease". They observed that this degeneration is diffuse but most prominent in the inner third of the myocardium. Areas of myocytolysis are common, especially in the papillary muscles and trabeculae carnae. There is no reactive exudation and the lesion progresses to a fibrous scar. Alterations of the endocardium were also observed but the Authors assign more importance to the myocardial changes. They stress that they have never seen areas of fibrinoid necrosis in the venous sinuses.

There are two main theories about the pathogenesis of SAEMC:

1) The basic lesion is myocardial [59, 90].
2) The disease is primary endocardial [18, 20, 33, 69, 120].

There is no doubt that there are pathological changes in both myocardium and endocardium. EDINGTON & JACKSON [59], in Ibadan (Nigeria), and HIGGINSON et al. [90], in South Africa, consider that the primary lesion is in the muscle and that the changes in the endocardium and subendocardium are secondary. EDINGTON & JACKSON [59] were, however, prepared to admit "that the histopathological changes in the myocardium could in many instances be explained by anoxia". Becker and his associates [18, 20, 33], think that

the disease begins with an acute serous or mucinous mural endocarditis which is either focal or diffuse. This may be virtually acellular or may show all changes up to an acute neutrophilic infiltration. Fibrin is deposited on, and incorporated into, the endocardium, and more extensive mural thrombus formation leads to secondary degenerative changes in the inner third of the myocardium.

The pathogenesis of SAEMC cannot be explained by a destruction of the intracardiac ganglion cells. Although the number of neurons is lower than in normal hearts, the difference is too slight and if it plays any role in the pathogenesis of the disease it is a secondary one [24].

Endomyocardial Fibrosis

Here again there are many synonyms — Endocardial Fibrosis [45, 83], Endomyocardial Sclerosis [111, 167], Endocardial Elastomyofibrosis[68] and Myocardial Fibrosis[100]. ABRAHAMS[3], an authority on EMF, gives a list of names similar to those given to South African Endomyocardiopathy. As the name Endomyocardial Fibrosis (EMF) [16, 52, 133, 183] is the most appropriate at present and it is universally used, it will be used in this discussion.

It is very difficult to say who "discovered" EMF. NEUWERCK [128] and JOSSERAND & GALLAVARDIN [97] described, in 1883 and 1901 respectively, diseases similar to EMF but their identity remains doubtful. In 1946, BEDFORD & KONSTAM [21] read a paper to the British Cardiac Society about "Heart Failure of Unknown Origin" in soldiers serving in West Africa (mostly Africans). It is not certain whether they were dealing with ane or several morbid conditions but possibly EMF was present among their patients. The first description of this cardiopathy as a "new disease" came from DAVIES [45], in 1948, and this pioneer contributed much to the understanding of this important African heart disease [45, 53].

Geographical, Racial, Sex and Age Distribution

EMF has been reported from Africa [16, 22, 38, 52, 56, 58, 74, 75, 87, 114, 125, 129, 130, 131, 138, 139, 142, 143, 144, 170, 174, 183], Asia [100, 102, 127, 152], Oceania [34, 67] and possibly [21, 166], and South America [12, 39, 64, 116]. PARRY [134, 135] in a very careful study of the geographical distribution of this disease concluded that "EMF is a cardiac disease which is limited to the hot and wet regions of the tropics". This is a very important statement and, although there may be some exceptions all recent epidemiological studies are in agreement. Case reports of EMF from outside "hot and wet areas" do exist [37, 38, 57, 63, 65, 66, 68, 76, 83, 95, 119, 120, 121, 141, 161, 168, 186]: not all cases reported in these papers were called EMF in the original communications but have subsequently been accepted by others as such. In reference to these cases the paper of COELHO & PIMENTEL [37] is particularly instructive. They published two cases of "Diffuse Endomyocardial Fibrosis". The first patient was a 21 years old white expatriate from the Congo. The Authors call attention to differences in these two cases and postulate the existence of two morphological types of EMF. If these descriptions are compared with the African ones, it becomes evident that the first case does not seem a typical one while the second conforms with a classical description of EMF. COELHO & PIMENTEL [37] accepted the possibility of an infectious etiology for the patient who came from the Congo. Some of these cases reported from regions outside the "hot and wet areas" of the world seems to be examples of familial cardiomegaly with a fibrotic reaction mainly in the myocardium [38, 63, 88]. The sole African paper reporting EMF in sibs — two brothers — admits that there is no evidence that this disease is hereditary [9]. Finally it must be remembered that any organ has limited possibilities of response to injuries of any nature and so cases may have similar morphological and clinical aspects but a different etiology. WILLIAMS et al. [183] wrote: "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".

EMF is not a disease restricted to Africans. Many examples occuring in Europeans who have lived in Africa have been reported [17, 37, 57, 70, 83] and publications from other continents (in "hot and wet" areas) reporting EMF in Caucasian and yellow races confirm this statement [12, 40, 64, 67, 102, 152]. O'BRIEN [131] reported 25 cases, many of whom were probably EMF, in Arabs living in the Sudan.

It seems unlikely that there is a significant racial incidence.

The disease affects both sexes equally and no age group is exempt. The youngest patient seen was 4 years old and the oldest over 70 years old [46] but EMF is commonest in the second and third decades with the highest incidence occurring in the second [134, 135].

It is not possible to estimate the general incidence. DAVIES [48] stated that EMF is the cause of death in 15% of the cases with cardiac failure in Mulago Hospital (Uganda) in the last fifteen years. LAUCKNER et al. [103] observed that EMF accounts for 1.6 per cent of admissions in the University College Hospital, Ibadan (Nigeria).

Etiology

Although the first extensive discussion on the etiology of EMF appeared in a paper by WILLIAMS et al. [183] in 1954, the disease is still shrouded in mystery [51, 62, 134, 135]. In 1955 DAVIES & BALL [52] wrote: "... virus infection, some antigen-antibody reactions, and malnutrition are possible etiological factors in the form of endocardial fibrosis common in Uganda". None of these have been confirmed.

WOODRUFF [185] observed that there are many diseases in the tropics characterized by marked fibrosis (EMF, cirrhosis of the liver, keloids, peptic ulcer with intense fibrosis, fibromata which appears to be much more common, organismal diseases with exuberant fibrosis such as juxta-articular nodes in yaws and subcutaneous nodules in onchocerciasis) and raised the question whether there is any link between these conditions. He discussed the possibility that malnutrition, reactivity to macro-molecules and reduced corticosteroide production are etiological factors. The role of these factors is still speculative.

SELYE [151] treated rats with steroids and sodium dihydrogen phosphate and produced myocardial necrosis localised predominantly in the subendocardial layers. He called it "electrolyte-steroid-cardiopathy-necrosis". Since then an electrolytesteroid factor is cited among the possible causes of EMF. It seems that up to the present this suggestion is nothing more than speculation. It must be added that DANTAS [44] published two cases in children of focal disseminated myocardial necrosis in the absence of vascular, inflammatory or toxic factors. He pointed out that the morphological findings were similar to those observed by Selye in experimental animals. Since from the same Department of Pathology cases of EMF have been published [12] which were not compared with Dantas'cases, this suggests that the resemblance between the disease called "infarctoid cardiopathy" by this Author and EMF is not striking.

ARNOTT [13] and CRAWFORD [42] suggested that 5-hydroxytryptamine might be responsable for the lesions of EMF in a similar way that the carcinoid tumor is said to produce endocardial changes. The staple diet of many Africans is banana and plantain (matoke) and these foods contain high levels of 5HT. Experimentally, lesions with certain similarities to EMF have been produced in guinea-pig hearts by mantaining the animals on plantain diet for several months [118]. There is controversy about the urinary excretion of 5-hydroxyindole-acetic-acid; some investigators did not find any abnormalities [136] but others found a lower excretion [132]. After banana meals high 5-HIAA values, comparable to the levels seen in carcinoid disease, have been found in both East-Africans [42] and West-Africans [71]. OJO & PARRATT [132] stated that apparently EMF occurs where there is a combination of malnutrition, parasitic infection and plantain ingestion. Furthermore CRAWFORD [43] supported this hypothesis with the observation that in the Mulago Hospital (Uganda) there is not one single case of EMF in members of the Luo tribe who because of a "tribal custom" do not eat bananas. In this article Crawford defends his point of view by pointing out that the three arguments against it: 1) that normal animal rapidly "detoxicates" serotonin; 2) that the anatomical lesions of carcinoid heart disease are different from those of EMF; and 3) that the microscopical aspects are not the same in these two morbid conditions, are not necessarily conclusive. The main problems of this hypothesis are that it does not explain the peculiar geographical distribution of EMF and not all patients with EMF are banana eaters. Recently, SHAPER [154] wrote that "... there is at present no convincing evidence that the serotonin content of the plan-

tain is a factor in the etiology of this condition".

It was suggested that EMF might be a new and different manifestation of a rheumatic process [1, 2, 158]. The studies of tribal distribution of EMF and rheumatic heart-disease and the degree of concurrence of these two conditions in autopsies make possible a relationship or association of some kind between EMF and RHD [153]. SHAPER [153] as a working hypothesis suggests that EMF represents another form of hypersensitivity response to infection with streptococci requiring a previous disturbed immunological state, perhaps caused by malarial infection. Van der GELD et al. [172] think that the high incidence of pericarditis and the immunological findings in cases of EMF "suggests a propensity to autoimmune reactivity".

An infectious agent has of course been suspected but up to the time of working no microorganisms have been demonstrated. DAVIES & COLES [53] suggest that viral myocarditis may be responsible for the destruction of endocardium which on healing produces the classical lesions of EMF. These Authors however acknowledge that the weakness of this theory is that in viral myocarditis the damage is widespread both in myocardium and endocardium thus producing lesions in areas of the heart not involved by EMF. Toxoplasma antibodies have been investigated and it seems that this parasite is not significant in the etiology of EMF [110]. Perhaps the most likely infectious agent is the microfilaria. There are many papers, mainly from French Authors on "cardiopathie filarienne" [10, 70, 75, 79, 113, 117, 126], and few doubt that microfilaria may cause a cardiac disease. Morphologically "cardiopathie filarienne" can be very similar to EMF although there are recognisable differences [75]. Typical cases of EMF were seen associated with filariasis [59, 70, 83, 113], and IVE & BROCKINGTON [96] clain that the incidence of filariasis in EMF approaches 100%. Parry wrote in this thesis [134]: "The inevitable conclusion from these patients is that there are moderately progressive or fulminant types of tropical EMF (if this is the correct diagnosis) which occur within months or years of probable filariasis". As cardiac lymphatic obstruction in dogs causes fibrosis of the endocardium [121] a parasitic lymphatic obstruction could be an explanation for EMF. MORENAS [126] and GERBAUX et al. [76] considered the possibility of an allergic mechanism caused by the micro-filaria which could act even in the absence of the parasite. There is therefore some evidence that micro-filaria is an etiological agent in EMF but this attractive hypothesis awaits verification. The absence of any evidence of the presence of microfilariae in the majority of hearts of patients with EMF and the lack of epidemiological evidences in Uganda [155] are serious obstacles to this theory.

The following quotation from PARRY [125] warrants serious consideration: "... any theory of the etiology must therefore embrace this geographical fact (the peculiar distribution of EMF preferential to "hot and wet areas"), in addition to embracing two very important clinical facts — the well documented occurrence of EMF in expatriates, and the undoubted acute initial illness and subsequent active disease".

Clinical Aspects

Since the classical paper on the clinical aspects of EMF by BALL et al. [16] many important observations have been made. Although only occasionally noted and recorded it seems that there is an initial phase with systemic symptoms, characterized by apathy, fever and loss of appetite and weight. This phase may last for a few days to three months before cardiac symptoms develop [134, 137]. NWOKOLO [129] observed that the earliest stage of EMF is elusive because it is subclinical. The first cardiac symptoms are those of acute carditis [130, 134, 137] presenting fever and tachycardia.

After the initial illness a small number of patients continue to have recurrent inflammatory episodes with pyrexia and symptoms and signs of myocarditis [130] which may lead to death after a steady downhill course over many months [3, 137]. In the majority of cases the inflammatory process subsides and the patients pass into a state of chronic illness with no signs of active disease [3].

There are three main types of established EMF [134, 137]: 1) EMF of the left ventricle; 2) EMF of the right ventricle; 3) Biventricular EMF.

The clinical features of left ventricular EMF have been described by ABRAHAMS [1, 2], ABRAHAMS & BRIGDEN [5] and PARRY [134, 135]. Pain in the chest, dyspnea, cough sometimes productive of blood-stained sputum and edema of the lower extremities are the prominent symptoms. The physical signs are those of mitral incompetence and pulmonary hypertension of varying degrees. Additional signs of acute carditis may be found [1].

Radiological studies [5, 35, 129] show a slight enlargement of the cardiac shadow, small aorta and prominent pulmonary segment. There are signs of pulmonary hypertension. The left atrium is enlarged but not to the extent seen in mitral disease.

The ECG pattern will be described later.

A fine paper about EMF of the right ventricle was published by ABRAHAMS [3]. Its main features are ascites generally without edema of the lower extremities, congestive hepatomegaly and a raised jugular pressure with a systolic wave. Atrial fibrillation occurs in about 50% of cases. Pericardial effusion may be found in many cases. Pansystolic murmur of tricuspid regurgitation is rare. Severe congestive heart failure is generally not present. With mild exercise the cardiac output rises significantly which might explain the absence of edema of the lower extremities. This later mentioned fact and the presence of ascites and high venous pressure led ABRAHAMS [3] to advance the following interesting explanation:

There is no congestive cardiac failure because the cardiac output is maintained by the very high venous pressure which forces blood through the heart. The increased intra-abdominal pressure, due to ascites, is responsible for "at least 30% of the total rise in central venous pressure and sometimes considerably more" [3]. Thus, the ascites is not a consequence of congestive heart failure but rather "a compensatory mechanism brought into play through the medium of "volume receptors" elsewhere in the body" [3]. In other words, EMF stimulates certain "volume receptors" which by a compensatory mechanism cause ascites, and the increased intra-abdominal pressure causes a substantial rise in central venous pressure which forces blood through the heart, thus, avoiding cardiac failure otherwise brought about by EMF.

The sustained high venous pressure has several consequences. In some chronic cases exophthalmos has been observed [134] and in others, arterial oxygen desaturation [7]. After careful studies in patients with arterial desaturation, ABRAHAMS & PARRY [7] suggested that shunting of venous blood from the azygos system to the pulmonary veins, caused by the extreme central venous pressure accounted for the arterial oxygen desaturation. This shunt may lead to mild cyanosis and clubbing of the fingers [3].

The presence of a pericardial effusion is readily confirmed by paracentesis. The fluid is frequently blood-stained and contains an excess of lymphocytes and protein [6]. Right ventricular EMF with pericardial effusion must be distinguished from cases of tuberculous pericarditis. "Important factors in the differential diagnosis are the presence of tricuspid incompetence with sistolic expansion of the neck veins, fibrillation, and the demonstration of cardiac enlargement, due to aneurysmal dilatation of the right atrium" [6].

Radiologically, in right-sided EMF, the heart is enlarged and globular. Frequently there is an aneurysmal dilatation of the right atrium [3]. An important radiological characteristic is pulmonary oligaemia [36]. Calcification within the cardiac shadow is an important finding [3, 164]. Tomography may be helpful for this purpose [164]. The localization of the calcified mass may be either within the area of the right ventricular apex [164] or in the fibrotic endocardium in the anterior part of the outflow tract of the right ventricle, just below the pulmonary valve [3].

Biventricular EMF. PARRY [134] divided this group of patients in two sub-divisions: 1) those with a large heart, and 2) those with a small heart. The first symptoms are generally dyspnea and coughing followed by ascites and edema. Signs of tricuspid regugitation of mitral incompetence or both are present. The main differences between Parry's two subgroups are less pronounced signs of atrio-ventricular incompetence, a quiet heart to precordial palpation and the absence of a loud pulmonary closure sound in the biventricular disease with small heart.

In biventricular EMF radiology is of little help, either showing a large heart or a normal to small one. The finding of a right-

side pleural effusion may be helpful because it is frequently seen in biventricular EMF with small heart [134].

Electrocardiogram in EMF. Many papers have described the ECG findings in EMF [3, 5, 16, 116, 160, 184]. Generally it can be said that the ECG pattern is not pathognomonic. In right ventricular disease atrial fibrillation is the commonest finding. Low voltage of the QRS complex and inverted T waves are frequent [3, 12, 134]. These findings together with abnormalities of the P wave are common in the later stages of this cardiopathy according to WILLIAMS & SOMERS [184].

Phonocardiograms have been done on 14 cases with EMF and mitral regurgitation by SOMERS & WILLIAMS [163]. Of these patients four also had tricuspid incompetence. The pansystolic murmur of atrioventricular regurgitation due to EMF is identical with that found in rheumatic heart disease. There is a difference in the ventricular filling sounds and both atrial and third sounds, which are constantly found, thus producing quadruple rhythm. The abnormal fourth sound is in some way related to the considerable atrial hypertrophy, particularly of the left atrial hypertrophy so frequently found in EMF [163].

Hemodynamic studies in EMF were made by several workers [2, 3, 6, 134, 160]. Generally there is no systemic hypertension. The pulse rate is usually elevated to 90 to 100 but the pulse wave is normal. The response of the pulse wave to the valsalva manoeuvre and to respiration is often abnormal [134].

The similarities of EMF to constrictive pericarditis have been emphasized many times [3, 12, 34, 64, 186], and hemodynamic studies support this impression [134, 160]. The venous and right atrial pressures were significantly raised in 13 of 15 patients studied by SHILLINGFORD & SOMERS [137]. The mean pressure ranged from 6 to 20 mmHg. The right atrial pressure falls after acute abdominal paracentesis [134], which supports the hypothesis of Abrahams explaining the role of ascites as a compensatory mechanism to avoid congestive heart failure. The right atrial pulse wave depends on the presence or absence of tricuspid regurgitation. When it is present, a systolic wave is dominant; in its absence the pulse is typical of that found in the constricted heart [134]. Catheterization of the right ventricle is difficult because of the problems of passing the catheter out of the enormously dilated atrium [3]. If the right ventricle is reached a "dip-and-plateau" type of tracing is a constant finding [3, 6, 34, 37, 76, 134, 160, 171], and it is typical of right ventricular EMF and of all other states in which the heart is constricted. The "plateau" frequently reaches 50% of the systolic peak [6]. The mean pressures recorded from the pulmonary artery and all parts of the right heart are virtually the same [6]. Right ventricular hypertension and increased pulmonary artery and pulmonary wedge pressures are present when the left ventricle is diseased [1, 134, 160]. The high pulmonary artery pressures are probably secondary to increased left atrial pressures [134]. Direct left atrial pulse has shown the characteristic wave of mitral regurgitation and the pressures in this chamber are elevated in left ventricular EMF [134]. ABRAHAMS [2] stated that EMF of the left ventricle can be distinguished from rheumatic mitral incompetence by the shape of the left ventricular pressure curve because there is a "dip-and-plateau" pattern in the former condition.

The cardiac output and stroke volume at rest is low because the cavity of the diseased ventricle is both small and constricted [3, 134] but as it has been stated before, in response to effort the cardiac output raises due to an increased cardiac rate.

The arterial blood is rarely fully saturated. The arterial oxygen saturation rises when acute abdominal paracentesis is performed [134]. The cause of the arterial desaturation is not understood. An azygos-pulmonary venous shunt has been suggested by ABRAHAMS & PARRY [7] but it could not be confirmed by injection techniques in cases of EMF coming to autopsy [134].

Although cardiac catheterization "probably does not contribute greatly to the diagnosis of EMF [160]" it may be helpful in establishing the anatomical diagnosis [134].

The angiocardiographic findings were described in detail by COCKSHOTT [36]. Deformities such as aneurysmal dilatation of right atrium, displaced aorta by the enlarged right atrium, narrowed right or left ventricular cavity, and impairment of the heart dynamics can be demonstrated by means of this

investigation and help in the diagnosis of EMF.

Laboratory investigations: No one test has diagnostic value in EMF; however, they may help to exclude other diseases. Eosinophilia can be present. Serum transaminase levels are usually within the normal range [32]. Because of the hypothesis that EMF may be due to an alteration of the fibrinogen-fibrinolysis mechanism the plasma fibrinogen levels have been investigated. It was found that they are essentially the same in the normal East-Africans as those found in United Kingdom [157]. Bromosulphthalein excretion and liver biopsy have been used to evaluate the duration of the disease, to confirm early disease and establish the diagnosis of an associated disease [134]. There is a high incidence of circulating heart antibodies, predominantly reactive with endomysial tissue and frequent occurrence of cryoprecipitates which may be responsable for the deposition of fibrin [172, 173].

Prognosis and Treatment: There is no adequate treatment for EMF[14]. BALL et al. [16] observed that response to treatment of heart-failure with bed rest, digitalis and diuretics is disappointing. Aspiration of ascitic fluid should generally be avoided because of the great loss of protein that it represents. PARRY [134] found that only spironolactone associated with thiazide diuretic had any hope of sucess in keeping the volume of ascites at a tolerable levels. Temporary improvement may be observed but generally the patients relapse quickly [3, 16].

The course of all types of EMF is unpredictable and it is governed rather by the "activity" of the initial phase (or its persistence) than by the static anatomical deformity of the heart [137]. EMF varies from a short fulminating disease to a very chronic one [134]. Cases have been followed up for more than three years [3], and one patient had symptoms for seven years [16]. Pulmonary hypertension in left ventricular EMF and ascites in right ventricular disease are important factors in the evolution of this cardiopathy[134]. Hepatic damage may well be as important to the prognosis as the cardiac lesion [3]. Possibly as a generalization it can be said that the majority of patients die within three years of their first symptoms.

Pathology: The pathological findings in EMF have been extensively studied [39, 49, 51, 52, 59, 134].

Macroscopical aspects: Pericardial effusion may be found [52] and when the right ventricle is severely involved it is almost invariably present [3, 6]. The frequently accepted image of a small and contracted heart should be considered rather the exception than the rule. The cardiac weight in the majority of the reported cases is above normal. However, it must be remembered, that it is rare to find cases of EMF with a heart weight above 500 g whereas in SAEMC it is common. DAVIES & BALL [52] in a series of 32 cases found only 3 atrophic hearts and of the rest 1/3 were normal in weight, 1/3 moderately hypertrophied and 1/3 considerably hypertrophied.

The majority of the hearts have naked-eye lesions. Those from cases of left ventricular EMF show endocardial fibrosis in the left ventricle extending from the apex to about the middle of the cavity. The region most commonly involved is the posterior wall, followed by the apex and lateral wall [52]. The fibrous process frequently involves the papillary muscle and chordae tendineae, which become thickened and apparently shortened, and the posterior cusp of the mitral valve may adhere to the damaged underlying ventricular wall [6, 134]. CONNOR [39] reported cases with only involvement of the posterior wall of the left ventricle behind the posterior mitral leaflet. The outflow tract of the ventricle and the aortic valve are not involved by the morbid process [2, 52]. The maximal thickness of the endocardium was usually 2 to 3 mm but occasionally it was 10 mm thick [52]. Mural thrombosis in various stages of organization was observed overlying the endocardial fibrosis in 1/3 of the cases [52]. It is commoner in severe cases of endocardial fibrosis and may almost fill the ventricular cavity. This feature is most frequently observed in the right ventricle. Areas of calcification in the endocardial fibrous tissue is common. Small patches of thickened endocardium in the left atrium may occasionally be found. It is important to remark that the fibrous tissue may originate in the apical endocardium, in the endocardium at the base of the papillary muscle of the posterior cusp of the mitral valve and in the endocar-

dium behind the chordae tendineae of the mitral valve, either independently or together [134]. DAVIES [49] described endocardial lesions of two types: a) The most important lesion being a deep endocardial sclerosis of the inflow tract which extends into the underlying myocardium but never throughout its entire thickness [51]. It may be of a pearly white colour or it may be covered with variable amounts of thrombus which may be so massive as to fill the cavity. b) A fine white filminess which is visible on the endocardium adjacent to the semilunar valves which is never covered with thrombus.

In right ventricular EMF there is more fibrous obliteration and organization of thrombus in the ventricle. This may cause retraction of the anterolateral wall of the ventricle producing classical external depression on the epicardial surface of the right ventricle in the proximity of its apex. Involvement of the papillary muscle and tricuspid valve causing valvular incompetence is common. The pulmonary valve is not affected in the fibrotic process [49]. The right atrium is enormously dilated in the majority of cases of right ventricular EMF.

In both clinically defined right or left ventricular disease minor degrees of fibrosis may be found in the other ventricular cavity. In biventricular disease there is involvement of both ventricles to varying degrees by the described morbid process.

There are no constant characteristic extracardiac findings. Despite the presence of mural thrombi, embolism is infrequent [46, 158, 165] compared to the incidence of embolism in SAEMC. The reported cases of EMF associated with infarction [12, 64, 72, 127, 131] were considered exceptional. SHAPER & WRIGHT [159], in a paper on this subject, stated that embolic phenomena was found in 15% of 117 autopsy cases of EMF not complicated by bacterial endocarditis. Even this figure contrasts with 35% and 78% of obvious visceral infarction recorded in SAEMC [20, 90]. If STEMMERMANN'S [166] case and the others revised by him are identical to EMF observed in Africa then pancreatitis is frequently associated with this cardiopathy, but such an association was not found in the papers from Africa.

Microscopical findings: There are a few observations in early cases of EMF [129, 130, 134]. NWOKOLO [129] raised the possibility that EMF starts with cellular infiltration which progresses toward fibrosis, and concluded that "... inflammatory cells are maximal when the disease is active, and gradually diminish as fibrosis becomes established" he added that "the original lesions preceding EMF are inflammatory edema, necrosis, and cellular infiltration, due to an injury the nature of which is at present unknown" [130]. PARRY [134] found some characteristic lesions in the active disease: The most significant histological findings are in the myocardium (in the subendocardial, intermediate and epicardial zones) and they are described as "star-shaped areas in which myocardial fibres were disappearing and in which fibrous tissue was replacing muscle which had completely disappeared". Near these areas small inflammatory foci can be found consisting of macrophages, plasma cells and lymphocytes. PARRY also stressed that these lesions in the heart muscle weve associated with small blood vessels. The changes described in the endocardium were: "1) An inconstant loose fibrin thrombus on the surface of the endocardium; 2) A superficial layer of young fibroblasts, separated by gaps from each other, evidently recently formed, and accounting for the thickened endocardium. Chronic inflammatory cells were often seen throughout this fibroblastic layer, and in some places plasma cells could be seen also; 3) Florid inflammatory changes in the deepest layer of the endocardium. In this layer lymphocytes abounded, and the vessels, both small and large, were choked with blood which had leaked among the fibroblasts [134]".

In the chronic cases the classical endocardial lesions are present. A thick layer of hyalinized and sometimes calcificated fibrous tissue, covered with thrombi. Only in the deeper zones are inflammatory cells present, consisting of macrophages, plasma cells and lymphocytes, and only rarely leucocytes or eosinophils. DAVIES [49, 50, 51], and PEUCHOT et al. [143] stressed that there is no fibroelastic proliferation; rarely, however, a very mild one is observed in the outflow tracts (where the endocardium is not thickened by the fibrotic process) below the semilunar valves, which is interpreted as secondary to hemodynamic factors. Next to the myocardium there is a zone of small blood vessels with a

few chronic inflammatory cells [52]. Tongues of fibrous tissue with large dilated blood vessels extend from the endocardium into the myocardium but rarely reach further than the inner two thirds of the heart muscle. The myocardial fibers show degenerative changes mainly in the areas adjacent to the endocardium but acute necrosis of the fibers is not seen [52]. DAVIES [162] emphasized that even when the heart valves are involved there is no evidence of valvulitis. NWOKOLO [130] observed mucoid degeneration in the mitral and tricuspid valves.

There are no characteristic extra-cardiac microscopical findings but deposition of fibrin in the kidney, spleen, liver, pancreas, thyroid and lung has been observed [172, 173].

Pathogenesis: DAVIES [46, 51] considers EMF a primary myocardial process. He thinks that the lesion starts in the sub-endocardial myocardium which may be damaged by a nutritional or metabolic factor. He suspects that the sub-endocardial layer is susceptible because it serves as the watershed between the coronary distribution and the supply from the cardiac chambers. In his opinion the involvement of the endocardium is secondary to the degeneration of the heart muscle. Davies stated that because of the rarity of embolism the thrombotic thickening must be a very slow process produced by an indolent deposition of fibrin which gets incorporated in the fibrous tissue. Finally Davies says: "... probably it is self aggravating in that as the scar tissue develops it occludes the channels of the Thebesian veins and this leads to dilatation of these vessels and to the development of fibrosis around them. The scar tissue thickens and replaces both the original endocardium and the subjacent myocardium". LYNCH & WATT [111] apparently agree with Davies that EMF may be due to malnutrition which affects the innermost layer of the myocardium but they accept other factors beside malnutrition as causative factors and think that EMF represents the terminal phase of various diseases.

GILLANDERS [78] suggested that EMF is the end-result of intracavitary thrombosis in a previously dilated heart. This mechanism is doubted by SHAPER & WRIGHT [159] mainly because dilatation is not a feature in EMF.

The possibility that EMF is primarily an endocardial disease has also been considered. PENFOLD [141] observed that the pathogenesis of EMF may be similar to Duguid's hypothesis for the formation of atherosclerosis and suggested the sequence of events as follows; a) Damage to the endocardium bye one of many possible factors; b) Deposition of fibrin on the affected areas, and c) Organization of the thrombi and incorporation in the endocardium as an apparent fibrosis. The idea that the lesion may commence as deposits of fibrin on the endocardium with subsequent incorporation in it was considered by SHAPER & SUMMERSCALES [157]. They investigated the plasma fibrinogen levels in East Africans in order to check a possible racial or geographical background. It was found that these levels are essentially the same as in the United Kingdom.

A quantitative study of the ganglion cells of the heart showed that the number of neurons is within the normal range [24]. So, the pathogenesis cannot be explained by a damage to the intracardiac nerve cells.

More than one etiological factor may be important in the pathogenic process. SHAPER & COLES [156] studying the tribal distribution of the disease in Uganda concluded that "an increased susceptibility to this disorder is associated with extremely poor socio-economic conditions. A chronic state of subnutrition, primarily dietary in origin but modified by many endemic diseases, constitutes the characteristic background to this disorder as seen in Uganda".

CONCLUSIONS

From the above data it may be concluded that SAEMC and EMF are two different cardiopathies with unknown etiologies occurring frequently in Africa.

The former shows a greater incidence in South Africa, it is commoner in the African than in other races and occurs in both sexes and in all age groups. The clinical picture is that of a heart failure, without valvular or coronary involvement, following dyspnea and edema. The circulation is hypokinetic or normokinetic and the blood pressure is normal. A minority of cases run a rapidly progressive course but the majority pursue a subacute, relapsing or chronic course which leads to death generally within one year

after the onset of the first symptoms. At post mortem examination the heart is greatly enlarged and hearts weighing more than 600 g are not uncommon. Mural thrombi, recent or organized, and extracardiac infarction are very frequent. There is no agreement on the microscopical aspects and on the pathogenesis of SAEMC; some Authors place importance on the endocardial changes and others on the myocardial alterations.

EMF seems to be limited to the "hot and wet" regions of the tropics. There is no particular racial incidence. It occurs in both sexes and it is commonest in the second and third decades. Clinically, there is an initial active illness with systemic inflammatory symptoms and myocarditis. This "activity" may persist leading to death or may pass into a state of chronic "inactive" disease involving either the left and/or right ventricles. Symptoms and signs of ventricular valve incompetence are very common. Hemodynamically EMF is similar to constrictive pericarditis. The majority of patients die within three years of the initial first complaints. Pathological examination shows a small to moderately enlarged heart weighing rarely more than 500 g. An external depression on the epicardial surface of the right ventricle in the proximity of its apex is often found. The ventricles undergo a deep endocardial fibrosis causing, frequently, valvular incompetence. However, the outflow tracts of the ventricles and the aortic and pulmonary valves are never affected. Mural thrombosis in various stages of organization is generally observed but embolism and infarction are less common. Histologically, degeneration of myocardial fibers with small inflammatory foci is the most significant finding in the initial phase of the disease. In chronic cases a thick layer of hyalinized and sometimes calcified fibrous tissue, covered with thrombi, which extend into the inner two thirds of the myocardium, is observed. Fibroelastic proliferation and valvulitis are not features of EMF. The pathogenesis of this morbid condition is still in question.

RESUMO

Endomiocardiopatia sul-africana e Fibrose endomiocárdica. Análise crítica

As investigações feitas sôbre duas cardiopatias, freqüentes na África e existentes no Brasil, chamadas de Endomiocardiopatia sul-africana e Fibrose endomiocárdica, são relatadas junto com uma extensa revisão bibliográfica. Tenta-se esclarecer a nomenclatura caótica existente e separá-las de outras doenças cardíacas com as quais são muitas vêzes confundidas. Conclui-se, considerando vários aspectos epidemiológicos, clínicos e patológicos, que são duas entidades mórbidas com características próprias e distintas entre sí.

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