

# Cardiac tumours in infancy and childhood<sup>1</sup>

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*With the aim of defining the clinical profile of cardiac tumours in childhood and of promoting their early recognition, a study of these relatively rare conditions was undertaken as a joint project by the members of the Association of European Paediatric Cardiologists. Within 5 years, 29 cases were collected from 15 centres. This report is limited to 22 primary cardiac tumours that were histologically verified and classified as 'benign'. There were 6 rhabdomyomas, 6 teratomas, 5 fibromas, 3 myxomas, and 2 haemangiomas. No patient with a well-documented primary malignant tumour was encountered. Though classified as 'benign', such tumours caused death in 11 patients by encroachment upon the cardiac cavities or compression of the conducting tissues. The salient clinical features and the macroscopical and histological findings are briefly reviewed. Thirteen cases were correctly diagnosed during life and before operation. Of the 11 children operated upon, 8 made a complete recovery: 4 had a teratoma, 3 a fibroma, and 1 a myxoma.*

In 1965 at the annual meeting of the Association of European Paediatric Cardiologists in St Andrews, Scotland, it was proposed to start a joint research project on the incidence and clinical profile of cardiac tumours in childhood. Within 5 years, 29 cases (Table 1) were collected from 15 centres: Amsterdam, Birmingham, Brussels, Göteborg, Helsinki, Leiden, Lille, Lisbon, Leuven, Nancy, Nijmegen, Rome, Rotterdam, Stockholm, and Zürich.

The final analysis was limited to primary cardiac tumours that were verified at necropsy or operation and in which histological proof was obtained. Of the original 29 cases, 5 had to be discarded as the patients were alive and not operated upon. Two malignant tumours, one haemangiosarcoma and one small cellular sarcoma, were excluded because they were probably due to secondary invasion from an extracardiac neoplasm. No patient with a well-documented primary malignant tumour was encountered.

The remaining 22 tumours (Table 2) may be classified as 'benign' in a strictly histological sense. It is obvious indeed that these new growths, because of their critical location within the heart, may readily encroach on the cardiac cavities or compress the conduction tissue. This is illustrated by the observation

that in 11 children in the present series death could be attributed directly to a histologically 'benign' tumour.

The salient clinical, macroscopical, and histological features in 22 patients are listed in Table 2. Cases that have been published separately are referred to by the name of the first author and the year of publication. In the following review, which does not intend to give a complete account of each individual patient, emphasis will be placed on signs that were common to several patients and appear to be of major clinical significance.

TABLE 1 *Distribution according to histological type*

	No. of cases
Benign tumours	
Rhabdomyoma	6
Teratoma	6
Fibroma	5
Myxoma	3
Haemangioma	2
Malignant tumours	
Haemangiosarcoma	1
Small cellular sarcoma	1
Total number with histological proof	24
Number without histological proof (4 living and being followed)	5
Total number	29

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TABLE 2

Case No. centre reference	Sex and age	Clinical findings	Diagnosis during life	Findings at operation or necropsy	Histological findings
1 Birmingham	M 4 dy.	Tracheo-oesophageal fistula; died following operation	Heart disease not suspected	<i>Necropsy</i> : multiple small nodules scattered through myocard.; brain: tuberous sclerosis	Rhabdomyoma
2 Birmingham	M 2 yr.	Murmur since age of 9 mth.; epileptic attacks; thrill and murmur in aortic area	Aortic stenosis; ? SBE	<i>Necropsy</i> : multiple subendocardial nodules in RV and LV; SBE vegetations on moderately stenosed aortic valve; brain: tuberous sclerosis	Rhabdomyoma
3 Lille: Dupuis, Ducoulombier, and Nuyts (1965)	M 6 wk.	Dyspnoea and cyanosis since birth; no murmur; x-ray: cardiomegaly + +; ECG: marked RVH; died following R paraplegia and L facial palsy	? Pulmonary stenosis ? cerebral thrombosis	<i>Necropsy</i> : large lobulated mass in RV narrowing P and T valves; several small nodules in RV; brain: not examined	Rhabdomyoma
4 Louvain	F 13 mth.	CHF; bradycardia (36/min.) alternating with tachycardia and bigeminy; Gr. 3/6 syst. murmur at 3-4L; x-ray: cardiomegaly; ECG: biventricular hypertrophy; intermittent pre-excitation syndrome and atrial reciprocal rhythm	Endocardial fibro-elastosis	<i>Necropsy</i> : large nodule (2 x 2 cm.) in upper part of IV septum producing obstruction of RV and LV outflow; multiple smaller nodules; brain: not examined	Rhabdomyoma
5 Rotterdam: de Villeneuve, Schenk, and Daamen (1969)	M 2 dy.	CHF, cyanosis, shock, no murmur; x-ray: extreme cardiomegaly; ECG: complete RBBB	? Hypoplastic LV ? myocarditis	<i>Necropsy</i> : large lobulated mass (3.5 x 3 cm.) in IV septum producing LV outflow obstruction; multiple smaller nodules; brain: tuberous sclerosis	Rhabdomyoma
6 Helsinki	F 15 dy.	CHF; Gr. 2/6 syst. murmur at 2L; x-ray: cardiomegaly; ECG: intraventricular conduction delay; died in ventricular fibrillation	Not specified	<i>Necropsy</i> : huge tumour in IV septum; slitlike RV and LV cavities; brain: not examined	Rhabdomyoma
7 Birmingham	M 8 yr.	Murmur since age 1 yr.; thrill and murmur. 2L; late P2; ECG: RVH; x-ray: calcification (ring shadow) in RV; cath.: moderate infund. gradient	Calcified mass in RV producing pulmonary stenosis (angio)	<i>Operation</i> : rounded tumour (2 cm.) in infund. RV; resection; complete recovery	Mass of acellular whorled collagen; extensive calcification; fibroma
8 Nijmegen	M 4 yr.	Bouts of tachycardia up to 220/min. gr. 2/6 murmur. 2R and 2L; x-ray: moderate cardiomegaly; ECG: sharply negative T waves in I, aVL, V3-V6, Q in aVL; intermittent ventricular tachycardia, LVH R and L cath.: N press	Mass compressing RV and LV to R and anteriorly (angio)	<i>Operation</i> : intracardiac tumour in LV; resection; recovery; (ECG remains abnormal)	Hamartoma
9 Stockholm: Björk <i>et al.</i> (1967)	M 13 mth.	Murmur detected at 8 mth.; gr. 4/6 murmur at 2L; wide splitting S <sub>2</sub> ; ECG: moderate RVH; x-ray: N; cath.: 15 mm. gradient AP-RV	Mass in RV outflow (angio)	<i>Operation</i> : rounded mass (3 x 3 x 4 cm.) in RV infund.; resection; complete recovery	Fibroma
10 Louvain: Van der Hauwaert, Corbeel, and Maldague (1965)	M 16 mth.	Diastolic murmur at 4L; pulsating liver; giant a-waves; cath.: a-waves 20 mm. Hg in RA	Mass in RV producing tricuspid stenosis (angio)	<i>Operation</i> : extensive mass in RV; inoperable; <i>Necropsy</i> : mass in RV and IV septum	Myoma or fibromyoma
11 Zürich	M 5 mth.	Pneumonia; severe gastro-enteritis; shock; x-ray: slight cardiomegaly; ECG: infarction pattern (Q neg. T wave in II, III, and aVF)	Septicaemia; cardiac tumour not suspected	<i>Necropsy</i> : egg-shaped tumour in posterior part LV (3 cm.)	Fibroma
12 Helsinki	M 10 yr.	Family history: mother operated for bi-atrial myxoma; presenting sign: femoral art. embolus; no murmur; ECG and x-ray: nl; cath.: N	LA myxoma (angio)	<i>Operation</i> : resection of soft friable tumour in LA (4 x 5 cm.) originating from LA septum; complete recovery	Myxoma
13 de Paiva <i>et al.</i> (1967)	M 16 yr.	Peripheral emboli; paresis; murmur changing with posture; x-ray and ECG: N	Space-occupying lesion in LV (angio)	<i>Operation</i> : pedunculated tumour in LV (3 cm.) originating from IV septum; resection; died postop.	Myxoma
14 Rome: Carile, Rutiloni, and Seganti (1968)	M 4 yr.	Dyspnoea; diast. rumble and accentuated S <sub>1</sub> at apex; x-ray: cardiomegaly + LA + hilar congestion; ECG: RVH and RAH; died in CHF	Rheumatic heart disease	<i>Necropsy</i> : jelly-like mass (3 x 5 cm.) in LA adherent to IA septum	Myxoma
15 Helsinki	F 5 yr.	Murmur at age 4 yr.; gr. 3/6 murmur at 2L and 2R; ECG: 2/1 AV block, ventricular extrasyst.; x-ray: slight cardiomegaly, bizarre contour; cath.: slightly increased PA pressure	LV fibroma; filling defect lateral wall LV (angio)	<i>Operation</i> : vascular tumour in LV narrowing outflow; died postop.	Haemangioma in LV and IV septum
16 Helsinki: Linder <i>et al.</i> (1965)	M 7 yr.	Murmur and complete AV block since age 2 yr.; slight syst. murmur; mid-diast. murmur at apex; ECG: complete AV block; x-ray: N; died in 1st Adams-Stokes attack	Congenital AV block; tumour not suspected	<i>Necropsy</i> : vascular tumour in IV septum, extending into IA septum	Haemangioma in IV septum, invading AV node and bundle

TABLE 2 (contd.)

Case No. centre reference	Sex and age	Clinical findings	Diagnosis during life	Findings at operation or necropsy	Histological findings
17 Nancy: Pernot <i>et al.</i> (1968)	F 11 dy.	Tachypnoea; cyanosis; CHF; no murm.; x-ray: extreme cardiomegaly; ECG: low voltage	Intrapericardial tumour, outlined by artificial pneumopericardium	Operation: intraperic. cystic tumour adherent to aorta; resection; complete recovery	Teratoma
18 Nancy: Pernot <i>et al.</i> (1968)	F 3 mth.	Acute respir. distress; CHF; no murm.; x-ray: extreme cardiomegaly; ECG: low voltage	Intrapericardial tumour, outlined by pneumopericardium and angio	Operation: identical findings as in previous case; resection; complete recovery	Teratoma
19 Leiden	M 3 mth.	Dyspnoea; anoxic spells; no murm.; x-ray: extreme cardiomegaly; ECG: low voltage; cath.: slight increase; RA, RV, and PA press.	Extracardiac mass displacing heart to the L and compressing RA (angio)	Operation: identical findings; resection; complete recovery	Teratoma
20 Stockholm	F 7 yr.	Incidental x-ray finding: bulging mass LV border containing small calcifications; ECG: N; cath.: N	Cardiac tumour compressing L upper part LV (angio)	Operation: Cystic tumour adherent to pericardium (10 × 5 × 3 cm.); resection; complete recovery	Teratoma
21 Birmingham	M 3 yr.	Hydrocephalus; no cardiac signs or symptoms; x-ray: nl.; died after emboli from ventriculo-jugular anastomosis	Heart disease not suspected	Necropsy: intrapericard. cystic tumour adherent to aorta	Teratoma
22 Louvain	M 1 dy.	Cyanosis and CHF at birth; loud syst. murm. lower L sternal border	Neonatal distress	Necropsy: huge multilocular cystic tumour originating from IV and IA septum	Teratoma (intracardiac)

N = normal; N press = normal pressure

### Rhabdomyoma

Six patients (Cases 1 to 6) had rhabdomyoma. All were less than 2 years of age, 4 being 6 weeks or younger.

In one patient (Case 2) a murmur suggested the possibility of aortic stenosis. At necropsy a moderately stenosed aortic valve, damaged by bacterial endocarditis, was found as well as scattered rhabdomyomas. The other patients had either no murmur or only a slight and non-specific murmur.

Congestive heart failure and conspicuous to extreme cardiomegaly on x-ray (Fig. 1) were present in the 4 children whose death may be attributed to tumour invasion. One of the two remaining patients (Case 2) died as a result of

bacterial endocarditis; and in the other (Case 1) a rhabdomyoma was an incidental finding at necropsy.

FIG. 2 *Rhabdomyoma (Case 4). Longitudinal section through the heart showing a large nodule (2 × 2 cm.) in the upper part of the interventricular septum. Smaller nodules are seen in the superior part of the free wall of the right atrium and in the apex of the heart. Scale at the bottom indicates cm.*

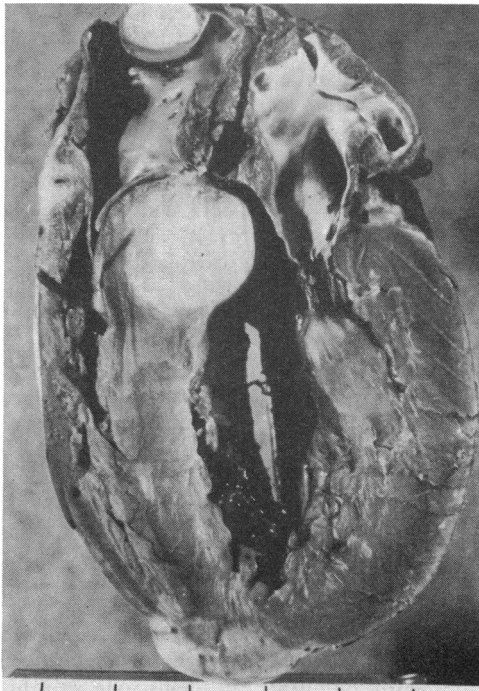
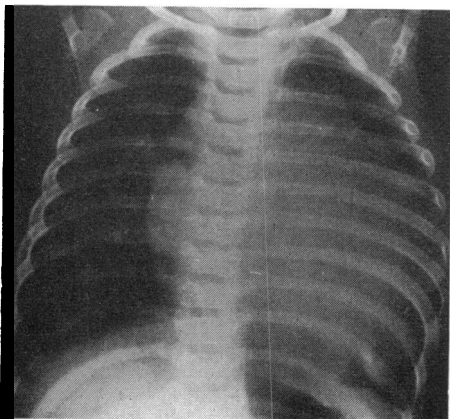


FIG. 1 *Obvious cardiomegaly in an infant (Case 4) with rhabdomyoma.*



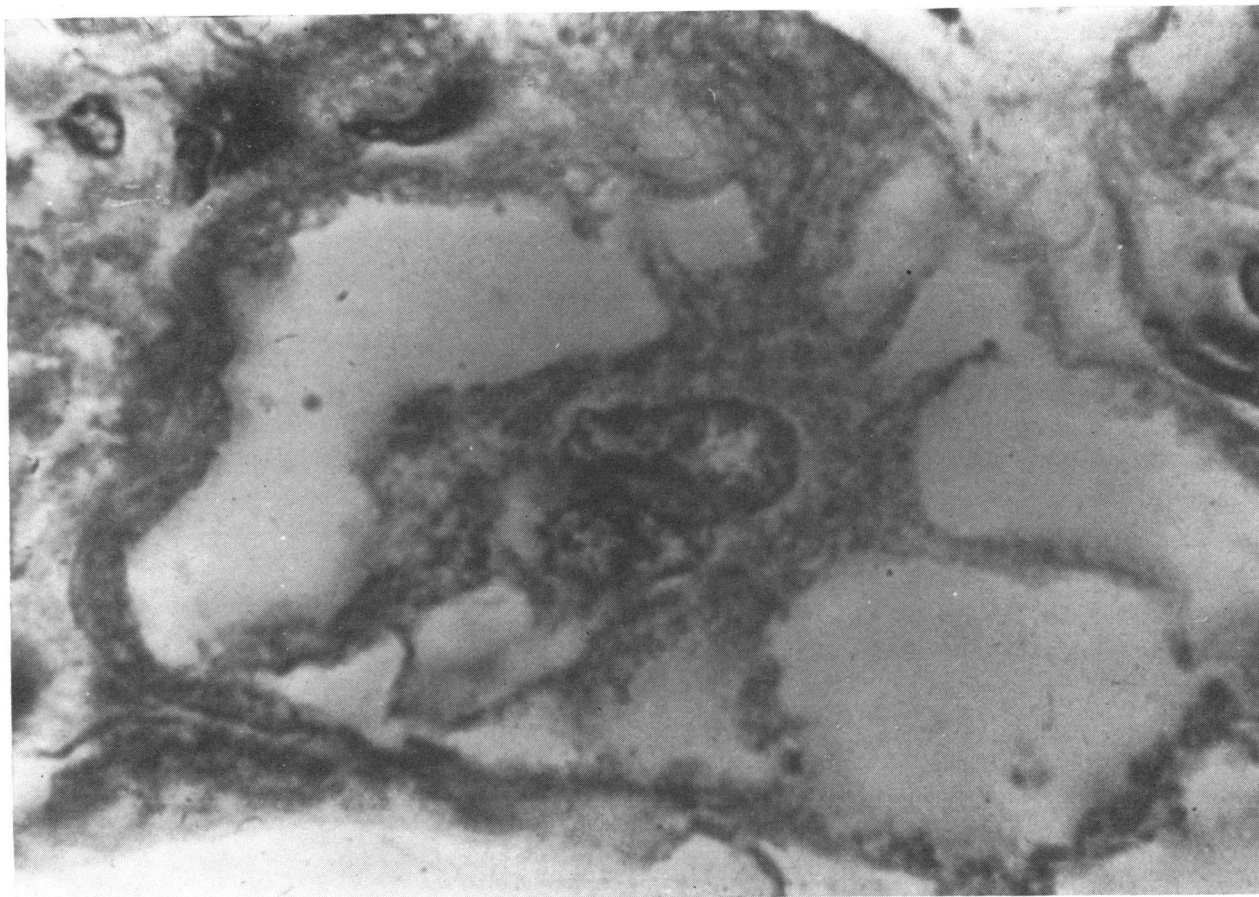


FIG. 3 *High magnification of rhabdomyomatous tissue (Case 5) showing characteristic spider cells.*

Cardiac rhythm disturbances were a major problem during life and the immediate cause of death in 2 infants. In one of them (Case 4) an intermittent pre-excitation syndrome and bouts of reciprocating tachycardia were possibly produced by impulse re-entry via accessory atrioventricular pathways in the rhabdomyomatous tissue. At necropsy (Fig. 2) a large nodule was found in the upper part of the interventricular septum, as well as smaller ones in the ventricles and atria. In one neonate (Case 5) complete right bundle-branch block was presumably caused by compression of the right bundle. In none of these 6 children was a cardiac tumour suspected during life. The presumptive diagnoses are listed in Table 2.

Macroscopical findings were strikingly similar: in all cases the nodules were multiple, firm, white, or greyish, scattered throughout the myocardium. The largest nodule (3 × 3.5 cm.) was found in the youngest

infant (Case 5). In 3 instances a nodule was situated in the upper part of the interventricular septum. Large nodules often produced narrowing of the right ventricular outflow tract. The microscopical finding of large vacuolated 'spider cells' (Fig. 3) confirmed the diagnosis. In 3 of the children in whom the brain was examined, typical lesions of tuberous sclerosis were found. This is in keeping with previous reports in which the common association of this brain lesion with rhabdomyomatosis has been stressed.

#### **Fibroma and hamartoma**

Five patients (Cases 7-11) belonged to this group which is histologically less well defined than the rhabdomyomas (Bigelow, Klinger, and Wright, 1954; Geha *et al.*, 1967). Of the 5 tumours in our series 3 were reported as fibromas, one as a hamartoma and one as a

myoma or fibromyoma. All the patients were male. Their ages ranged from 5 months to 8 years.

In one infant (Case 11) who died from an unrelated cause, the tumour was an incidental post-mortem finding. Ventricular tachycardia was the presenting sign in one child (Case 8, Fig. 4). The 3 remaining patients were admitted to hospital for evaluation of heart murmurs (Cases 7, 9, and 10) which suggested the presence of tricuspid stenosis in one and pulmonary stenosis in 2 patients. In these 3 patients the electrocardiogram was compatible with the diagnosis of 'stenosis', which was further confirmed by the measurement of a pressure gradient at cardiac catheterization.

In 2 patients the electrocardiogram revealed an infarction-like pattern, one over the high lateral part of the left ventricle (Case 8, Fig. 5), the other in the inferior leads (Case 11). X-ray examination was practically diagnostic in one patient (Case 7) in whom it showed a calcification within the heart. In the others slight or moderate cardiomegaly were noted but added little to the diagnosis.

It is noteworthy that in the 4 patients who presented with cardiac signs, the correct diagnosis of an intracardiac space-occupying lesion was made on angiocardiograms. Three of them were operated upon successfully. In one the tumour was too extensive to be resected.

### Myxoma

In contrast to its relatively high incidence in adults, myxomas are rare in childhood. Only 3 cases (Cases 12-14) were encountered. These patients were older than the average age in the other diagnostic groups, which confirms the impression that the incidence increases with age.

In 2 patients (Cases 12 and 13) the presenting symptoms were produced by peripheral arterial emboli. In one patient this immediately raised the suspicion of atrial myxoma in view of an unusual family history: the child's mother had been operated for a bi-atrial myxoma. In the other patient, who sustained at least three arterial emboli, the diagnosis was suggested by the variable character of mitral murmurs that changed with body posture. In both patients angiography showed a mass which was localized in the first patient to the left atrium and in the second to the left ventricle. The former was successfully resected but the boy with the left ventricular myxoma died in the postoperative period. In the third patient (Case 14) the diagnosis was not made during life. His clinical signs mimicked mitral valve

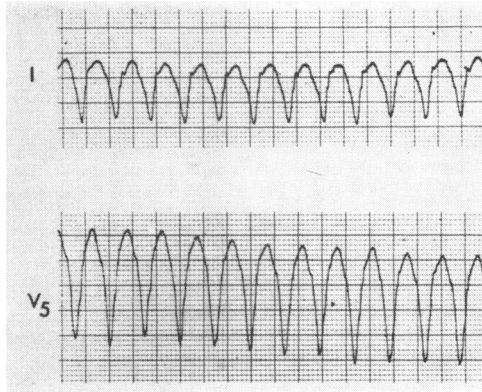


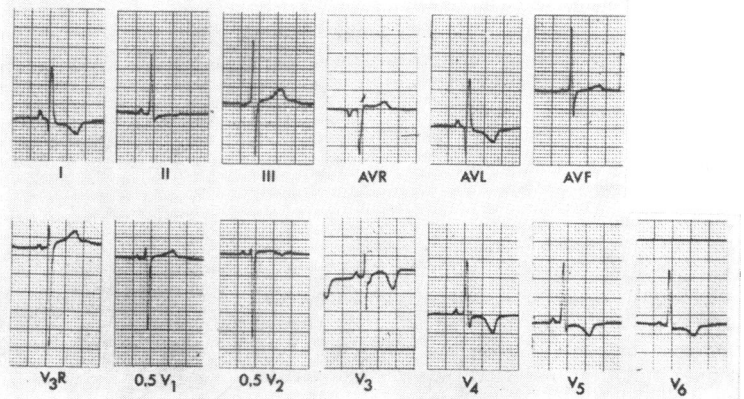
FIG. 4 Ventricular tachycardia was the presenting sign in a boy with a left ventricular fibroma (Case 8). He was resuscitated and later operated upon successfully.

disease. Systemic reactions consisted of a raised sedimentation rate and increased plasma globulins, the  $\alpha_2$  fraction being as high as 17.8 per cent of a total protein concentration of 6.8 g./100 ml. At necropsy a large left atrial myxoma was found attached to the interatrial septum.

### Haemangioma

The 2 patients with a cardiac haemangioma (Cases 15 and 16) presented with similar signs: in both a systolic murmur of moderate intensity at the pulmonary area and an atrio-ventricular conduction disturbance were noted. One child, who had been known to have complete atrioventricular block since

FIG. 5 Electrocardiogram in the same patient (Case 8) during sinus rhythm, showing a deep Q wave in I and aVL and inverted T waves in I, aVL, V<sub>3</sub> through V<sub>6</sub>.



the age of 2 years, died suddenly in his first Adams-Stokes attack at the age of 7 years. Histological studies (Linder *et al.*, 1965) indicated haemangiomas in the free wall of the left ventricle and in the interatrial and the interventricular septum, where it had invaded the atrioventricular node.

The other patient had a 2:1 atrioventricular block. Angiocardiography showed a filling defect in the lateral wall of the left ventricle which was thought to be due to an intramural fibroma. At operation a vascular tumour, bulging from the lateral wall of the left ventricle, was seen and partially excised. The patient died the next day. The haemangioma was localized in the free wall of the left ventricle as well as in the interventricular septum.

### Teratoma

Of the 6 teratomas (Cases 17–22), only one was intracardiac, the others were extracardiac but remained intrapericardial. All were true teratomas containing a wide variety of structures derived from two or three primitive germ layers, in contrast to some bronchogenic cysts that have been reported as teratomas (Dabbs, Peirce, and Rawson, 1957).

Three infants (Cases 17, 18, and 19) were admitted in acute distress and presented with almost identical signs: tachypnoea, cyanosis, absence of murmurs, low voltage on the electrocardiogram, and a huge 'heart' on the radiograph. In the youngest infant a pericardiocentesis yielded 60 ml. of clear straw-coloured fluid. A pneumopericardium revealed an intrapericardial mass. In the second patient a combination of a pneumopericardium and angiocardiography distinctly outlined the pericardial sac within which a mass was seen to displace and distort the cardiac cavities, especially the superior vena cava, right atrium, and ventricle. In the third infant (Case 19) cine-angiocardiography demonstrated the compression of the right atrium and its downwards displacement by a large extracardiac mass. The operative findings in these three cases were identical: upon opening the pericardium a large, firm, multicystic, well-encapsulated extracardiac tumour was found, attached by a short pedicle to the root of the aorta. All three tumours were successfully removed.

In a 7-year-old symptomless boy (Case 20) cardiac investigation was performed because of an unusual x-ray finding which showed an irregular bulging mass on the left cardiac border (Fig. 6). Within this shadow several small calcifications were seen. Angiocardio-

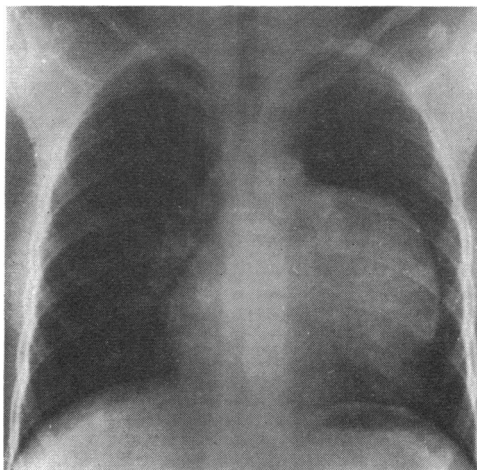


FIG. 6 *Irregular bulging left cardiac border in a 7-year-old symptomless boy with an intrapericardial teratoma (Case 20). Small calcifications within this mass, visible on the original x-ray, are not clearly shown.*

FIG. 7 *Teratoma incidentally found at necropsy (Case 21). The lobulated tumour, attached to the aortic root, extends mainly over the right atrium. (By courtesy of Dr. A. Cameron.)*





graphy delineated an extracardiac tumour compressing the upper part of the left ventricle. At operation a large cystic tumour adherent to the pericardium was found and easily resected. In one child (Case 21) who died from an unrelated condition, a teratoma adherent to the aortic root was found at necropsy (Fig. 7).

The only patient (Case 22) with an intracardiac teratoma was a neonate. The baby survived only 15 hours. The neoplasm was a huge multilocular cystic tumour which occupied most of the right atrial and right ventricular cavities and had grown through the tricuspid orifice. It appeared to have originated from both the interatrial and interventricular septa. Histologically, derivatives of all three primitive germ layers were identified.

### Discussion

Whereas in previous decades cardiac tumours were usually reported as post-mortem findings, more recently they have shifted to the clinician's domain. This is borne out by the fact that in a 5-year period 29 children with cardiac tumours (24 with histological proof) were collected by members of the Association of European Paediatric Cardiologists. In 13 cases a correct diagnosis of intracardiac or intrapericardial mass was made during life and before operation (Table 3).

TABLE 3 *Preoperative or premortem diagnosis*

Total number of histologically verified cases	24
Number of cases diagnosed during life	13
Fibroma	4
Teratoma	4
Myxoma	2
Malignant	2
Haemangioma	1
Diagnosis based on	
Angiocardiogram	9
Pneumopericardium	1 (teratoma)
Pneumopericardium + angio	1 (teratoma)
Biopsy	1 (malignant)
Clinical context	1 (malignant)

The present series, limited to children, comprises a wide variety of benign cardiac tumours in contrast to most reports in adults where the vast majority are atrial myxomas. Teratomas usually present at a very early age; 13 of the 22 patients listed by Pernot *et al.* (1968) were infants below the age of 3 months, and 5 were between the age of 3 months and 2 years. In a recent review (Van der Hauwaert, 1968) it was found that out of 78 cases

of rhabdomyoma only 8 occurred in patients older than 15 years. Geha *et al.* (1967) reviewed 36 cases of intramural cardiac fibroma and noted that 31 were reported in children.

On the basis of the present report one may conclude that in childhood the following clinical findings or associations of signs and symptoms are suggestive of a cardiac neoplasm.

(1) Congestive heart failure and obvious cardiomegaly in infancy, unexplained by congenital heart disease, myocarditis, or endocardial fibroelastosis; (2) the association of congestive heart failure or a cardiac murmur or both, with rhythm disturbances, either atrioventricular block or bouts of tachycardia; (3) the association of heart disease with peripheral arterial emboli; (4) any atypical feature in a condition that otherwise would be labelled as 'valvar stenosis', e.g. changing character of the murmur, influenced by posture, rhythm disturbances, disproportion between obvious cardiomegaly and signs of only moderate 'valvar' obstruction, or an infarction-like electrocardiographic pattern; (5) even as an isolated finding a bulging mass on the cardiac border outlined by x-ray, is highly suggestive. It is almost diagnostic of a hamartoma or teratoma if it contains calcifications.

Once the suspicion has been raised, angiocardigraphy is the only method to confirm the diagnosis before operation. As suggested by Pernot *et al.* (1968), it may be used in conjunction with a pneumopericardium to visualize better an intrapericardial tumour.

The importance of early and correct diagnosis is indicated by the relatively good surgical results in the present series (Table 4). Of the 11 children operated upon, 8 had a complete recovery, 2 died after operation, and 1 was found to be inoperable. From the surgical and pathological reports it appears that teratomas, myxomas, fibromas, and hamartomas in childhood may be completely resected. In

TABLE 4 *Operations*

Number of patients operated upon: (all correctly diagnosed as pericardial or intracavitary mass)		11
Teratoma	4: complete recovery	4
Fibroma	4: complete recovery	3
	inoperable	1
Myxoma	2: complete recovery	1
	postoperative death	1
Haemangioma	1: postoperative death	1
Complete recovery:	8	

the case of a teratoma special care has to be taken to avoid bleeding from the vascular pedicle by which the tumour is usually attached to the aortic root. It is unlikely that rhabdomyomas will ever be amenable to surgery because of their multifocal distribution.

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