

# Necropsy Study of Endomyocardial Fibrosis and Rheumatic Heart Disease in Uganda 1950-1965

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Endomyocardial fibrosis is a relatively common form of heart disease in Uganda (Davies, 1948; Shaper and Williams, 1960) and accounts for some 10 per cent of heart disease seen at necropsy in Kampala (Davies, 1961). It is characterized in the established condition by fibrosis in the endocardium and subjacent myocardium affecting particularly the inflow tract and the apex of one or both ventricles. The aetiology of this disorder is not known, and hypotheses have been put forward in attempts to incriminate virus or filarial infections, plantain diets, and rheumatic heart disease. The disorder has also been described in West Africa, Ceylon, South India, and Central Africa, and well-authenticated cases have been seen in Europeans resident in tropical areas (Brockington, Olsen, and Goodwin, 1967).

Mulago Hospital, Kampala, is situated in Buganda, the largest province of Uganda, and about half the patients admitted to the hospital belong to the local Ganda tribe (Fig. 1). There is also a large immigrant population in Buganda, coming in particular from Rwanda and Burundi (herein referred to as 'Rwandans') and from the Western Province of Uganda (Kigezi, Ankole, Toro, and Bunyoro districts). An analysis of the tribal origins of cases of endomyocardial fibrosis coming to necropsy at Mulago Hospital in the period 1950-1961 showed a preponderance of this condition among those groups immigrant to Buganda, in particular those originating from Rwanda and Burundi. The condition was far less common than expected among the indigenous Ganda people (Shaper and Coles, 1965).

This analysis of the tribal origins of subjects with endomyocardial fibrosis has now been extended to cover the period 1950-1965, and a similar analysis

has been made of subjects with rheumatic heart disease over this 16-year period. The present study examines the age and sex distribution and the tribal origins of subjects in whom endomyocardial fibrosis or rheumatic heart disease has been established at necropsy, attempts to assess the significance of tribal predominance in these conditions, and examines the possible significance of the concurrence of these two disorders in the same person. The patterns of cardiac pathology seen in rheumatic heart disease and in endomyocardial fibrosis are described, and comment is made on intracardiac thrombosis, embolic phenomena, and bacterial endocarditis.

## SUBJECTS AND METHODS

The necropsy records of Mulago Hospital, Kampala, were studied for the years 1950-1965 and all cases in which a diagnosis of endomyocardial fibrosis or rheumatic heart disease had been clearly established were included in this study. Several cases in which endomyocardial fibrosis or rheumatic heart disease was of moderate degree occur in this series and no attempt has been made to include only advanced cases. However, isolated patches of endocardial thickening irregularly distributed over the ventricular surface were not accepted as evidence of endomyocardial fibrosis. These lesions are frequently seen in other cardiac disorders, e.g. idiopathic cardiomegaly (Hutt *et al.*, 1965). Death was usually but not always due to the presence of endomyocardial fibrosis or rheumatic heart disease. Three subjects diagnosed at necropsy as having endomyocardial fibrosis have been included in this study, as they possibly represent the more acute lesions of endomyocardial fibrosis. The material comprises 356 African subjects, and information on tribal origin was available in all except 6, and an age assessment had been made in all except 5 subjects.

The Mulago Hospital register of deaths and necropsies for the years 1950-1965 was studied and an analysis made by tribe, age, and sex to establish the necropsy

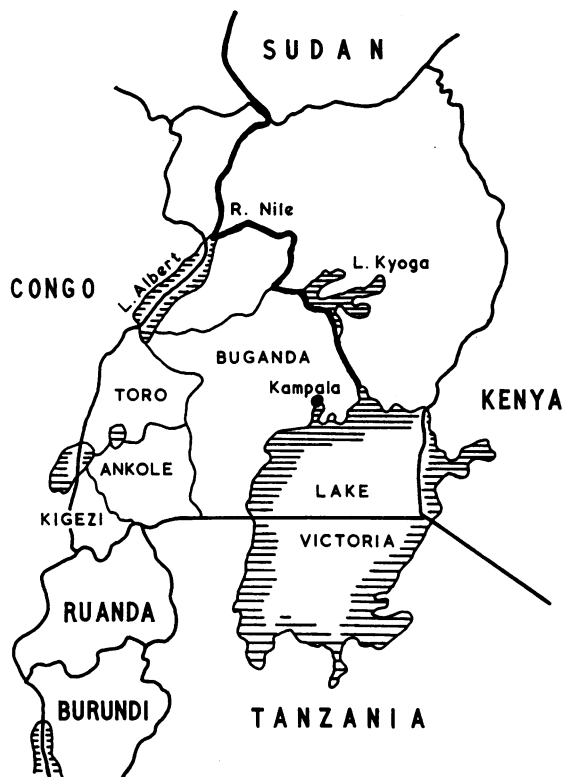


FIG. 1.—Map of Uganda: some of its provinces and neighbouring countries.

rates for these various groups. Data are not presented for stillbirths or for necropsies on subjects under 1 year of age, but medico-legal necropsies, which comprise about 15 per cent of all necropsies, are included. This analysis of deaths and necropsies by sex, age, and tribe was made for each year separately and a table drawn up for the whole 16-year period under review\*. A summary of this analysis is given in Table I.

By reference to the observed figures for endomyocardial fibrosis (Table II) and rheumatic heart disease (Table III), and the detailed table of necropsies from which the summary in Table I is derived, the expected number of deaths due to either of these causes in each sex and age category for each tribal group (if there were no difference in incidence between the tribal groups) can be calculated by simple proportion. For example, 746 necropsies were performed on men aged 15–24 years in the 1950–1965 period and 19 cases of endomyocardial fibrosis were observed. Since 243 necropsies among men in this age-group were from the Rwandan tribal group, the number of endomyocardial fibrosis cases expected for male Rwandans aged 15–24 years can be

calculated as  $243 \times 19/746 = 6.2$ . A similar calculation for all other age, sex, and tribal groups leads to the figures presented in Tables II and III in which the observed distributions of necropsy cases of endomyocardial fibrosis and of rheumatic heart disease are compared with the expected distributions. A  $\chi^2$  (chi squared) test was carried out for men and women separately in both series in order to assess the significance of any differences between the observed and expected figures.

*Concurrence.* If endomyocardial fibrosis and rheumatic heart disease are two completely independent conditions, it is possible to calculate the number of occasions on which both should occur in the same subject, given the details of the necropsy population and the detailed incidence of each condition in this population. These expected concurrence rates have been calculated for both men and women for each age-group in each of the main tribal groups, and the differences between the observed and expected figures subjected to a  $\chi^2$  test.

## RESULTS

*Endomyocardial Fibrosis* (Table II). Only 19 (11%) of the 172 cases of endomyocardial fibrosis

\* Copies of the full analysis of deaths and necropsies 1950–1965 are available on request.

TABLE I  
NECROPSY RATES IN VARIOUS TRIBAL GROUPS AT MULAGO HOSPITAL 1950-1965

	Ganda		Rwanda		Ankole		Others		Total	
	M	F	M	F	M	F	M	F	M	F
Deaths Necropsies	4250 1934	2474 854	2129 1583	613 391	442 298	178 104	3960 2666	991 479	10781 6481	4256 1828
Necropsy rate (%)	46	35	74	64	67	58	67	48	60	43
Tribal necropsy rate (%)	42		72		65		64		55	

TABLE II  
OBSERVED AND EXPECTED DISTRIBUTION, BY SEX, AGE, AND TRIBE, OF SUBJECTS WITH  
ENDOMYOCARDIAL FIBROSIS 1950-1965 (EXPECTED NUMBERS IN BRACKETS)

Age (yr)	Ganda		Rwanda		Ankole		Others	
	M	F	M	F	M	F	M	F
1-4	0 (1.0)	0 (0.3)	3 (0.9)	1 (0.3)	0 (0.1)	0 (0.1)	0 (0.9)	0 (0.3)
5-14	2 (4.8)	1 (6.2)	7 (1.3)	10 (3.1)	1 (0.6)	1 (0.4)	2 (4.4)	1 (3.3)
15-24	1 (4.2)	2 (2.9)	15 (6.2)	4 (1.5)	2 (1.2)	0 (0.4)	1 (7.4)	1 (2.1)
25-34	2 (8.2)	2 (9.7)	30 (12.3)	11 (5.8)	1 (1.6)	5 (1.3)	6 (16.9)	4 (5.1)
35-44	2 (7.1)	2 (3.5)	17 (6.8)	5 (1.7)	1 (1.3)	0 (0.6)	7 (11.8)	1 (2.2)
45-54	2 (3.8)	2 (1.9)	3 (1.7)	1 (0.3)	2 (0.5)	0 (0.1)	3 (4.0)	0 (0.6)
55-64	1 (2.9)	0 (1.4)	1 (0.8)	1 (0.2)	0 (0.3)	0 (0.0)	4 (2.0)	1 (0.3)
	10 (32.0)	9 (25.9)	76 (30.0)	33 (12.9)	7 (5.6)	6 (2.9)	23 (47.4)	8 (13.9)

TABLE III  
OBSERVED AND EXPECTED DISTRIBUTION, BY SEX, AGE, AND TRIBE, OF SUBJECTS WITH  
RHEUMATIC HEART DISEASE 1950-1965 (EXPECTED NUMBERS IN BRACKETS)

Age (yr.)	Ganda		Rwanda		Ankole		Others	
	M	F	M	F	M	F	M	F
1-4	1 (0.7)	1 (0.7)	1 (0.6)	0 (0.7)	0 (0.1)	1 (0.1)	0 (0.6)	0 (0.6)
5-14	5 (4.4)	9 (7.2)	3 (2.1)	2 (3.5)	1 (0.6)	0 (0.5)	2 (4.1)	4 (3.8)
15-24	5 (3.3)	4 (4.2)	2 (4.9)	2 (2.2)	1 (1.0)	0 (0.6)	7 (5.9)	4 (3.1)
25-34	17 (7.8)	8 (8.8)	9 (11.7)	3 (5.3)	2 (1.5)	2 (1.2)	8 (16.0)	7 (4.7)
35-44	7 (6.8)	11 (4.8)	7 (6.6)	0 (2.4)	3 (1.2)	0 (0.9)	9 (11.4)	0 (3.0)
45-54	7 (6.5)	11 (8.2)	0 (2.9)	0 (1.5)	2 (0.8)	0 (0.6)	8 (6.7)	2 (2.6)
55-64	16 (9.6)	3 (2.9)	1 (2.7)	0 (0.4)	1 (0.9)	0 (0.1)	2 (6.8)	1 (0.7)
65+	2 (2.3)	3 (2.1)	1 (0.5)	0 (0.1)	0 (0.1)	0 (0.1)	1 (1.1)	0 (0.6)
	60 (41.4)	50 (38.9)	24 (32.0)	7 (16.1)	10 (6.2)	3 (4.1)	37 (52.6)	18 (19.1)

over the 16-year period are from the local Ganda tribe, who contribute 34 per cent to the total necropsies at Mulago Hospital. The remainder are from several tribal groups all of whom are immigrant to Buganda. The subjects originating from Rwanda and Burundi (Rwandans) provide 109 (63%) of the cases and only 24 per cent of the total necropsies. If the number of cases found at necropsy in the various tribal groups is expressed as a percentage of all necropsies performed on members of that tribe, the incidence is substantially higher in the Rwandan group (5.8%) than in the Ganda group (0.7%) or 'other tribes' (1.1%), while the Ankole occupy an intermediate position (3.5%).

The value of probability resulting from the  $\chi^2$  test carried on the data in Table I is less than 0.001 both for males ( $\chi^2 = 100.8$ ;  $f = 6$ ) and females ( $\chi^2 = 47.5$ ;  $f = 6$ ).

Direct comparison of the observed and expected numbers shows that this is principally due to a conspicuous excess of endomyocardial fibrosis among the Rwandan group, apparent in both sexes and in all age-groups. There is a suggestion of some excess occurrence in the female Ankole group. There are also far fewer cases observed in almost all Ganda male and female age-groups than expected.

*Rheumatic Heart Disease* (Table III). Half of

TABLE IV

CHANGES IN INCIDENCE AT NECROPSY OF ENDOMYOCARDIAL FIBROSIS AND RHEUMATIC HEART DISEASE OVER TWO 8-YEAR PERIODS, 1950-1957 AND 1958-1965

	Ganda		Rwanda		Others	
	M	F	M	F	M	F
<i>Endomyocardial Fibrosis</i>						
1950-1957	8	2	43	11	15	4
% necropsies	1.0	0.6	5.2	6.7	1.0	1.8
1958-1965	3	7	33	22	17	8
% necropsies	0.3	1.4	4.4	9.6	1.1	2.2
<i>Rheumatic Heart Disease</i>						
1950-1957	16	16	11	2	21	4
% necropsies	2.0	4.5	1.3	1.2	1.5	1.8
1958-1965	44	34	15	5	28	17
% necropsies	3.9	6.8	2.0	2.2	1.8	4.7

the rheumatic heart disease cases (52%) are from the local Ganda tribe who provide 34 per cent of the total necropsies at Mulago Hospital, while the Rwandan group, who provide 24 per cent of the total necropsies, account for 15 per cent of the cases. If the numbers of cases found at necropsy in the various tribal groups is expressed as a percentage of all necropsies performed on members of that tribe, the incidence is lower in the Rwandan group (1.7%) than in the Ganda group (4.2%), with the Ankole group (3.5%) again occupying an intermediate position. In the "other tribes", the percentage incidence related to all necropsies (2.0%) is closer to the Rwandan figure than to the Ganda incidence.

The value of probability resulting from the  $\chi^2$  test carried out on the data in Table III is  $<0.01$  both for males ( $\chi^2 = 28.0$ ,  $f = 12$ ) and females ( $\chi^2 = 23.7$ ;  $f = 10$ ). Direct comparison of the observed and expected numbers shows that this is principally due to an excess number of cases in the Ganda group and a diminished number in the Rwandan group, while the male Ankole group shows a slight excess of observed over expected figures. There were 9 cases of rheumatic heart disease in subjects of the Toro tribal group over this 16-year period, in contrast to a complete

absence of endomyocardial fibrosis in this group over the same period. The Toro group come to necropsy most frequently after the Ganda, Rwanda, and Ankole groups, and endomyocardial fibrosis has been recorded in several other tribal groups coming to necropsy far less frequently.

*Changing Incidence of Endomyocardial Fibrosis and Rheumatic Heart Disease at Necropsy.* If the incidence of these two lesions at necropsy in the two 8-year periods 1950-1957 and 1958-1965 are compared, certain very striking changes are seen. We initially compared the necropsy rates for these two 8-year periods, and there was virtually no change seen in any group by tribe and sex, i.e. the necropsy rates as shown in Table I were seen in both of the two periods. In Table IV is shown the number of cases of both conditions by tribe and sex in these two 8-year periods. The most striking feature of the figures for endomyocardial fibrosis is the reversal of the sex ratio in the Ganda and Rwandan groups. In the figures for rheumatic heart disease there is a marked increase in the number of cases of rheumatic heart disease seen at necropsy, most strikingly evidenced in the Ganda subjects, both male and female, and in the female "Other" group.

*Age Distribution of Endomyocardial Fibrosis and Rheumatic Heart Disease.* From Table V it can be seen that both these conditions present over a very wide age range, and that the similarities in age and sex distribution in these necropsies are more striking than the differences.

*In men,* a similar proportion of both disorders are found in the under 15-year age-group. A slightly larger proportion of endomyocardial fibrosis cases present in the 15-34 year period compared with the rheumatic series, but the difference between these two proportions is not significant and the proportions are similar in the 35-54-year period. Significantly more rheumatic heart cases come to necropsy past 55 years of age, and the observed difference (13.2%) is 3.3 times its standard error.

TABLE V

AGE DISTRIBUTION OF SUBJECTS WITH ENDOMYOCARDIAL FIBROSIS (EMF) AND RHEUMATIC HEART DISEASE (RHD) COMING TO NECROPSY, 1950-1965

		Age-groups (yr.)							
		1-4	5-14	15-24	25-34	35-44	45-54	55-64	65+
Male (%)	EMF	2.6	10.3	16.4	33.6	23.3	8.6	5.2	0
	RHD	1.5	8.4	11.4	27.5	19.8	13.0	15.3	3.1
Female (%)	EMF	1.8	23.2	12.5	39.3	14.3	5.4	3.6	0
	RHD	2.6	19.2	12.8	25.6	14.1	16.7	5.1	3.8

In women, in both the series there is twice the percentage of cases found under 15 years of age compared with the respective male series. The difference between the endomyocardial fibrosis and rheumatic series in the 15-34-year group is not significant. Over 35 years of age there is a smaller proportion of endomyocardial fibrosis (23.3%) than of rheumatic heart disease (39.7%), and the observed difference is 2.1 times its standard error. When the 35-54 years and over 55-year groups are taken separately, there is no significant difference between the two series.

*Heart Weights in Endomyocardial Fibrosis and Rheumatic Heart Disease.* The average heart weights in subjects with both conditions are shown in Table VI, and are compared with heart weights found at necropsy at Mulago Hospital in subjects with normal hearts (Coles and Davies, 1959). All hearts weighed with the aortas are excluded as well as those hearts in which both disorders were concurrently present. The heart weights refer only to subjects aged 15 years or more in both series and to subjects aged 20 years or more in the routine necropsy series of Coles and Davies (1959).

The findings in this study show that hearts with endomyocardial fibrosis tend to be on average some 80-110 g. heavier than normal hearts, while rheumatic heart disease hearts weigh about 150-180 g. more than normal hearts. The range, however, is wide and many hearts with either disorder fall within the normal range. No attempt has been made to correlate the type of heart lesion with the weight of the heart.

*Pattern of Pathology in Rheumatic Heart Disease.* The mitral valve was involved in 188 cases (88.3%), with mitral stenosis in 100, i.e. 47 per cent of all those with rheumatic heart disease (Table VII). The aortic valve was involved in 94 cases (44%), with aortic stenosis in 21 cases. Tricuspid valve involvement was present in 31 cases (14%), with stenosis in only 3 cases, and in only 2 cases was the pulmonary valve involved.

The age distribution of subjects with mitral stenosis was not significantly different from that of other rheumatic heart disease subjects, but mitral stenosis was present in 40 per cent of male subjects and 59 per cent of female subjects. The observed difference (19%) is 2.7 times its standard error, suggesting that this finding is of some significance.

Lone mitral valve disease without stenosis occurred in 39 cases and associated endomyocardial fibrosis was present in 7 of these. Of the 16 cases in Ganda subjects, only 2 were male (aged 7 and 10

TABLE VI

HEART WEIGHTS OF ADULT SUBJECTS WITH ENDO-MYOCARDIAL FIBROSIS AND RHEUMATIC HEART DISEASE COMPARED WITH HEART WEIGHTS OF SUBJECTS WITHOUT HEART DISEASE

Groups	Sex	No.	Mean weight (g.)	SD (g.)	Range (g.)
Normal subjects (Coles and Davies, 1959)	F	130	226	—	134-320
	M	456	267	—	230-346
Endomyocardial fibrosis	F	28	308	76	190-460
	M	65	379	100	145-680
Rheumatic heart disease	F	41	372	86	170-580
	M	90	444	138	160-760

TABLE VII

DISTRIBUTION OF LESIONS IN RHEUMATIC HEART DISEASE, MULAGO HOSPITAL NECROPSIES, 1950-1965

Mitral valve alone	= 99	(Mitral stenosis in 61)
Mitral and aortic valves	= 57	(Mitral stenosis in 25, aortic stenosis in 15, combined mitral stenosis and aortic stenosis in 10)
Aortic valve alone	= 25	(Aortic stenosis in 4)
Mitral and tricuspid valves	= 18	(Mitral stenosis in 10, tricuspid stenosis in 2, both with mitral stenosis)
Mitral, tricuspid, aortic valves	= 12	(Mitral stenosis in 4, aortic stenosis in 2, tricuspid stenosis in 1, with mitral stenosis)
Mitral and pulmonary valves	= 1	
Mitral, tricuspid, and pulmonary valves	= 1	

years), indicating that in this study mitral incompetence as a lone lesion in a male Ganda subject over 15 years of age was singularly uncommon. Mitral incompetence and tricuspid incompetence as a combined lesion occurred in 8 subjects, with associated endomyocardial fibrosis in 2 of these.

*Bacterial endocarditis* occurred in 26 per cent of rheumatic heart disease cases, affecting 33 per cent of the male subjects and 14 per cent of the female subjects (Table VIII). The observed difference (19%) is 3.4 times its standard error.

*Ante-mortem atrial and/or ventricular intracardiac thrombi* were present in 31 cases (14.6%), but in

TABLE VIII

BACTERIAL ENDOCARDITIS IN NECROPSIED CASES OF RHEUMATIC HEART DISEASE, MULAGO HOSPITAL, 1950-1965

	Male	Female
Mitral valve	18	8
Mitral and aortic valves	9	0
Aortic valve	17	3
Mitral, aortic, tricuspid valves	1	0
	45	11

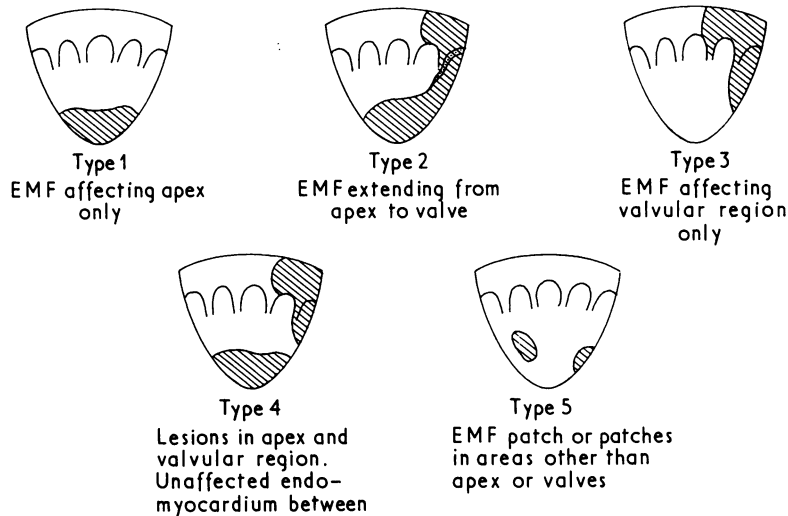


FIG. 2.—The distribution of endomyocardial fibrosis in the left or right ventricle.

only 5 were ventricular thrombi present (2.3%). Cases with associated endomyocardial fibrosis were excluded from this analysis (Table IX).

*Embolic phenomena* in the absence of bacterial endocarditis were present in 36 subjects with rheumatic heart disease, 4 of whom also had endomyocardial fibrosis. If these latter 4 cases are excluded, embolic phenomena occurred in 15 per cent of the rheumatic heart disease subjects. Eighteen of these 32 subjects had mitral stenosis.

*Pattern of Pathology in Endomyocardial Fibrosis.* The 172 hearts with endomyocardial fibrosis were separated into several descriptive groups based on the distribution of the lesions (Fig. 2).

*Type 1.* Apex only involved, extending for a variable distance along the inflow tract.

*Type 2.* Lesion involving the apex and with extension along the ventricular wall to involve the mitral or tricuspid valve.

*Type 3.* Lesion of the ventricular wall involving the atrioventricular valve but with no apical lesion.

*Type 4.* Apical lesion and a separate lesion of the ventricular wall involving the atrioventricular valve.

*Type 5.* Lesion of the ventricular wall away from the apex and the atrioventricular valve.

The following method of abbreviation will be used in the ensuing text: R1 will indicate a Type 1 lesion on the right side of the heart and L2 will indicate a Type 2 lesion on the left side of the heart, and so on.

*Pure right ventricular lesions* were present in 19 cases (11%), with apical involvement alone in 6 (R1), apical involvement extending to the tricuspid valve in 11 (R2), separate apical and tricuspid valve lesion in 1 (R4), and an isolated ventricular wall patch in 1 (R5).

*Pure left ventricular lesions* were present in 66 cases (38%), with apical involvement alone in 26 (L1), and an apical lesion extending right up to involve the posterior mitral valve cusp in 25 (L2). In 10 cases without apical involvement the posterior mitral valve cusp was adherent to the ventricular wall fusing with an area of endomyocardial fibrosis (L3), and in 2 further cases this lesion was present with a separate lesion at the apex (L4). In 3 cases there was a large area of endomyocardial fibrosis in the left ventricular wall separate from the apex and the mitral valve (L5).

TABLE IX  
DISTRIBUTION OF INTRACARDIAC THROMBI IN  
RHEUMATIC HEART DISEASE AT NECROPSY, 1950-1965

Site	No.
Right atrium	13
Left atrium	10
Right and left atria	3
Right atrium and right ventricle	2
Right atrium, right ventricle, and left ventricle	1
Right ventricle	1
Left ventricle	1

**Combined Lesions.** Both right and left ventricles were affected by endomyocardial fibrosis in 88 cases (51%), the involvement being predominantly left-sided in 39 cases, predominantly right-sided in 22, and both sides being about equally affected in the remaining 27 cases.

In Table X, the pattern of combined right- and left-sided endomyocardial fibrosis is shown using the system described above, and in addition indicating (in brackets) which side of the heart was more involved, or whether both sides were equally involved. From the Table it can be seen that in those cases in which the right-sided lesion affected only the ventricular apex (R1, 38 cases) the major involvement by endomyocardial fibrosis was most frequently on the left side of the heart (28 cases), and in 29 of the 38 cases the mitral valve was involved. From the necropsy description the effect of the right ventricular apical lesion on the function of the tricuspid valve was not always possible to assess. It must be presumed that in many of these cases tricuspid incompetence was present, but its frequency or degree could not be estimated.

If one examines those right ventricular apical lesions which were sufficiently extensive as to involve the tricuspid valve and/or its attachments (R2, 35 cases), the predominant pathology was either on the right side of the heart (18 cases) or both sides were equally affected (16 cases). In 29 of these 35 cases the mitral valve was involved so that both mitral and tricuspid incompetence were presumably present. Several other combinations of lesions occurred apart from these main groupings and the pattern of these can be seen from Table X.

**Bacterial Endocarditis.** Bacterial endocarditis was present in 10 of the 173 cases of endomyocardial fibrosis, but in 7 of these cases rheumatic heart disease was also present. In the 3 cases of bacterial endocarditis occurring in pure endomyocardial fibrosis the mitral valve was involved in one case and the left ventricular endocardium in 2 cases. In the 7 RHD + EMF cases with bacterial endocarditis the mitral valve was involved in 6 cases and the aortic valve in 1 case.

**Ante-mortem atrial and/or ventricular intracardiac thrombi** were present in 74 cases (43%) of endomyocardial fibrosis and involved the ventricles in 50 of these cases (29%). The left ventricle had intracardiac thrombi in 43 subjects and the right ventricle in 16 subjects (Table XI).

**Emboic phenomena** in the absence of bacterial endocarditis were present in 36 cases, 9 of which had associated rheumatic heart disease. If these

TABLE X  
PATTERNS OF COMBINED RIGHT- AND LEFT-SIDED  
ENDOMYOCARDIAL FIBROSIS

	R-1	R-2	R-3	R-4	R-5
L-1	8 (5L/1R/2B)	8 (7R/1B)	3 (3L)	—	2 (2L)
L-2	18 (16L/B2)	14 (3R/1L/10B)	1 (1L)	2 (2L)	2 (2L)
L-3	3 (1L/2R)	8 (7R/1B)	2 (2B)	—	—
L-4	8 (6L/2B)	5 (4B/1R)	—	2 (2B)	—
L-5	1 (1R)	—	—	—	1 (1B)

*Note:* Figures in brackets indicate frequency with which one or other side of heart is more severely affected, i.e. L, R, or B indicates that the more advanced lesion was on the left (L) or right (R) side or that both sides (B) were equally affected.

TABLE XI  
DISTRIBUTION OF INTRACARDIAC THROMBI IN ENDO-  
MYOCARDIAL FIBROSIS AT NECROPSY, MULAGO  
HOSPITAL, 1950-1965

Site	No.
Left ventricle	29
Right atrium	22
Right and left ventricles	5
Right ventricle	5
Right atrium and both ventricles	4
Left atrium and ventricle	2
Right atrium and ventricle	2
Right atrium, left ventricle	2
Both atria, left ventricle	1
Both atria	1
Left atrium	1
	74

TABLE XII  
DISTRIBUTION OF 26 CASES WITH CONCURRENT  
ENDOMYOCARDIAL FIBROSIS AND RHEUMATIC HEART  
DISEASE: MULAGO HOSPITAL, 1950-1965

	Ganda	Rwanda	Ankole	Others
1-4	—	2	—	—
5-14	—	1	1	—
15-24	—	—	—	—
25-34	—	5*	1	4†
35-44	2†	2	—	1
45-54	2*	—	1	1
55-64	—	1	—	2
	4	11	3	8

\* Includes 1 female. † = Includes 2 female.

latter are excluded, embolic phenomena occurred in 16 per cent of the endomyocardial fibrosis subjects. Aortic embolization occurred in 7, and as these constitute a syndrome apparently peculiar in Kampala to endomyocardial fibrosis and not seen in this rheumatic heart disease series, they will be fully described in a separate paper.

**Concurrence of Endomyocardial Fibrosis and Rheumatic Heart Disease** (Table XII). Characteristic macroscopical lesions of both rheumatic

heart disease and endomyocardial fibrosis were present in 26 hearts: 20 male and 6 female. We are aware of the problems inherent in retrospective studies of necropsy material, and in most cases under discussion the hearts had been fully described, often by several pathologists, and photographs were frequently available.

The number of occasions on which both conditions might be expected to occur in the same subject was calculated separately for both male and female subjects for each age-group in each of the main tribal groups. As the Ankole group had behaved in an intermediate way in the assessment of tribal predominance in both series they were included in "other tribes" for the purpose of this particular statistical evaluation. It was calculated that 2.2 cases of combined lesions were to be expected in the 6481 male necropsies and 2.5 cases in the 1828 female necropsies, in striking contrast to the 20 male and 6 female cases in which these two disorders were considered to be concurrently present.

#### *Description of Cases showing Concurrence of Both Conditions*

*Group A:* (7 cases). In this group advanced mitral stenosis was present without other valvular lesions of a rheumatic nature. In addition, there were characteristic lesions of endomyocardial fibrosis. In 3 cases the fibrosis was quite separate from the mitral valve lesion, obliterating the apex of the right ventricular cavity in all 3, and, in addition, involving the apex of the left ventricular cavity in 2.

In the other 4 there was typical rheumatic mitral stenosis, but in each case the posterior mitral cusp was also adherent to the ventricular wall, the chordae tendineae were short, thick, and often fibrosed, and disappeared into an area of endomyocardial fibrosis. In 2 of these 4 cases, there was left ventricular apical endomyocardial fibrosis in one case separate from the area on the posterior wall, and in the other it was continuous with the area behind the posterior mitral cusp. In addition, 2 of these 4 cases had severe endomyocardial fibrosis of the right ventricle.

*Group B:* (11 cases). In this group both the anterior and posterior cusps of the mitral valve were considered to be abnormal in a manner consistent with rheumatic fever, but there was no stenosis. In addition, there were lesions in the ventricular cavities characteristic of endomyocardial fibrosis, and the posterior cusp of the mitral valve was usually involved in a lesion suggestive of endomyocardial fibrosis.

In 9 cases the posterior mitral cusp, in addition to being thickened, irregular, and contracted in a rheumatic manner, was associated with thickened and sometimes fibrosed chordae tendineae and was adherent to the posterior ventricular wall. Here it fused with a patch of endomyocardial fibrosis of varying size. In 2 cases there were further but separate patches in the

left ventricle but not at the apex and in 4 cases there was apical endomyocardial fibrosis—separated from the patch on the posterior wall in 3 cases and continuous with it in 1 case. In 7 cases there was fibrosis involving the right ventricular apex, 3 of a gross degree with distortion and 3 of less degree.

In 2 cases there was rheumatic mitral incompetence with involvement of both anterior and posterior cusps, but the posterior cusp was free and not affected in the manner described above. In both cases there was fibrosis of the left ventricular apex quite separate from the mitral lesion and the right ventricular apex was similarly affected.

*Group C:* (3 cases). In this group the mitral and aortic valves were both involved in an apparent rheumatic process, together with lesions of endomyocardial fibrosis.

In one subject with mitral stenosis there was well-defined fibrosis running from the posterior cusp to the posterior wall of the left ventricle and down to the apex. There were other patches within the left ventricular cavity and also a small patch near the right ventricular apex. All three valves of the aortic cusp were involved in an apparent rheumatic process, with small pale vegetations on the edges of two cusps and scarring of the third cusp. In the second case both mitral cusps were thickened, nodular, and almost cartilagenous, with slight narrowing of the mitral ring. The anterior leaflet was adherent to the ventricular wall by a mass of organizing material, and there was a patch of fibrosis at the apex of the cavity. The aortic valve was nodular, calcified, and incompetent. In the third case both the mitral and aortic valves showed thickening and calcification without gross distortion, and there was a sharply defined plaque of fibrosis on the wall of the right ventricular cavity.

*Group D:* (5 cases). In this group the aortic valve disease was the main site of rheumatic heart disease, together with lesions of endomyocardial fibrosis.

In all 5 cases there was endomyocardial fibrosis of the left ventricular apex, often of a gross degree, with extensive fibrosis and occasional calcification and overlying thrombus. Two of these cases showed, in addition, fibrosis of the left ventricular wall behind the posterior mitral cusp, tethering the papillary muscles and chordae, and one of these had additional patches in the right ventricle. In one case the tricuspid valve showed slight thickening of the free margins, and the chordae of the posterior cusp were adherent to each other and to the ventricular wall, with small patches of yellowish-white thickening over the papillary muscles. Aortic stenosis was present only in 1 of these 5 cases associated with a large and dense fibrotic scar at the apex of the left ventricular cavity.

#### DISCUSSION

This paper is intended to provide information rather than to review the whole subject of endomyocardial fibrosis or rheumatic heart disease in a



tropical area. The discussion will be brief and will merely indicate the possible significance of some of our observations.

In the previous study of the tribal origins of subjects coming to necropsy at Mulago Hospital over a 12-year period, it was evident that endomyocardial fibrosis particularly affected the immigrants to Buganda from Ruanda and Burundi (Shaper and Coles, 1965). The condition occurred less frequently than expected among the local Ganda tribe. The present study over a 16-year period confirms the conspicuous preponderance among the Rwandans and the relative freedom from the disorder seen in the indigenous group. Endomyocardial fibrosis was present at the rate of 1 in every 147 necropsies in the Ganda subjects and in 1 in every 18 necropsies in the Rwandan subjects. The observed incidence of cases in the Ankole female group is in excess of the expected number, but the numbers involved are too small to do more than suggest an increased susceptibility in this group to endomyocardial fibrosis.

Rheumatic heart disease occurs even more frequently at necropsy than endomyocardial fibrosis, and appears to affect the Ganda group more than expected and the Rwandan group less than expected, though the level of statistical significance is not as high as in the endomyocardial fibrosis figures. In the Ganda subjects, rheumatic heart disease is present in 1 in every 25 necropsies; in the Rwandans in 1 in every 64 necropsies.

In the previous study, attention was drawn to the absence of endomyocardial fibrosis in subjects from the Toro group, the tribal group coming to necropsy most frequently after the Ganda, Rwanda, and Ankole groups, though endomyocardial fibrosis had been recorded in several other tribal groups coming to necropsy far less frequently. In the present 16-year study this remains true, and no case of endomyocardial fibrosis is recorded at necropsy in a subject belonging to the Toro group. On the other hand, 9 cases of rheumatic heart disease were observed at necropsy in people originating in Toro.

The migrant status of the people originating from Rwanda and Burundi, and the history of their pattern of movement into Buganda, has been fully described in our earlier publication. It must again be emphasized that, according to the 1959 Uganda Census, a considerable proportion of Rwandans living in Buganda claim to have been born in Buganda, and this is almost certainly true of many of those in the younger age-groups. We suggested in our earlier study that, whatever the initiating factor in endomyocardial fibrosis, a state of increased susceptibility was associated with poor socioeconomic

conditions such as is seen in the Rwandan, while a degree of protection was conferred on the Ganda by a dietary and social background which would however still be regarded as suboptimal by western standards. In an attempt to move the field of interest from nutritional factors to those concerned with infection and immunity, a hypothesis was later put forward that emphasized the previous immunological experiences in the immigrant community, in particular that resulting from parasitic infestation, such as malaria, and suggested that endomyocardial fibrosis might represent in the Rwandans an altered response to infection with haemolytic streptococci (Shaper, 1966).

A comparison of the two 8-year periods at present under review (1950-1957 and 1958-1965) shows that there have been certain temporal changes in the incidence and sex ratios of both endomyocardial fibrosis and rheumatic heart disease (Table IV). In the Rwanda group, the former constitutes 5.5 per cent of necropsies in both 8-year periods, but whereas in the first period there was a nearly similar sex ratio, by the second 8-year period, female subjects had more than double the incidence at necropsy. In the Ganda group the proportion of endomyocardial fibrosis at necropsy fell from 0.84 per cent to 0.61 per cent over the two 8-year periods, but with a similar appearance of a conspicuous female predominance in the second 8-year period. In rheumatic heart disease neither the Ganda nor the Rwanda groups showed any change in sex ratio over the years, but the proportion of rheumatic heart disease cases at necropsy rose from 2.7 to 4.8 per cent in the Ganda, and the Rwanda showed a slight increase from 1.3 to 2.0 per cent of necropsies.

In the majority of cases of both conditions presenting at necropsy, we are confronted with a chronic fibrotic lesion in the heart. As the age distribution at necropsy of these two conditions is similar, perhaps the least that can be concluded is that both have a similar natural history.

From these necropsy findings it appears that in recent years both endomyocardial fibrosis and rheumatic heart disease have shown an increasing predilection for female subjects, and that in both disorders mortality rates are much higher in female subjects in the 1-14 age period than in the male. Clinical studies at Mulago Hospital have also indicated a female preponderance in endomyocardial fibrosis of 2:1 (D'Arbela, Kanyerezi, and Tulloch, 1966), and in recent unselected necropsies the female sex has predominated (Connor, 1964).

It is not intended to discuss in detail the pattern of pathology seen in the hearts with rheumatic

disease. One point of interest is the greater frequency of mitral stenosis in female subjects with rheumatic heart disease than in men. The fact that twice as many female subjects with this lesion present at necropsy in the 1-14-year age-group, suggests that the intensity of rheumatic heart disease is greater in women, a concept supported by the smaller proportion of female rheumatic heart disease subjects surviving past 55 years of age.

In describing the pattern of pathology encountered in endomyocardial fibrosis we have put forward a descriptive method (Fig. 2) which might be of general use in recording the lesions in this disorder. It is not really possible to compare our findings with those of any other study, for our material represents a 16-year period while every other report concerns selected material, often selected over very short periods of time. It is unfortunate that many generalizations regarding the pattern of endomyocardial fibrotic lesions have been made from clinical studies in which it has not been possible to exclude the presence of lesions on both sides of the heart.

*Concurrence of Endomyocardial Fibrosis and Rheumatic Heart Disease.* In this paper we have drawn attention to the striking degree of concurrence of rheumatic heart disease and endomyocardial fibrosis. In the review of the pathology of endomyocardial fibrosis in Uganda, Davies and Ball (1955) gave a very detailed description of 32 hearts and referred to mitral stenosis in 2 cases, one of which also has a scarred and thickened aortic valve. They mentioned that anterior cusp involvement was less frequent and less severe than posterior cusp involvement, and it is this latter lesion that is stressed by all observers. It might, however, be of some value to draw attention to the fact that isolated lesions of the posterior (mural) cusp of the mitral valve are not pathognomonic of endomyocardial fibrosis. From a study of 240 cases with rheumatic mitral valve disease, Nixon, Wooler and Radigan (1959) described 29 with unusual auscultatory findings, 11 of which at operation had a relatively healthy anterior cusp but a diseased posterior cusp. Connor (1964) in a prospective necropsy study of gross unexplained endocardial lesions at Mulago Hospital, reviewed 17 cases over a 20-month period, and excluded 3 because of the presence of associated rheumatic heart disease.

The various possibilities that arise from the high degree of concurrence of endomyocardial fibrosis and rheumatic heart disease have been discussed in detail elsewhere (Shaper, 1966, 1967). The material in this present paper provides no immediate answer to the many questions raised by the patterns of tribal predominance or the degree of concurrence

of these two disorders, but nevertheless it appears that there are many similarities in their natural history.

#### SUMMARY

This paper is a review of 356 cases of endomyocardial fibrosis and rheumatic heart disease presenting at necropsy in Mulago Hospital, Kampala, Uganda, during 1950-1965. Endomyocardial fibrosis is predominantly a disorder affecting immigrants to the Kampala region from Rwanda and Burundi, and the indigenous Ganda people are seldom affected. Rheumatic heart disease affects the Ganda group more than is expected, and the Rwandan people coming to necropsy in Kampala are less affected than expected.

Over the past 16 years, cases of endomyocardial fibrosis have shown a reversal of the sex ratio, with an increase in the proportion of female subjects affected. There has been an increase at necropsy of cases of rheumatic heart disease. The age and sex distribution of necropsy cases of endomyocardial fibrosis and rheumatic heart are similar, particularly in the 1-14 age-group.

The patterns of pathological involvement in both conditions are described, together with comment on the frequency of bacterial endocarditis, intracardiac thrombi and embolic phenomena.

Characteristic lesions of both endomyocardial fibrosis and rheumatic heart disease were present in 26 hearts in this series, whereas concurrence was expected to occur on only 5 occasions. The cases of concurrence are fully described. There is a brief discussion concerning the significance of the findings in this necropsy study.

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#### REFERENCES

- Brockington, I. F., Olsen, E. G. J., and Goodwin, J. F. (1967). Endomyocardial fibrosis in Europeans resident in tropical Africa. *Lancet*, **1**, 583.
- Coles, R. M., and Davies, J. N. P. (1959). The normal heart weight of Uganda Africans. *E. Afr. med. J.*, **36**, 76.
- Connor, D. H. (1964). Africa cardiomyopathies. A report on a visit to Africa. *W.H.O. internal document*.
- D'Arbela, P. G., Kanyerezi, R. B., and Tulloch, J. A. (1966). A study of heart disease in the Mulago Hospital, Kampala, Uganda. *Trans. roy. Soc. trop. Med. Hyg.*, **60**, 782.
- Davies, J. N. P. (1948). Endomyocardial fibrosis in Africans. *E. Afr. med. J.*, **25**, 10.
- (1961). The heart of Africa. Cardiac pathology in the population of Uganda. *Lab. Invest.*, **10**, 205.

- , and Ball, J. D. (1955). The pathology of endomyocardial fibrosis in Uganda. *Brit. Heart J.*, **17**, 337.
- Hutt, M. S. R., Ikeme, A. C., Lucas, A. O., Prata, A., Puigbo, J. J., Shaper, A. G., and Fejfar, Z. (1965). Cardiomyopathies. *Bull. Wld Hlth Org.*, **33**, 257.
- Nixon, P. G. F., Wooler, E. H., and Radigan, L. R. (1959). Mitral incompetence caused by disease of the mural cusp. *Circulation*, **19**, 839.
- Shaper, A. G. (1966). Endomyocardial fibrosis and rheumatic heart-disease. *Lancet*, **1**, 639.
- (1967). On the nature of some tropical cardiomyopathies. *Trans. roy. Soc. trop. Med. Hyg.*, **61**, 458.
- , and Coles, R. M. (1965). The tribal distribution of endomyocardial fibrosis in Uganda. *Brit. Heart J.*, **27**, 121.
- , and Williams, A. W. (1960). Cardiovascular disorders in an African hospital in Uganda. *Trans. roy. Soc. trop. Med. Hyg.*, **54**, 12.