Prednisone Treatment of Endocardial Fibroelastosis: Two Years' Experience

By

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Endocardial fibroelastosis (endocardial fibrosis) appears to be an independent clinical entity, but its pathomechanism is still obscure. There is little doubt that various pathological processes evolving in the same phase of the disease produce similar results.

A study of the pertaining literature clearly reflects the increasingly growing interest in the problems of endocardial fibroelastosis. Here we would refer to two major statistics only. According to FRUHLING and ADAM [9] the condition is responsible for 1 per cent of the total mortality of children up to 10 years of age. KELLY and ANDERSEN [13] found post mortem endocardial fibroelastosis in 20 per cent of 270 infants who had died from heart disease.

The outstanding pathological feature of endocardial fibroelastosis is a marked thickening, with an icing-like surface, of the endocardium lining both ventricles, but mostly the left one only, followed necessarily by hypertrophy or hypertrophy and dilatation of the left ventricle or both ventricles. The substrate of the fibroelastic layer is still a controversial subject. While it is now known to consist of collagenous and elastic fibres, its ground substance has not yet been identified with certainty, either by staining reactions, chemical investigations, or electron microscopy (BEVERIDGE, 5). Generally, this rigid layer does not extend to the cardiac valves, but it does penetrate the subendocardial musculature, interposing itself between the fibres or even breaking up bundles of them (FRUHLING and ADAM, 9; SCHWEISGUTH and NOUAILLE, 21; BLUMBERG and LYON, 6; STADLER *et al.*, 22).

Some authors claim to have recognized at necropsy different phases of an inflammatory process in the myocardium and the endocardium, depending at what stage of the disease the heart is seen (FRUHLING and ADAM, 9).

Until recently attention has been devoted almost exclusively to the morbid anatomy of the disease; it has been difficult to diagnose it in life, and very little has been said concerning its treatment. The hesitancy about the therapy is understandable: the cause of the disease is unknown. Its appearance in newborns and young

infants would suggest a congenital defect. Numerous other aetiological considerations have, however, been advanced including anoxia (ANDERSEN and KELLY, 3; BLUMBERG and LYON, 6), hyperoxaemia (KELLY and ANDERSEN, 13), vitamin deficiency (GRAY, 11), circulatory strain (SCHWEISGUTH and NOUAILLE, 21), and foetal endocarditis (FRUHLING and ADAM, 9; PANKE and ROTTINO, 17). Some authors regard the condition as a collagen disease (BÁNHIDI and BERKI, 4; HILL and REILLY, 12), while others, basing their view on certain analogies, suggest an allergic origin. Arguments can be put forward both in support of and against each of the aetiological hypotheses, but the question is still an open one.

The sum and substance is: we know of no causal therapy, and the clinician falls back on supporting the heart with digitalis to extend life as long as possible. Occasionally we may learn of sporadic attempts at treatment with adrenal cortical hormone. HILL and REILLY [12] were the first to report such an attempt and were followed by others [4, 16, 21, 23], but Hungarian authors had pointed to this possibility as long ago as 1955 (BÁNHIDI and BERKI, 4). Lasting results, however, have not been attained; survival has been prolonged from one or two months to a year.

The most promising results have been achieved by PAUL and ROBBINS [18, 19]. With a view to improving the blood supply to the myocardium these authors brought about sterile pericarditis by means of talc. One to five years later they could claim good general condition of their patients.

CASES AND TREATMENT

We have observed nine infants with endocardial fibroelastosis in the course of the last two and a half years.

According to the histories the first symptoms had appeared in one infant immediately after birth, in six infants at the age of 4 months, and in one each at 6 and 8 months. Gastrointestinal disorders had been recorded in five children. All but one had had repeated respiratory infections. Several had had pneumonia, often without fever. Usually during an intercurrent febrile disease, cyanotic episodes had been observed in four infants, and dyspnoea with paroxysmal cough in seven children. Such paroxysms had been accompanied in three cases by loss of consciousness but with no seizures; one had had typical Adams–Stokes attacks. At admission seven patients were markedly underdeveloped. All had anorexia.

The following symptoms characteristic of endocardial fibroelastosis were encountered. Tachycardia was obvious in six patients; in one there was bradycardia associated with complete atrioventricular dissociation. In all nine patients the heart was enlarged, especially the left ventricle. The most prominent abnormality, and one of value in differential diagnosis, was the not pulsating or barely pulsating, enlarged left ventricle. It was revealed by the X-rays in eight of the nine patients. A short functional systolic

murmur was heard in seven patients, but never a diastolic murmur. In three cases an apical gallop rhythm, extremely rare to occur in infancy, was audible. Seven children had severe dyspnoea, five of them with cyanosed lips. X-ray indicative of pulmonary congestion proved the stress laid on the small circulation in all the patients; in two infants pneumonia was actually observed.

Left heart insufficiency was accompanied by decompensation of the systemic circulation. Each of the nine patients had a markedly enlarged liver, and one of them developed extensive oedema.

Electrocardiography showed left heart preponderance in four patients. In three children normal R vector, and in two infants hypertrophy of both ventricles were found. In six patients the ST segment was depressed. A negative T_1 was recorded in four, and flat T_{1-2} in three cases. A negative T wave in V_4—V_6 was registered in four children. With the exception of one, in all our cases there was a deep negative Q_1 wave.

On the strength of these signs and symptoms endocardial fibroelastosis was diagnosed in all but one of the nine patients. In differential diagnosis three conditions were to be taken into consideration, glycogen storage disease, anomalous origin of the coronary artery, and viral myocarditis. Of these, glycogen storage disease could be ruled out in each of the cases. In one child, anomalous coronary artery was suspected on account of sudden shrill shrieks, similar to those heard from infants suffering anginal pain, and because of a peaked negative T wave in the electrocardiogram. Although no decisive proof could be produced on which to exclude viral myocarditis, a barely pulsating left ventricle and the general course of the disease seemed to lend more credence to a diagnosis of fibroelastosis.

In a 4-year-old child, the endocardial fibroelastosis was revealed only post mortem. There had been complete atrioventricular dissociation, and several Adams—Stokes attacks and the condition had been thought to be a congenital valvular defect. In addition to endocardial fibroelastosis aortic hypoplasia was found. A second child died 24 hours after admission. The clinical diagnosis was confirmed at necropsy, when in addition to endocardial fibroelastosis and anomalous origin of the coronary artery, a persistent ductus arteriosus, an open foramen ovale, and verrucous endocarditis were revealed. These two cases have been mentioned separately because in them fibroelastosis was associated with a congenital defect, constituting a syndrome which in recent literature has been discussed as an independent clinical entity (ANDERSEN and KELLY, 3).

On account of the symptoms of decompensation all patients were treated with digitalis which, however, produced but mild and transient improvement.

Considering the condition's appearance in infancy, the absence of congenital heart defects and the general post mortem findings, we share FRUH-

LING and ADAM's [9] view who principally regard endocardial fibroelastosis as a condition resulting from foetal endomyocarditis or possibly as a collagen disease. In spite of the current counterarguments, we feel we must insistently consider fibroelastosis as a progressing process and not a stationary condition.

Considerations on the pathomechanism of the condition and scant and summary references to its treatment with cortisone induced us to institute such therapy with the hope that it will inhibit progression and enhance the action of digitalis. Seven patients were treated with prednisone, in daily doses of 20 mg, which after some weeks were reduced to 10, 5 and 2.5 mg, respectively. After this course a maintenance dose was prescribed, like in rheumatoid arthritis; as a matter of fact, the patients are still taking the drug. For preventive purposes benzathine penicillin G was administered in due intervals and treatment was complemented with digitalis according to need. After 6 to 13 weeks in each of the patients there was marked improvement, with compensated circulation, return of appetite, and gain in weight.

RESULTS

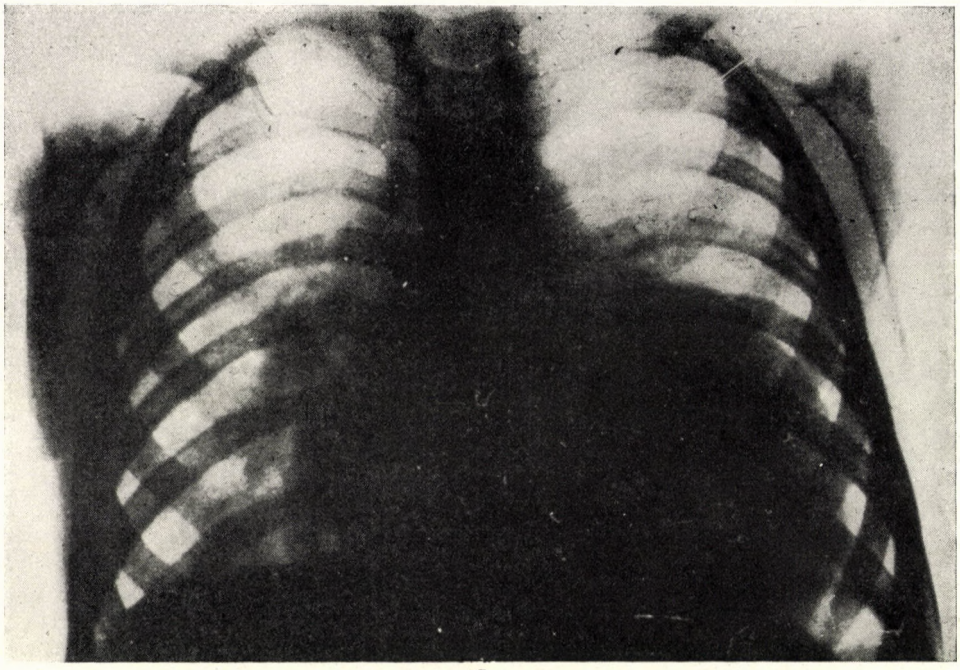
The patients were followed up regularly. Two of them have recently failed to appear; their fate is unknown to us. Five children are normally developed for their age, completely free of complaints, with their circulation compensated.

The X-rays in Figs. 1a, b and 2a, b

TABLE 1

Heart pressure and oxygen saturation in five patients with endocardial fibroelastosis as revealed by cardiac catheterisation after 18 months of treatment with prednisone

Case	V. c. Sup. %	V. c. inf. %	R. atrium		R. ventricle		A. pulm.		L. atrium		P. cap.		Capac.
			Hgmm	%	Hgmm	%	Hgmm	%	Hgmm	%	Hgmm	%	%
B. I.	75	71.5	17/12	73.5 74.5 70	30/15	67	30		22/15	100			
K. I.	69	65	23/17	71 69.5 65.5	34/12	65.5	40/20	50			22/14		
M. T.	67	73	6/0	69 73.0 70.0	40/7	58	45/25	65			32/20		
M. A.	70	70	5/2	71 68 67.5	60/10	65	38/20	65				100	
K. K.			15/6	73	58/4	71.5	60/30	71.5			12/3		94.8



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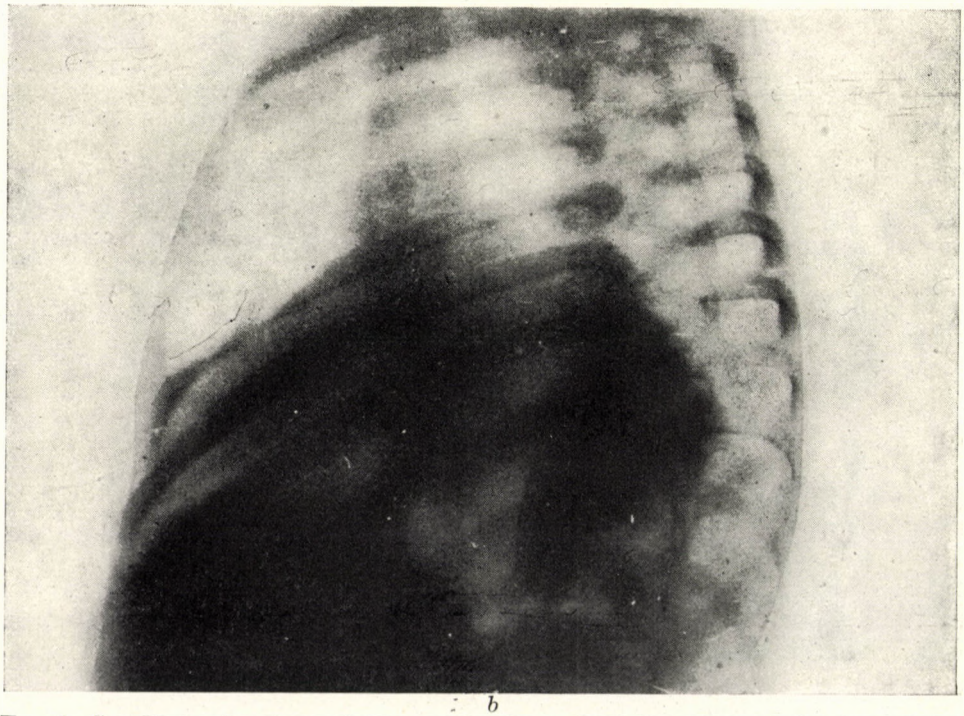

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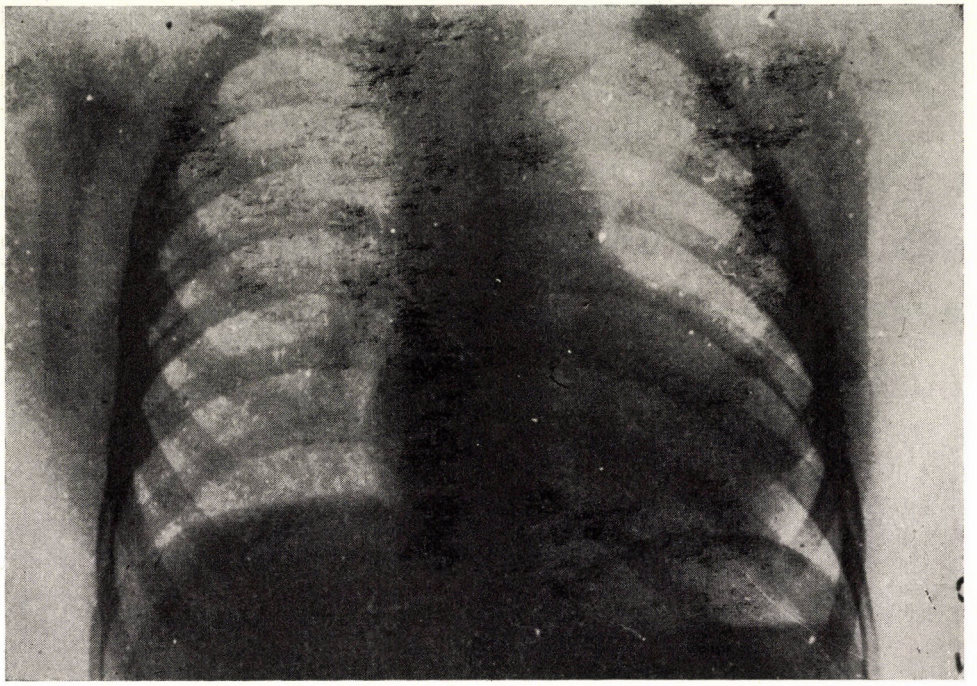
FIG. 1. Case M. A., female aged 18 months. X-rays in (*a*) anteroposterior and (*b*) left anterior oblique view prior to beginning treatment with prednisone



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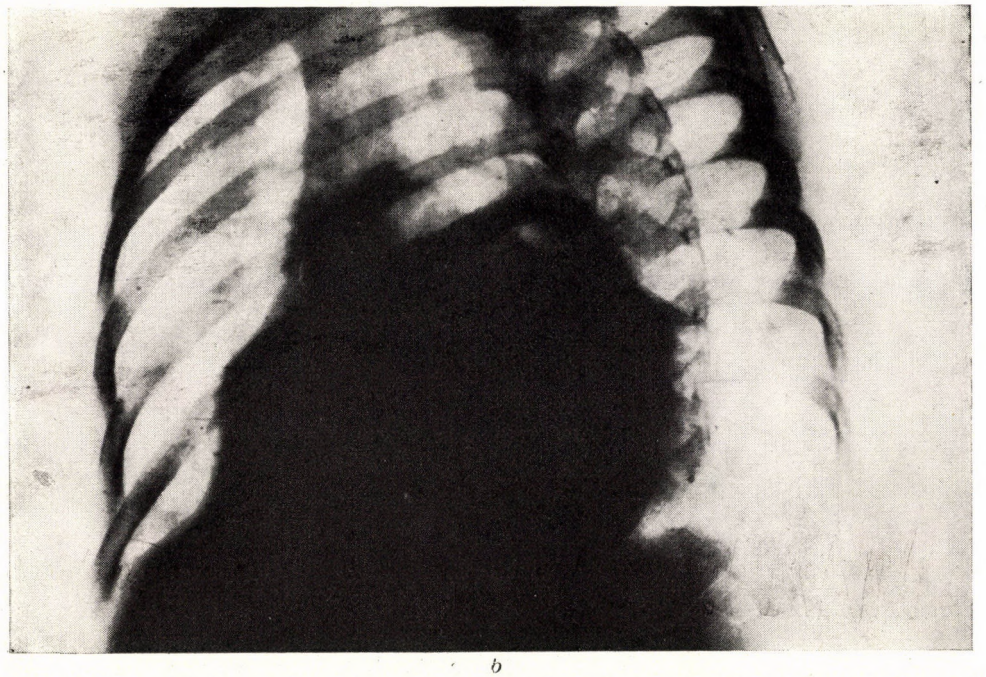

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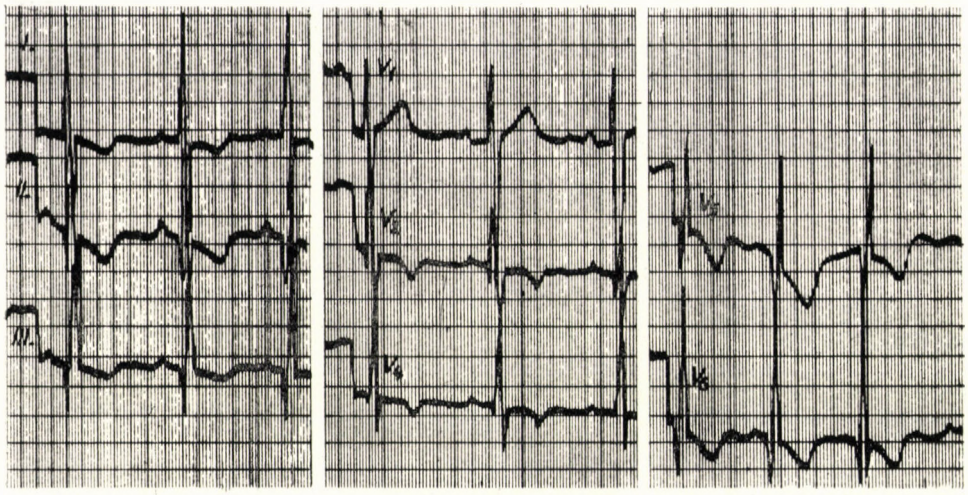
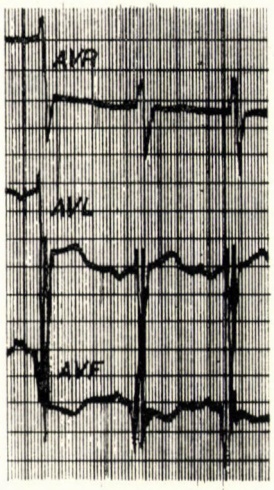
FIG. 2. Case M. A., a female aged 18 months. X-rays in (*a*) anteroposterior and (*b*) left anterior oblique view two years after beginning treatment with prednisone



M.A. 1270

10. XII. 1957



a

illustrate the favourable change in the size of the heart and the state of the left ventricle in one of our patients after 2 years of treatment with prednisone.

In all five patients the heart has decreased in transverse diameter; of course, without disappearance of the left ventricular enlargement. Pulsation of the left ventricle is still barely perceptible in three children, but satisfactory in the remaining two. The lung pattern became normal in each of the patients.

The electrocardiograms show no change in the left heart preponderance, but the ST segment has ceased to be depressed and the previously negative T waves in limb leads and V_4—V_6 have turned positive (Figs. 3a, b).

Cardiac catheterization had not been done at the inception of treat-

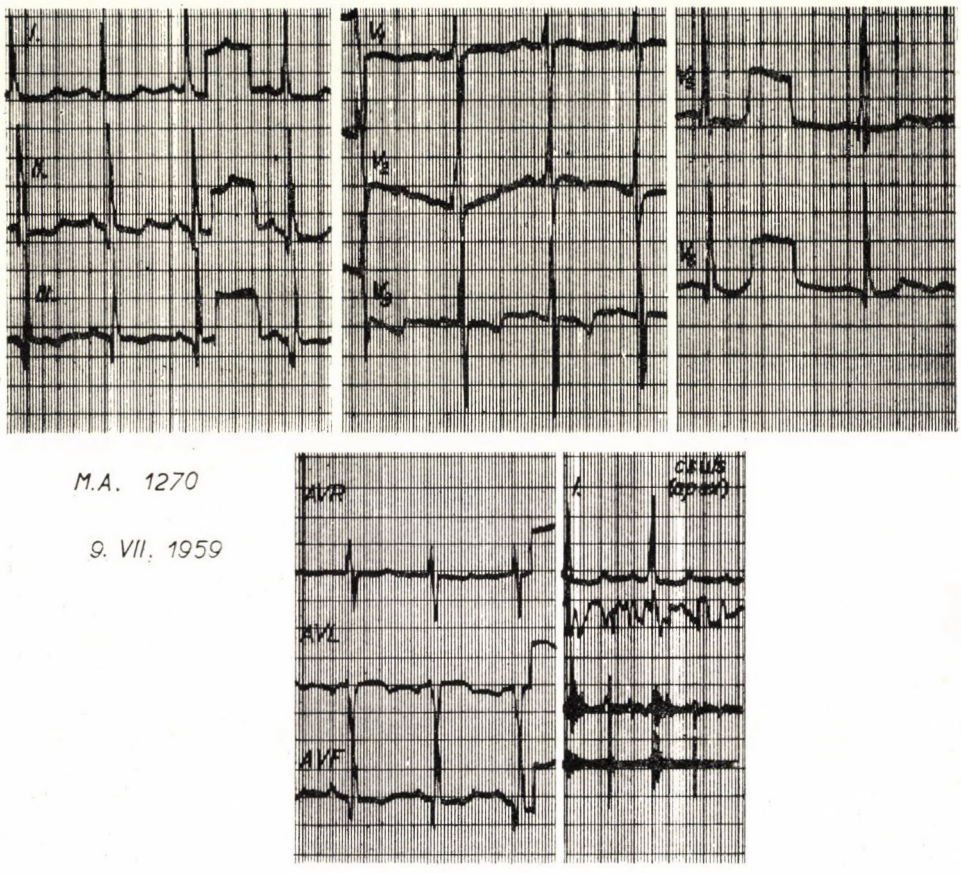


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FIG. 3. Case M. A., a female aged 18 months. Electrocardiogram (*a*) at beginning of treatment with prednisone and (*b*) two years later

ment, but was performed in all five patients at the follow-up examination (Table 1). On right-heart catheterization the elevated diastolic pressure and diastolic plateau formation, features currently held to be characteristic of endocardial fibroelastosis (LINDE *et al.*, 14; NADAS, 16) were still present in all of these children after a year and a half (Fig. 4). The explanation undoubtedly is that the thickly lined hypertrophic left ventricle limits the contraction of the right ventricle as well.

At present, after two years' continuous treatment, all the patients are doing well.

The marked improvement seen to persist after two years appears to show that — though the anatomical changes are seemingly irreversible — cortisone is capable of arresting

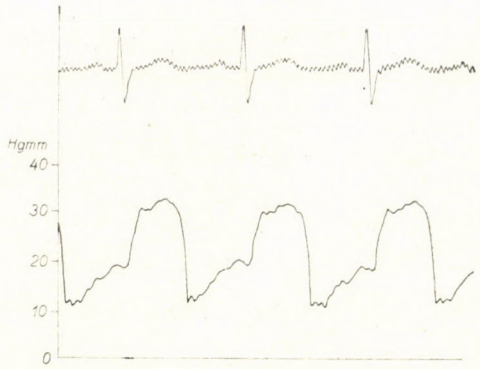

FIG. 4. K. I., a male aged 2 years. Intracavitary pressure curve of right ventricle with simultaneously recorded electrocardiogram

the progress of the condition, maintaining the circulatory balance, and ensuring normal development.

A follow-up of two years is of course too short to warrant any definite conclusions. Many more years will have to elapse before we shall be able to appraise the full merits of treatment with prednisone, although the present evidences of improvement seem to be more promising than those known from the literature or derived from our earlier attempts.

SUMMARY

Seven cases of endocardial fibroelastosis with all the classical signs characteristic of the condition have been subjected to continuous treatment with prednisone. The results after two years' treatment suggest that, although the original anatomical change is irreversible, prednisone is capable of inhibiting further progression of the condition and of ensuring circulatory balance and normal development of the patients.

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