and in the right 10·5 g. All tumours were shown to be neuroblastomas. The fifth child was carefully followed prospectively because of the extraordinary family history. At the age of 5 months a tumour mass was detected radiologically in the thorax at the level of T8. This was resected and shown to be yet another neuroblastoma. This child was vigorously treated and is well, now aged 4 years (J. Chatten, personal communication, 1969).

In this family there was also evidence of neural crest anomalies on the father’s side, in that the father and 3 of his sibs had café-au-lait spots. This evidence makes it difficult to reject the idea that some genetic factor may play a part in the aetiology of at least some neuroblastomas.

**Summary**

Two families are reported in each of which 2 children developed neuroblastoma. These are only the fifth and sixth families in which neuroblastoma has been conclusively shown to occur in sibs.

Our thanks to Mr. A. B. Maclean of the Cumberland Infirmary, Carlisle, to Mr. J. E. Monro, late of that hospital, to Mr. J. Oldfield of Eston Hospital, South Teeside, and Mr. J. Scott of the Departments of Surgery and Child Health, University of Newcastle upon Tyne.

**References**


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**Primary endocardial fibroelastosis**

**An inherited condition**

The name endocardial fibroelastosis (EFE) was introduced by Weinberg and Himelfarb in 1943, though the condition had been described under other names. Gowing (1953) defined endocardial fibroelastosis as a ‘congenital condition of unknown aetiology in which there occurs a diffuse thickening up of the mural endocardium associated in most cases with myocardial hypertrophy and leading to early death’. Andersen and Kelly (1956) divided their series of endocardial fibroelastosis into the common variety associated with other congenital cardiac anomalies and the rarer primary form without such anomalies, and found a familial incidence in 23% of the primary variety. Forfar et al. (1964), reviewing 72 cases of endocardial fibroelastosis, found multiple familial incidence only in the primary group which accounted for 22% of their cases. A familial incidence has also been described in the primary form by Dordick (1951), Winter et al. (1960), and Sellers, Keith, and Manning (1964).

The aetiology of primary EFE remains a mystery. Possible theories fall into 3 categories (1) inflammatory, (2) mechanical, and (3) hereditary.

A recent and attractive view is that EFE is a secondary response in certain individuals either to an intrinsic inherited myocardial defect, which results in inefficient myocardial function, or to grossly abnormal haemodynamics associated with a congenitally malformed heart (Moller et al., 1964). This view accords well with the clinical and haemodynamic findings in the natural history of primary and secondary varieties.

Though a number of authors have dealt with the hereditary element in EFE, most have not assessed the two forms separately. Generally the mode of inheritance has been assumed to be an autosomal recessive type. Our experience in Edinburgh suggests a higher incidence in families with affected children than would be expected from recessive inheritance. This paper deals with 4 families having more than one child affected. In each family at least one child has been confirmed at necropsy as suffering from primary EFE.

**Case material**

The clinical, electrocardiographic, and pathological data are presented in the Table.

**Family I**. There were 3 children in this family. The first child (Case 1, female) had the typical clinical picture of EFE in infancy but remains well on digoxin, though with reduced exercise tolerance. Cardiac catheterization has not been carried out. The second child (female) is apparently normal. The third child (Case 2, male) died in infancy after a brief but typical illness, and primary EFE was confirmed at necropsy. There is no family history of heart disease.

**Family II**. There were only 2 children in this family. The first (Case 1, male) died suddenly and a procurator...
**Short reports**

**Clinical data of families and affected children**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sex</th>
<th>Onset of symptoms</th>
<th>Age at death</th>
<th>Initial radiological findings</th>
<th>Initial ECG findings</th>
<th>Necropsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>F</td>
<td>2 mth</td>
<td>—</td>
<td>Left atrial and left ventricular enlargement</td>
<td>LAD, LVH, and 'strain'</td>
<td>Large dilated LV with EFE affecting only this chamber; no other cardiac abnormality</td>
</tr>
<tr>
<td>Case 2</td>
<td>M</td>
<td>2 mth</td>
<td>2 mth</td>
<td>Left atrial and left ventricular enlargement</td>
<td>LVH and 'strain'</td>
<td></td>
</tr>
<tr>
<td><strong>Family II</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>M</td>
<td>6 wk</td>
<td>2½ mth</td>
<td>Not x-rayed</td>
<td>No ECG</td>
<td>Cardiac enlargement with EFE affecting all chambers, particularly LV and LA; no other cardiac abnormality</td>
</tr>
<tr>
<td>Case 2</td>
<td>F</td>
<td>2 mth</td>
<td>2½ yr</td>
<td>Left atrial and left ventricular enlargement</td>
<td>LVH and 'strain'</td>
<td>LV large and dilated with EFE; other chambers normal; no other cardiac abnormality</td>
</tr>
<tr>
<td><strong>Family III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>M</td>
<td>6 wk</td>
<td>7½ mth</td>
<td>Left atrial and left ventricular enlargement</td>
<td>LVH</td>
<td>LV large, dilated with marked EFE; mitral valve cusps involved by process; no other cardiac abnormality</td>
</tr>
<tr>
<td>Case 2</td>
<td>F</td>
<td>3 mth</td>
<td>3½ mth</td>
<td>Left ventricular enlargement</td>
<td>LVH and 'strain'</td>
<td>Both RV and LV were large, dilated with marked EFE particularly affecting the LV; no other cardiac abnormality</td>
</tr>
<tr>
<td>Case 3</td>
<td>F</td>
<td>3 mth</td>
<td>4 yr</td>
<td>Left ventricular enlargement</td>
<td>LVH</td>
<td>LV dilatation and enlargement; all four chambers affected by EFE but particularly the LV; no other cardiac abnormality</td>
</tr>
<tr>
<td><strong>Family IV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>F</td>
<td>4 mth</td>
<td>4 mth</td>
<td>Left atrial and left ventricular enlargement</td>
<td>LVH and 'strain'</td>
<td>Large dilated LV with marked EFE; no other cardiac abnormality</td>
</tr>
<tr>
<td>Case 2</td>
<td>F</td>
<td>1 mth</td>
<td>8 mth</td>
<td>Generalized cardiac enlargement, mainly left atrial</td>
<td>Normal initially; later showed LVH and 'strain'</td>
<td>RA and LA enlargement; RV hypertrophied with EFE; LV dilatation and hypertrophy with marked EFE; no other cardiac abnormality</td>
</tr>
</tbody>
</table>

LVH, left ventricular hypertrophy; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; EFE, endocardial fibroelastosis; LAD, left axis deviation.

fiscal necropsy confirmed primary EFE. The second (Case 2, female) presented with typical findings in infancy, was investigated by cardiac catheterization, and made reasonable progress on medical therapy. She died at 2½ years and primary EFE was found at necropsy. There is no family history of heart disease.

**Family III.** Of 9 children born to these parents, 4 are dead. The eldest died of 'birth injuries' at 5 weeks—no further information is available. The other 3 deceased children (Case 1, male, and Cases 2 and 3, female) all had classical clinical history and a picture of primary EFE. The third was investigated by cardiac catheterization. At necropsy all these cases showed primary EFE. The parents are normal and there is no other heart disease in the family.

**Family IV.** The mother of this family is the full sister of the mother in Family III. She had 2 children (both females) by different fathers. Both children (Cases 1 and 2) died in infancy with a history compatible with primary EFE. Necropsy confirmed primary EFE in both cases. There is no other heart disease in the family.

**Discussion**

Mitchell et al. (1966) laid down stringent criteria for the diagnosis of endocardial fibroelastosis. The disease can be diagnosed with reasonable certainty clinically, and cardiac catheterization and angiocardiography give characteristic findings. Absolute confirmation of the diagnosis however is only possible at necropsy. The endocardium is smooth, porcelain-like, and greatly thickened with proliferation of elastic and fibrous tissue and these changes frequently extend to involve the valves...
(particularly the mitral and aortic). The papillary muscles and chordae tendineae are enlarged. Though all 4 heart chambers may be involved, the left atrium and left ventricle are most frequently affected. Myocardial hypertrophy or dilatation are usually present.

We are confident that our cases fulfil the criteria for primary endocardial fibroelastosis. In 8 out of 9 the diagnosis was confirmed at necropsy, and in the case of the surviving child in Family I the diagnosis was based on investigation and clinical assessment in 2 hospitals. Virus studies have been carried out in this case and were negative. Clinical electrocardiographic and radiological evidence points to EFE as the diagnosis. The 4 families reported include all the cases of primary endocardial fibroelastosis diagnosed in the Edinburgh Northern Group of Hospitals in the last 5 years. In each family more than one child has been affected, and in Families III and IV, 2 sisters have had affected children by 3 fathers. 9 affected children out of a total of 16 is a remarkably high incidence. The parents are all apparently normal. This striking familial incidence appears to indicate a strong hereditary element in the aetiology of EFE. None of these children had EFE secondary to other congenital cardiac defects, and in the overall series of children seen in this unit with EFE there is no family with more than one child affected when EFE was associated with other cardiac anomalies. The hereditary element appears confined to the primary type of EFE. Though the number of families is too small to make dogmatic statements concerning the mode of inheritance, the 1 : 1 ratio of affected and unaffected children and the equal proportion of the sexes affected at least suggests autosomal dominant inheritance.

To our knowledge there has been only one report of primary EFE in mother and child (Moller et al., 1966). The child died at 11 months in cardiac failure, and primary EFE was found at necropsy. The mother had died two weeks after delivery at 22 years of age and her necropsy also confirmed EFE.

A familial incidence of primary EFE affecting several sibs in one family has been reported frequently. Not all of these reports give full details of other sibs in the family. A scrutiny of these reports does suggest that the familial pattern occurs in primary EFE and not in the secondary variety. In 1968 Hallidie-Smith and Olsen described a family of 3 sibs apparently suffering from primary EFE who had no other intracardiac abnormalities, but had coarctation of the abdominal aorta.

There are several reports of one of monozygous twins being affected (Kelly and Andersen, 1956; Kempton, 1959; Studler, 1961). Ullrich (1938) described triplets of whom two were monozygotic and died of EFE. The third baby was normal and lived.

Vestermark (1962) described 2 affected sibs whose parents were first cousins, and Rafinski et al. (1967) described a similar family with 3 sibs dying at 10, 11, and 13 years. Consanguinity in the parents is not described in the other reported families with multiple occurrence of EFE.

In 1965 Nielsen surveyed the published reports of multiple primary EFE. These collected cases with Rafinski’s families and Hallidie-Smith and Olsen’s family of 3 give a total of 17 families recorded as having more than one child affected by primary EFE.

Where details of all sibs are known, the number of affected children exceeds or equals the number of normal children in each family. This accords well with the findings in our own cases. However, too much significance must not be placed on the reports of multiple occurrence in families as there is no corresponding information in families where only one child is affected. Such families are not usually reported in the literature and the conclusions regarding incidence and inheritance might be radically different if such information were available.

Where population studies have been undertaken as in the National Institutes of Health studies in Bethesda, Maryland, an incidence of primary EFE in 1 in 4000-6000 total births has been noted, but no incidence of more than one affected child in a family found.

Primary endocardial fibroelastosis is an important cause of death in infancy and early childhood, and according to Lambert and Vlad (1958), it may account for half as many deaths in infancy as transposition of the great arteries. If it is accepted, as our cases and the review of the literature suggest, that heredity plays an important part in the aetiology, then correct genetic counselling is of vital importance for parents who have had an affected child. Nielsen (1965) has suggested that primary EFE is a recessive autosomal trait. Our findings favour rather the dominant autosomal mode of inheritance with incomplete penetrance. But, more information, perhaps from large-scale population studies, is necessary before a definite pattern of genetic inheritance can be proved.

**Summary**

Four families each with more than one child affected by primary endocardial fibroelastosis are
reviewed. The diagnosis was made at necropsy in 8 out of the 9 children. On the basis of these families and a review of reported familial incidence in the literature, it is suggested that this condition may be a dominant autosomal trait rather than a recessive autosomal as previously suggested.

The first child in Family III was under the care of Professor J. L. Henderson; the second child in Family III and the second child in Family IV were under the care of the late Professor R. W. B. Ellis. We are indebted to Dr. Douglas Bain for details of the necropsies which he carried out.

REFERENCES


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Glomerulonephritis associated with Staphylococcus albus in a Spitz Holter valve

The association of glomerulonephritis with infection of a ventriculoatrial shunt by Staphylococcus albus was first described by Black, Challacombe, and Ockenden (1965), and the presence of γ-globulin and complement in the glomeruli suggested that the glomerulonephritis was due to an immune response. The findings of immune deposits on the glomeruli in similar cases was also reported by Stickler et al. (1968) and Rames et al. (1970), who in addition described electron dense deposits in the glomeruli of their 3 patients. Staphylococcal antigen in the glomeruli of a further case of shunt nephritis was found by Kaufman and McIntosh (1971). 5 cases presented at clinical meetings were quoted by Rames et al. (1970) and 2 more cases were reported briefly by Leumann, Stauffer, and Wegmann (1971).

In this paper we report the findings in a 3-year-old boy who developed the nephrotic syndrome in association with Staph. albus infection of a ventriculoatrial shunt, and describe the light and electron microscopic changes in his kidney. He had a very high level of antibodies to Staph. albus, providing, for the first time, direct evidence of antibody response to this organism.

Case report

This boy had a Spitz Holter valve inserted at the age of 10 months for hydrocephalus due to aqueduct stenosis. He had hypospadias, undescended testes, slight webbing of the third and fourth fingers, incurved little fingers, and was mentally retarded. Chromosomal analysis showed an elongated short arm of chromosome 2.

At the age of 3½ years his spleen became palpable and soon afterwards he began to sweat excessively. Three months later he was admitted to hospital for surgical correction of a strabismus. He was febrile (temp. 37-8 °C), sweating, and had generalized oedema.
Primary endocardial fibroelastosis. An inherited condition.
A S Hunter and A J Keay

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