Myocardial Infarction and Ischaemic Heart Disease in Infants and Children

Analysis of 29 Cases and Review of the Literature

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Myocardial infarction, the hallmark of heart disease in adults, has been generally held to be virtually non-existent in infants and children. That this view is probably incorrect is suggested by the finding of 29 proven examples from the necropsy files of the Second Paediatric Department of Charles University, Prague, between 1945 and 1960†, where there are approximately 2000 admissions per year.

The underlying causes of myocardial infarction in these cases can be classified into five categories: embolic, inflammatory, degenerative, congenital, and functional. The distribution of the 29 cases by category is shown in Table I. Clinical and pathological features of the 29 cases are shown in Table II. An illustrative case report and a review of pertinent literature are given for each category.

Embolism

In 8 cases clear evidence of embolism of the coronary arteries could be demonstrated. In 5 of these instances the embolism was associated with bacterial endocarditis. In 2 there were thrombi in the pulmonary veins and in 1 there was a thrombus in a peripheral vessel which led to paradoxical embolism.

Case 4. A 13½-year-old boy was admitted with signs and symptoms of occlusion of the tibial artery after a febrile illness. Subsequently signs of bacterial endocarditis involving the aortic valve and heart failure led to transfer to the medical department. A chest x-ray showed enlargement of the heart and pulmonary-oedema. ECG (Fig. 1) showed the evolution of an antero-lateral infarction during the two days before death. Necropsy confirmed the clinical diagnosis:

infarction of the anterior wall of the left ventricle and ulcerative endocarditis of the aortic valve.

Embolic myocardial infarction is rare, even in adults (Moragues, Bawell, and Shrader, 1950; Braun, 1956; Dufek, 1957; Shrader, Bawell, and Moragues, 1956). Only two cases in childhood could be found in a review of the literature: coronary embolism from ulcerative endocarditis (Stryker, 1946a) in an 8-year-old boy, and from coronary thrombosis (Ramsay and Crumrine, 1931) in a 4-month-old girl. Two additional infants with sudden myocardial infarctions after exchange transfusion, which were probably embolic, have been described in an unpublished report (J. D. Keith, 1964, personal communication).

Inflammatory Diseases

Inflammatory disease of the coronary arteries was the apparent cause of myocardial infarction in 9 children. 5 of them had acute rheumatic carditis, in one associated with bacterial endocarditis, and 3 had severe non-rheumatic myocarditis. In 1 child, the diagnosis was lupus erythematosus disseminatus, with Libman Sacks endocarditis and coronary arteritis.

TABLE I

Classification of 29 Cases of Myocardial Infarction in Infants and Children
Charles University, Prague, 1945-1960 (Bor, 1964)

Groups	Aetiology	No. of Cases
I	Embolism into coronary arteries	8
II	Inflammatory diseases of coronary arteries	9
III	Degenerative changes of coronary arteries	3
IV	Congenital abnormalities of coronary arteries	4
V	Functional disturbances of coronary blood flow	5

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† Some of these cases were reported to the World Congress of Cardiology (Bor, 1958), and a fuller discussion subsequently appeared in the Czech literature (Bor, 1964).

FIG. 1.—Case 4. 13½-year-old boy. Electrocardiogram in vertical lines shows evolution of antero-lateral infarction pattern. Necropsy: fresh infarction of the anterior wall of left ventricle.

Rheumatic

Case 10 was a 3½-year-old boy who was admitted with fulminating rheumatic pancarditis, severe dyspnoea, heart failure, and severe headache and abdominal pain. ECG (Fig. 2) showed a pattern of posterior infarction. Death occurred 14 days after admission, and necropsy confirmed rheumatic pancarditis, inflam-

mation of the coronary arteries, and recent infarction of the posterior wall of the left ventricle.

Among reports of inflammatory disease of the coronary arteries in association with rheumatic fever are 3 patients (Gross, Kugel, and Epstein,

TABLE II

Summary Table of 29 Cases of Myocardial Infarction or Ischaemic Heart Lesions in Infants and Children
(Charles University, Prague, 1945-1960)

Case No.	Sex	Age at Death	Age at Onset of Symptoms	Symptoms	Death After Admission	Group	Clinical Diagnosis	Principal Necropsy Diagnosis	Myocardial Infarction	Other Findings	
<i>Embolism</i>											
1	M	58 dy.	58 dy.	Dyspnoea vomiting, cyanosis, pain	Same dy.	Ia: 'Fetal' endocard.	CHD	Aortic stenosis and insufficiency	Recent	Chronic aneurysm of apical part of LV	Embolus descend. LCA
2	M	12 dy.	5 dy.	Dyspnoea, fever, cyanosis, CHF	2 dy.	Ia: 'Fetal' endocard.	CHD	Aortic atresia	Posterior part of ventric. septum		
3	M	24 dy.	9 dy.	Fever, pallor, vomiting, cyanosis, CHF	1 dy.	Ia: 'Fetal' endocard.	Necrosis of lateral wall LV	As clinical diagnosis			LCA obstruction
4	M	13½ yr.	Sudden	Fever, CHF, pain	2 dy.	Ib: Bacterial ulcerous endocard.	Bacterial endocard. embolism into tibial artery	Ulcerative endocard.	Recent ant. wall LV		Embolism
5	F	12 4/12 yr.	3 mth., CHD 1½ yr.	CHF	4 mth.	Ic: CHD, bact. endocard.	CHD, bact. endocard. MI	CHD, VSD, bact. endocard.		Löhlein's nephritis	Micro-embolism
6	F	8 yr.	8 yr., post-pneumonic lung abscess	Fever, dyspnoea	5 dy.	Id: Thrombosis PV		Thrombosis PV	Multiple ant. and post. wall of LV and ventr. septum		Embolism in rt. descend.
7	F	3 yr.	1 mth. after measles	Dyspnoea, cyanosis, vomiting, CHF, coma, cachexia	5 dy.	Id: Thrombosis PV	MI	Thrombosis PV; interstitial myocard.	Apex	Multiple kidney, spleen, brain infarct.	
8	M	7 yr.	Abscess in cubital region	CHF, cachexia	2 wk.	Ie: Paradoxical embolism	Hodgkin's disease	Hodgkin's disease	Posterior wall LV	Spleen infarct.	Paradoxical embolism
<i>Inflammatory Diseases of Coronary Arteries</i>											
9	F	14 yr.	3 mth. after RF recurr.	stroke	1 dy.	Iia: Rheumatic	Recurr. rheum. card. bact. endocard.	Rheum. and bact. endocard.	MI posterior wall	Apex myo-fibrosis	
10	M	3½ yr.	Peracute	Dyspnoea, CHF, pain	14 dy.	Iia: Rheumatic	Rheum. pancard.	Rheum. pancard.	Recent MI posterior wall	Arteritis of coron. art.	
11	M	8 yr.	Rheum. card.	CHF, pain, vomiting, shock	3 wk.	Iia: Rheumatic	Rheum. card.	Rheum. card.	Necrosis LV	Arteritis of coron. art.	
12	F	13 4/12 yr.	7 and 11 yr. RF	Fever, pain, CHF	Prolonged	Iia: Rheumatic	Rheum. card. aorto-mitral bact. endocard.	Rheum. card., aorto-mitral, bact. endocard.		Fibrosis LV	
13	F	14 4/12	12 yr. chorea, 14 yr. recurr. card.	Fever, CHF, pain	1 wk.	Iia: Rheumatic	Rheum. pancard.	Chronic rheum. pancard., aorto-mitral	Necrosis of post. LV	Arteritis of coron. art.	
14 yr.	F	2 11/12 yr.	2 6/12 yr. subacute	Dyspnoea, shock, transit. cyanosis	2 dy.	Iib: Myocarditis	Rheum. card.	Subacute myocard.		Inter-stitial fibrosis	

TABLE II—continued

Case No.	Sex	Age at Death	Age at Onset of Symptoms	Symptoms	Death After Admission	Group	Clinical Diagnosis	Principal Necropsy Diagnosis	Myocardial Infarction	Other Findings
15	F	8 yr.	Subacute	Dyspnoea, CHF, cough	1 wk.	IIb: Myocarditis	Interstit. myocard.	Interstitial myocard.		Diffuse myofibrosis
16	M	7 yr.	Lobectomy for bronchiectasis at 6 yr.	Fever, dyspnoea, pallor	4 dy.	IIb: Myocarditis	Thrombosis PV	Extensive interstitial myocard.		Fibrosis
17	M	10 yr.	Acute dissem. lupus erythem.	Shock, coma, convulsions	2 wk.	IIc: Dissem. lupus erythem.	Dissem. lupus erythem.	Dissem. lupus erythem., Libman-Sacks endocard.	Recent large MI	Arteritis of coron. art.
<i>Degenerative Changes of Coronary Arteries</i>										
18	M	3 yr.	Acute	3 wk. after adm. BPN; pain	3 wk.	IIIA: Coronary arteriosclerosis	Hyper-tension	Renal calculi, LV hypertrophy		Apex, foci of myomalacia
19	F	2 5/12 yr.	2 4/12 yr.	Fever, cough, dyspnoea	1 mth.	IIb: Fibroelastosis	Fibroelastosis	Fibroelastosis		Fatty changes
20	F	2 mth.	Acute	Dyspnoea; tempor. cyanosis	At operation	IIc: Fibroma LV	Tumour LV	Fibroma LV		
<i>Congenital Abnormalities of Coronary Arteries</i>										
21	F	6 mth.	5 mth.	CHF, Pain	1 wk.	IV: Anatomical	Anom. origin LCA from PA	Anom. origin LCA from PA		Chronic aneurysm of post. wall of LV
22	M	13 wk.	13 wk.	CHF, pain	1 dy.	IV: Anatomical	Anom. origin LCA from PA	Anom. origin LCA from PA	MI anterior wall LV	Aplasia of horiz. branch
23	M	3 mth.	Sudden	Pallor, convulsion	20 min.	IV: Anatomical	Moribund	Anom. origin LCA from PA	Recent and older necroses of LV	
24	F	6 mth.	Acute	Dyspnoea, pain, cyanosis	1 dy.	IV: Anatomical	Anom. origin LCA from PA	Anom. origin LCA from PA		Fibrosis and aneurysm of apex
<i>Functional Disturbances of Coronary Blood Flow</i>										
25	F	5 6/12 yr.	2 6/12 yr.	CHF, dyspnoea, pain	1 mth.	Va: Aortic stenosis	Congenital aortic stenosis	As clinical diagnosis		Myofibrosis, chronic aneurysm of apex LV
26	M	10 mth.	Acute	Fever, dyspnoea, CHF	Same dy.	Vb: Pulm. AV aneurysm	Pulm. AV aneurysm	As clinical diagnosis		No changes
27	M	8 yr.	Acute	Coma	4 dy.	Vc: Poisoning	Mushroom poisoning (<i>Amanita phalloides</i>)	As clinical diagnosis		Fatty changes
28	F	4 yr.	Acute	Coma	4 dy.	Vc: Poisoning	Mushroom poisoning (<i>Amanita phalloides</i>)	As clinical diagnosis		Fatty changes
29	M	7 mth.	Acute	Fever, CNS lesions	2 dy.	Vd: Hyperpyretic, syndrome CNS	Microcephalus; spastic quadriplegia; hyperpyretic	As clinical diagnosis		Lesions of myomalacia in LV

CHD, congenital heart disease; LCA, left coronary artery; CHF, congestive heart failure; VSD, ventricular septal defect; BPN, bronchopneumonia; PA, pulmonary artery; MI, myocardial infarction; RF, rheumatic fever; PV, pulmonary vein.

FIG. 2.—Case 10, a 3½-year-old boy. Posterior infarction pattern. Necropsy: fresh posterior infarction.

1935) with acute necrotizing arteritis, a 14-year-old girl with rheumatic carditis without bacterial endocarditis (Otero, del Zar, and Hojman, 1956), and a 2-year-old child with acute rheumatic carditis who died suddenly (Rae, 1937). Necropsy of the latter showed myocarditis, pericarditis, and aortitis, with marked inflammatory lesions of the main coronary arteries.

Lupus erythematosus. Myocardial infarction secondary to lupus erythematosus has been attributed by Siegenthaler (1958) to coronary arteritis. This occurred in one case in our series in a 10-year-old boy with Libman Sacks endocarditis.

Syphilis. Cases with luetic involvement of the coronary arteries and complicating myocardial infarction have been described (McDonald, 1932; Norris, 1935; Baggenstoss and Keith, 1941; Stryker, 1946a; Goormaghtigh, de Vos, and Blanquaert, 1955) in children.

McMichael (1929) reported an unusual example of coronary inflammatory disease in an 18-month-old infant, with *extensive visceral endarteritis obliterans* and fibrosis of the myocardium which he attributed to syphilis, though the serological reactions of the child and of the mother and father were negative.

Polyarteritis nodosa. Coronary artery involvement in polyarteritis nodosa has been reported in childhood. An 11-year-old girl (Stryker, 1946a)

with periarteritis nodosa of at least 6 years' duration showed, at necropsy, occlusion of the posterior descending branch of the right coronary artery and an infarct of the apex. A 15-month-old girl (Pickard, Owen, and Dammin, 1947) and a 9-month-old with aneurysm of the coronary artery (Sinclair and Nitsch, 1949), and a 3-month-old with myocardial necrosis and thrombi in the left anterior descending branch of the coronary artery (Crocker, Sobin, and Thomas, 1957; Fager, Bigler, and Simonds, 1951; Munro-Faure, 1959) have been described.

Interstitial myocarditis. In typical interstitial myocarditis it has not been uncommon to find electrographic patterns of infarction when necropsy has shown only inflammatory change (Neubauer, 1944; House, 1948; Tedeschi and Stevenson, 1951; Williams, O'Reilly, and Williams, 1953; De la Chapelle and Kossmann, 1954; Rossi, 1954; Doll, 1955; Bor, 1956; Van Creveld and De Jager, 1956; Koch, Schmidt, and Doll, 1957; Saphir and Cohen, 1957; Saphir and Field, 1954; Huttman and Cimpoesu, 1958; Kaplan, 1958; Keith, Rowe, and Vlad, 1958; Blumenthal and Sapin, 1959; Burwell and Robin, 1959; Dominguez, Lendrum, and Pick, 1959; Saphir, 1959; Brigden *et al.*, 1960; Apley, 1961; Fowler, Gueron, and Rowlands, 1961; Hadorn, 1961; Scholer, 1961; Goldman, 1962; Pruitt, Curd and Leachman, 1962; Nadas, 1963; Wegelius and von Knorring, 1964) while the majority of children with myo-

carditis do not show these ECG changes. The principal histological finding is interstitial cellular infiltration together with focal necrosis of muscular fibres. Gross coronary arterial obstruction, inflammation, or degeneration have not been shown at necropsy though changes in smaller coronary arteries were not excluded. It is probable that the ECG changes are due to diffuse involvement of myocardial fibres. The typical ECG changes would be expected if a greater number of anatomically and functionally compromised myocardial fibres were located close to the epicardium or extended transmurally (Dominguez *et al.*, 1959).

Degenerative Diseases

In adults degenerative disease of the coronary arteries is the most common cause of ischaemic changes of the myocardium. In infants and children the causes of degenerative changes of the coronary arteries are manifold. The structure of the coronary vessels may be altered by calcification, hypertension, haematological disorders, or other systemic diseases. The changes are not restricted to the coronary arteries.

Minor histological alterations of the coronary vessels are not uncommon in infants. Gruenwald (1949) found necroses in the media of coronary arteries in 21 newborn or stillborn infants, or in 9.5% of the necropsies performed in infants dying in the first three days of life. Small thrombi were revealed in 2 cases. Thickening of the intima was found in the coronary arteries in newborns (Minkowski, 1947; Fangman and Hellwig, 1947; Schornagel, 1956; Moon, 1957; Scott, 1961).

Moon (1957) studied coronary arteries in fetuses, infants, and juveniles. Early stages of the arteriosclerotic lesions were occasionally present in infants, and these processes appeared identical to the early phases of arteriosclerosis in adults.

Stryker (1946b) published a review of *calcification of coronary arteries in infancy*. Only 3 of 20 infants showed infarction at necropsy. The principal pathological findings in the cases he reported were calcification of the internal elastic membrane of all arteries of the body, coronary occlusion, and myocardial ischaemia, with areas suggesting infarcts. There are 13 additional reported cases with coronary artery disease or calcification and myocardial infarction (Hughes and Perry, 1929; Forrer, 1930; Lightwood, 1932; Brown and Richter, 1941; Baggenstoss and Keith, 1941; Lipman, Rosenthal, and Lowenburg, 1951; Traisman, Limperis, and Traisman, 1956; Cochrane and Bowden, 1954; Leach, 1955; Gault and Usher, 1960). Stryker

(1946a) reported a 3-month-old boy with infarction. Lipman *et al.* (1951) described a 5-month-old boy with cardiomegaly and an ECG showing anterior infarction. Necropsy revealed primary disease of the coronary, renal, and pulmonary arteries, together with infarction of the left ventricle and ventricular septum. The earliest arterial lesions were those of necrosis and exudation followed by granulomatous proliferation and calcification. Cochrane and Bowden (1954) published the ECG of a 5-month-old girl with signs of infarction. The diagnosis was confirmed by necropsy, fibrosis and foci of recent necroses being found at the apex of the left ventricle. In 5 other cases only microscopic infarcts were found (Forrer, 1930; Lightwood, 1932; Brown and Richter, 1941; Baggenstoss and Keith, 1941; Leach, 1955).

More typical 'adult' forms of coronary disease are found in older children (Kambolis, Lebhar, and Barnett, 1958). Three papers with classical myocardial infarction in a younger age-group were published (Scott and Miller, 1946; Ravich and Rosenblatt, 1947; Martelle, 1955; Jokl and Greenstein, 1957). Benda (1925) reported a 13-year-old girl who died suddenly. Atherosclerosis was present in the aorta and large arteries. The anterior descending branch of the left coronary artery was obliterated. Myocardial infarction with rupture of a resulting ventricular aneurysm and arteriosclerotic nephropathy completed the necropsy picture.

Sprague and Orgain (1935) presented a 15-year-old boy who had substernal pain for three years. The coronary arteries showed moderate atheromatous degeneration with calcification. The left circumflex branch was completely occluded by a peripheral thrombus, as was the posterior portion of the right coronary artery. Better known causes for arteriosclerosis are diabetes and progeria. Shivelhood (1948) diagnosed myocardial infarction on the basis of the ECG in a 12-year-old boy with diabetes.

Keay, Oliver, and Boyd (1955) reviewed cases of progeria and atherosclerosis in children. Myocardial infarctions were found in only 2 out of 5 (Guild, Kindell, and Gibson, 1938; Talbot *et al.*, 1945; Atkins, 1954).

Thickening of coronary arteries in children with gargoylism has been described by Lindsay (1950). In 7 of 9 of this series the lumen of the coronary arteries was considerably narrowed by changes of the intima. The ECG of a child with gargoylism reproduced in Nelson's textbook (1959), shows an infarction pattern. Strauss and Platt (1957) described a 5-month-old girl with a clinical picture

of gargoylism, with small area of acute myocardial necrosis.

Nadas, Alimurung, and Sieracki (1951) described myocardial infarction in a child with Friedreich's ataxia. Microscopical examination revealed extensive fibrosis, the few remaining muscle fibres showing fatty degeneration. The coronary arteries had marked medial hypertrophy, intimal proliferation, and various degrees of obstruction. The authors collected five additional cases ranging from 4 to 13 years of age, all of whom had pathological T wave changes in the standard and praecordial leads of their ECG.

Thorén (1964) reported cases with heart disease as the initial manifestation of Friedreich's ataxia. Certain clinical features such as improvement of ischaemic changes in serial electrocardiograms. (Keith *et al.*, 1958; Thorén, 1964) have suggested that coronary artery disease plays an important role in this disease.

Coronary disease does not, however, appear to be an important cause of cardiopathy in other myopathic diseases, such as progressive muscular dystrophy (Weisenfeld and Messinger, 1952; Schott, Jacobi, and Wald, 1955; James, 1962, 1964; James and Fisch, 1963; Thorén, 1964).

Hypertensive cases

Case 18. Hypertension was found in a 3-year-old boy; the ECG revealed a pattern of anterior infarction. Three weeks after admission he developed chest pain with severe bronchopneumonia, and died. Necropsy revealed renal calculi and hypertrophy of the left ventricle, foci of myomalacia in the apex and in the trabecular muscles, with arteriosclerosis of the coronary arteries.

Diseases associated with *hypertension* mostly due to renal disease can be complicated by myocardial ischaemia. Electrocardiographic changes in acute and chronic glomerulonephritis have been demonstrated (Keith *et al.*, 1958; Nadas, 1963).

Parrott, Joseph, and Nesbit (1951) reported a 10-week-old boy with hypertension and myocardial infarction pattern in the ECG. Necropsy revealed polycystic kidney disease and degenerative changes of the myocardium with fibrous replacement. Mehrizi *et al.* (1964) recently described a 9-year-old boy with polycystic kidneys whose ECG showed an infarction pattern.

Adrenal tumours. These are another cause of hypertension. Kremer (1936) described a 14-year-old boy with myocardial infarction on his ECG. At necropsy, pheochromocytoma, marked sclerosis, and myocardial infarction were found. Among 7 adult patients of Kline (1961) with pheochromocytoma, myocardial changes were

found at necropsy in 4. The outstanding lesions were the severe degenerative changes in groups of muscle fibres combined with focal necrosis and chronic interstitial inflammation. Even though there was no evidence of fatty degeneration, the myocardial alterations closely resembled those seen in experimental animals treated with nor-epinephrine.

Miscellaneous.

Thrombocytosis. Spach, Howell, and Harris (1963) reported an unusual case of an 8-year-old girl with primary thrombocytosis. ECG and vectorcardiographic study showed myocardial infarction. Multiple thromboses were also found.

Traumatic. Jokl and Greenstein (1944) published a history of a 10-year-old boy who died three minutes after participation in a boxing match. At necropsy the left descending branch of the coronary artery was occluded by thrombus for a distance of 2.5 cm. No other abnormalities of the arterial system were found.

The ECG pattern of myocardial infarction due to trauma has been observed by the author in 4 children. One such example resulted from puncture of the lungs for biopsy in a case of pulmonary haemosiderosis, while in 3 other children the changes were noted after operation for congenital heart disease by extracorporeal circulation. In all 4 children, electrocardiographic resolution coincided with clinical recovery.

Aneurysms. Kempton (1951) described a 9½-year-old girl who suddenly died while playing hockey. Necropsy revealed myocardial fibrosis with two large calcified aneurysms of the coronary arteries.

Ellis (1935) found infarcts and aneurysms of a branch of the coronary artery in a 9-month-old infant; the cause was not revealed. The majority of coronary artery aneurysms in infants and children reviewed by Crocker *et al.* (1957) did not show ischaemic changes of the myocardium, though many died suddenly from rupture of the aneurysm and cardiac tamponade, without ischaemic changes being evident at necropsy.

Fibroelastosis. Endocardial fibroelastosis is not rare. The ECG picture has been described by Vlad, Rowe, and Keith (1955). The high voltage QRS and left ventricular hypertrophy pattern differs from the low voltage QRS and T wave changes of patients with myocarditis. Yet some infants and children with evident ischaemic changes on the ECG and at necropsy have been reported (Edmonds and Seelye, 1951; Adams and Katz, 1952; Thomas *et al.*, 1956; Auld and Watson, 1957; McCormick, 1958;

FIG. 3.—Case 20, a 2-month-old girl. *Electrocardiogram shows extensive anterior infarction. Necropsy: fibroma in the wall of the left ventricle.*

Lambert and Vlad, 1958; Hastreiter and Miller, 1964). In 36 cases with the necropsy finding of fibroelastosis in Prague (Bor, 1956), myocardial infarction was found only in one instance.

Tumours.

Case 20. A full-term infant of 2 months was admitted for anorexia, transitory cyanosis, tachycardia, and gallop rhythm. X-ray showed, in the left anterior oblique position, the upper part of the shadow of the heart overlapped by the shadow of the spine. ECG (Fig. 3) showed anterior infarction pattern. Tomography and angiocardiography indicated a tumour of the left ventricle. During exploratory thoracotomy, cardiac arrest occurred. At necropsy there was a fibroma in the wall of the left ventricle.

Nadas (1963) describes a 10-day-old newborn with rhabdomyoma. The ECG with Q in the first standard lead is presented, and ST changes are evident. Engle and Glenn (1955) published the case of a 4-year-old boy with sudden congestive heart failure with ST elevation and negative T₅, 6. A diagnosis of myocardial infarction pattern was made before death. The tumour (rhabdomyosarcoma) had practically obstructed the lumen of the anterior descending branch of the left coronary artery.

Glycogenosis. Lambert and Vlad (1958) described an anterior infarction in a newborn with a necropsy finding of glycogenosis of the heart.

Congenital Abnormalities

Anomalous origin of the left coronary artery from the pulmonary artery.

Case 21. Death at the age of 6 months. ECG showed antero-lateral infarction pattern. Necropsy surprisingly revealed an aneurysm of the posterior wall of the left ventricle.

Case 22. At the age of 13 weeks, heart failure and symptoms of pain appeared. X-ray showed cardiomegaly; ECG posterior infarction pattern. He died next day, and necropsy revealed infarction of the anterior wall of the left ventricle.

Because of the possibility of benefiting from operation, anomalous origin of the left coronary artery is an important entity causing myocardial ischaemia. Keith (1959) found the incidence of anomalous origin of the left coronary artery from the pulmonary artery was 1 in 300,000 children. The diagnosis should be suspected in an infant in the first year of life who develops signs of heart failure, has an enlarged heart, and ECG with evidence of myocardial ischaemia in the anterior portion of the left ventricle. The diagnosis may be confirmed by an aortogram, the technique best demonstrating the anomaly being injection of contrast material into the aortic root, with the

FIG. 4.—Case 25, a 5½-year-old girl. Electrocardiogram shows posterior infarction. Necropsy: aneurysm of the apex.

patient in the left oblique position. A large coronary artery is obvious at once, and only later does the left coronary artery become visible, and subsequently the pulmonary artery (Sabiston, Neill, and Taussig, 1960a; Sabiston, Pelargonio, and Taussig, 1960b; Sabiston *et al.*, 1963; Noren *et al.*, 1964; Bookstein, 1964).

Nadas, Gamboa, and Hugenholtz (1964) recommend surgical ligation of the anomalous left coronary artery near its origin only in cases with aortographic demonstration of flow from the coronary artery to the pulmonary artery. Since this is the most common finding, operation should be beneficial for most cases. Dominguez *et al.* (1959) suggest that the particular localization of the infarction by ECG is of help in the differential diagnosis. Posterior wall infarction in their view indicates an aetiology other than anomalous origin of the left coronary artery. This has not been always true, as for Case 22 (above) or for other reported cases (Keizer and Rochet, 1952; Keith, 1959; Sabiston *et al.*, 1960a, b, 1963; Noren *et al.*, 1964; Bookstein, 1964; Nadas *et al.*, 1964). Ruttenberg *et al.* (1964) showed how the clinical and laboratory examination can be misleading: examination of an 8-month-old infant suggested anomalous origin of the left coronary artery from the pulmonary artery; ECG and VCG showed left ventricular hypertrophy, with extensive myocardial infarction; angiocardiography revealed an aneurysmally dilated left ventricle with unusual internal septations and loculations; and the necropsy showed concentric semicircular muscular ridges

and grooves in the apical portion of the left ventricle and a peculiar fibrous endocardial network of the same chamber. The coronary arteries were normal.

Grossman and Adams (1964) state that angina pectoris or myocardial infarction in a child, youth, or young adult often results from anomalies of coronary arteries, particularly when hypertension and metabolic disease are not present.

Not all types of anomaly of the coronary arteries have unfavourable consequences in childhood. Alexander and Griffith (1956) have collected 54 cases of anomalous coronary circulation, only 10 showing myocardial infarcts.

Miscellaneous

Case 25. Congenital aortic stenosis with left heart strain was diagnosed at the age of 2½ years. At 5 years heart failure appeared. The child developed severe chest pain, with dyspnoea and cyanosis. The next day ECG (Fig. 4) showed a pattern of posterior infarction. Necropsy showed fibrosis of the left ventricle with aneurysm of the apex; the tight aortic stenosis had caused ischaemia of the hypertrophied myocardium; and the apex of the left ventricle was so thin that it was transparent.

Functional disturbances of the myocardium can be divided into cases with left or right ventricular outflow obstruction, anaemia, and unknown causes.

(A) Ventricular outflow obstruction: Prescott, Quinn, and Littmann (1963) published electrocardiograms in 4 adult cases, with hyper-

trophic subaortic stenosis which simulated myocardial infarction. A similar picture in congenital pulmonary stenosis has been described by Dimond and Lin (1954). The disproportion between the muscle mass of the ventricle and the adequacy of the coronary flow is the only possibility that seems feasible as an explanation for myocardial infarction. This has been found at necropsy in a child of 3½ years. Lasser and Jenkins (1957), in a detailed study, examined the causes of chest pain simulating angina pectoris in 5 adult cases with severe, isolated valvular pulmonary stenosis. In each instance the symptomatology was completely relieved by operation. An unusual case of the anterior wall myocardial infarction pattern in the ECG occurred in a 7-week-old infant, with transposition of the great vessels (Bernreiter, 1958).

(B) Anaemia. Infarction in haemolytic disease has been reported. Hogg (1962) studied 40 infants who died of haemolytic disease of the newborn: increased heart weight was found in 18. Dilatation of the heart was difficult to quantitate, but was thought to be present in many cases; small myocardial infarcts were present in 6 of the hearts, which were confined to the inner myocardium and papillary muscles of either ventricle. Varying degrees of endocardial fibroelastosis were present in 26 cases, but in no case was it recognizable grossly. It was considered likely that the changes were related to relatively long sustained anaemic hypoxia and to cardiac dilatation. There were no electrocardiographic data.

Severe anaemia or leukaemia is another well-known cause of ischaemic changes in the ECG, and ischaemic changes may be found at necropsy in these disorders. This group has been fully described by Friedberg and Horn (1939) and others (Klinefelter, 1942; Case, Berglund, and Sarnoff, 1955; Lindo and Doctor, 1955; Bär, Zeilhofer, and Heckel, 1957; Sanghvi *et al.*, 1958), and will not be discussed further here. Sick cell anaemia also produces these changes (Nelson, 1959). Relative or transient ischaemia in which the electrocardiographic signs rapidly returned to normal as adequate coronary perfusion was achieved may occur during open-heart surgery when air emboli enter the coronary arteries, or in tracings after prolonged attacks of supraventricular tachycardia (Keith *et al.*, 1958).

(C) Unknown cause. Dominguez *et al.* (1959) published the case of a 10-week-old infant with a posterior infarction ECG pattern where histology of the heart showed no abnormality, and also a

13-month-old girl with antero-lateral infarction and clinical improvement. Doherty and Dood (1957) published an antero-lateral infarction ECG pattern in a 5-year-old girl whom they followed for 3 years and whose ECG picture later became normal.

Clinical Features

The diverse aetiology of ischaemic heart disease has been shown in our patients and in cases published elsewhere (Bor, 1964). It follows that the clinical picture is not likely to be uniform. Differences will arise if the obstruction of the coronary arteries is sudden as in embolism, or slow and progressive as in some degenerative types. The extent and location of myocardial ischaemia play a role. Dyspnoea is always present in varying degree, and it is interesting that even in infants and small children with myocardial infarction it is possible to observe behaviour suggesting that chest pain is present. There is an unjustified tendency to neglect symptoms of this kind. Shock may be an early manifestation of the disease, occurring in 4 cases in the Czech series. Signs such as cough, vomiting, and cyanosis occurred in the majority, often in association with congestive failure. Headache is a common complaint in older children. Loss of consciousness occurred frequently, but was usually a terminal event.

There was no significant sex difference in this series nor in the literature.

The chest x-ray usually shows cardiomegaly; however, the leading tool to the diagnosis of myocardial infarction is the electrocardiogram. Descriptions of classical infarction patterns are given in many textbooks. The difficulties in electrocardiographic diagnosis of myocardial infarction have been outlined by Pruitt, Dennis, and Kinard (1963).

Laboratory Findings

Electrocardiographic analysis. Since the typical adult history suggesting myocardial infarction is usually lacking, the ECG has great importance in recognition of the disease. The Q wave has been said to have no great significance in paediatrics (Nadas, 1963). Its vital role in the diagnosis of myocardial infarction in adults is well known, but in children a sizeable Q wave is often normally present in leads II, III, aVF, and V5, 6. In V6, the Q wave averages 1.5 mm. and does not usually exceed 4.5 mm. (Keith *et al.*, 1958). It is not commonly found in lead I, and, when present, is not deep, and is certainly not wide. A prominent

Q will be followed by a tall R wave and is associated most often with other evidence of left ventricular hypertrophy. Ziegler (1951) found no Q in the leads V1 and 2 in any normal children. It is customary to accept as the upper limit a Q wave no greater than 25% of the following R wave in leads other than III, where 50% is acceptable, or a VR where Q is normally prominent.

Keith and colleagues (Keith *et al.*, 1958; Watson and Keith, 1962) concluded that a Q in V6 of more than 2 mm. was a reliable indication of left ventricular overload, especially of the diastolic type. They differentiated the Q of overload pattern from that in ischaemia, which is seen in the tracings of patients with anomalous origin of the left coronary artery from the pulmonary artery, by the amplitude of the following R wave (absent or low in ischaemic cases) and by the increased duration of the Q and association with T and ST segment changes in the ischaemic group (Keith, 1959).

A Q wave duration of 0.04 sec. is accepted as pathological in adults. In our series of ischaemic changes, it was encountered in 9 infants and children. In the total number of ECG tracings, pathological Q wave was absent only in 5: Case 2 (no chest leads were obtained), Case 13 (leads V7-9 were not recorded), Case 16 (interstitial myocarditis), Case 18 (arteriolosclerosis), and Case 19 (fibroelastosis).

Vectorcardiographic diagnosis. Three main vectorcardiographic abnormalities in myocardial infarction were outlined by Grant and Estes (1951). Firstly, the initial vectors of the QRS loop point away from the area of infarction—the so-called infarction vector. Secondly, the terminal QRS vector may be normal, or if 'peri-infarction' block occurs, it may be directed toward the infarcted region. Thirdly, during the acute process, the ST vector tends to point toward the infarcted zone, and the T vector away from the infarct.

Vectorcardiographic patterns of myocardial infarction in infants and children have been published by three groups (Spach *et al.*, 1963; Noren *et al.*, 1964; Nadas *et al.*, 1964) using different lead systems. For the diagnosis of myocardial infarction in anomalous origin of the left coronary artery from the pulmonary artery, the QRS sE loop in the horizontal plane was found to be most helpful: the loop was inscribed in a clockwise direction and was oriented posteriorly and to the left; the T sE loop was oriented anteriorly and to the right. In the case of inferior myocardial infarction described by Spach *et al.* (1963) the frontal plane showed the initial deflection of the QRS sE loop

directed superiorly and to the left, and an arch-like deformity of the efferent limb was observed. The maximum QRS vector was in a position of 16° in the presence of clockwise rotation of the QRS loop.

The features of the electrocardiograms in the Czech series are shown in Table III.

An electrocardiographic pattern of myocardial infarction was positively identified in 18 of 21 patients where tracings were available in the Czech series. Anatomical localization of the ischaemic changes in the Czech series is shown in Table IV. In the 21 cases where electrocardiograms were available for comparison with the morbid findings, clinical localization of the ischaemic changes was confirmed at necropsy in 14 instances.

TABLE III

Summary of Electrocardiographic Study of 29 Cases (Bor, 1964)

Electrocardiogram	No. of Cases
Positive pattern of myocardial infarction	18
No definite infarction pattern (one where recording of leads V7-9 should have shown myocardial infarction)	2
Left bundle-branch block	1
No ECGs available (lost or not performed in the time of acute illness)	8
	29

TABLE IV

Localization of Ischaemic Changes at Necropsy (Bor, 1964)

Site of Ischaemic Changes	Case No.	Total No. with a Particular Ischaemic Change
Apex of left ventricle	1, 9, 18, 24, 25	5
Apex of right ventricle	7	1
Ventricular septum	2, 6	2
Lateral wall of left ventricle ..	3	1
Anterior wall of left ventricle ..	4, 6, 22	3
Posterior wall of left ventricle ..	6, 8, 9, 10, 13, 21	6
Left ventricle without demarcation	11, 14, 15, 16, 17, 19, 23	7

This experience suggests that a diagnosis of myocardial infarction in infants and children is possible.

Paediatricians rarely consider myocardial infarction in the differential diagnosis of heart disease. Ischaemic changes should be suspected from atypical and more discrete ECG disturbances. Careful study of Q waves, with examination for QS com-

plexes, elevation and depression of ST and T waves, can improve diagnostic accuracy. It is important to follow the evolution of any such changes. As in adults, complementary leads are necessary in suspect cases. The value of vectorcardiography for the diagnosis of ischaemic heart disease in infants and children is frequently not appreciated. Since myocardial fibrosis from any cause may produce ECG patterns suggestive of infarction, aortographic studies are essential in patients suspected of having anomalous origin of left coronary artery.

Conclusion

The incidence of ischaemic heart disease in infancy and childhood is higher than generally believed. Detailed study of the heart and coronary vessels at necropsy is of fundamental importance in obtaining the true picture of myocardial infarction in this age-group. History and physical examination are not usually helpful in determining the nature of the heart disorder.

Clinical diagnosis is possible from the electrocardiogram, but the electrical changes may be subtle, or non-specific. Serial electrocardiograms and vectorcardiograms should be performed in suspected cases.

Review of the literature shows a wide spectrum of the clinical picture and aetiology of myocardial infarction in children, and indicates the need for a greater appreciation of the diagnostic problem in this age-group.

Some patients with ECG infarction patterns require special studies to find surgically correctable disease such as anomalous coronary arteries.

Summary

Twenty-nine infants and children with post-mortem findings of myocardial infarction or ischaemic heart disease were retrospectively studied to obtain information regarding the prevalence, aetiology, and clinical description of this entity.

The material was divided into five groups according to aetiology. Emboli led to myocardial infarction in 8 patients, inflammatory disease of the coronary arteries in 9, and degenerative disease of the coronary arteries in 3. Anomalies of the coronary arteries led to myocardial infarction changes in 4 patients, and functional disturbances of the coronary circulation created ischaemic changes in 5.

These patients and a review of the literature suggest that myocardial infarction in infants and children is by no means rare; it presents an extremely variable clinical picture, and also suggests that diagnosis can be made by electrocardiography.

Necropsies were performed at the First Institute of Pathology (Director, Professor B. Bednář), at the Department of the Faculty of Paediatrics (Director, Professor D. Benešová), and at the Second Institute of Pathology (Director, Professor V. Jedlička). Their skill and industry which enabled the collection of this material is acknowledged with gratitude.

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REFERENCES

- Adams, F. H., and Katz, B. (1952). Endocardial fibroelastosis. *J. Pediat.*, **41**, 141.
- Alexander, R. W., and Griffith, G. C. (1956). Anomalies of the coronary arteries and their clinical significance. *Circulation*, **14**, 800.
- Apley, J. (1961). Primary myocardial disease in infancy: clinical aspects. *Arch. Dis. Childh.*, **36**, 366.
- Atkins, L. (1954). Progeria. Report of a case with post-mortem findings. *New Engl. J. Med.*, **250**, 1065.
- Auld, W. H. R., and Watson, H. (1957). Fibro-elastosis of the heart in adolescence. *Brit. Heart J.*, **19**, 186.
- Baggenstoss, A. H., and Keith, H. M. (1941). Calcification of the arteries of an infant. Report of a case. *J. Pediat.*, **18**, 95.
- Bär, C. G., Zeilhofer, R., and Heckel, K. (1957). Chronic anemia and its repercussions on heart and circulation. *Circulation*, **16**, 468.
- Benda, C. (1925). Über einen Fall von schwerer infantiler Koronararteriosklerose als Todesursache. *Virchows Arch. path. Anat.*, **254**, 600.
- Bernreiter, M. (1958). Myocardial infarction in an infant with transposition of the great vessels. *J. Amer. med. Ass.*, **167**, 459.
- Blumenthal, S., and Sapin, S. O. (1959). Left ventricular hypertrophy syndrome in infancy. *Dis. Chest.*, **36**, 179.
- Bookstein, J. J. (1964). Aberrant left coronary artery. *Amer. J. Roentgenol.*, **91**, 515.
- Bor, I. (1956). Kardiiden im frühen Kindesalter. *Ann. paediat. (Basel)*, **187**, 399.
- (1958). Myocardial infarctions in infants and children. In Third World Congress of Cardiology, Brussels. Communications, p. 242.
- (1964). Ischemická nemoc srdeční u kojenců a dětí. (Ischemic heart disease in infants and children.) *Acta. Univ. Carol. Med. (Praha)*, **10**, 3.
- Braun, A. (1956). Následky embolií do věnitých tepen. (Consequences of emboli into the coronary arteries.) *ibid.*, **2**, 435.
- Brigden, W., Bywaters, E. G. L., Lessof, M. H., and Ross, I. P. (1960). The heart in systemic lupus erythematosus. *Brit. Heart J.*, **22**, 1.
- Brown, C. E., and Richter, I. M. (1941). Medial coronary sclerosis in infancy. *Arch. Path.*, **31**, 449.
- Burwell, C. S., and Robin, E. D. (1959). Diagnosis of diffuse myocardial fibrosis. *Circulation*, **20**, 606.
- Case, B. R., Berglund, E., and Sarnoff, S. J. (1955). Ventricular function. VII. Changes in coronary resistance and ventricular function resulting from acutely induced anemia and the effect thereon of coronary stenosis. *Amer. J. Med.*, **18**, 397.
- Cochrane, W. A., and Bowden, D. H. (1954). Calcification of the arteries in infancy and childhood. *Pediatrics*, **14**, 222.
- Crocker, D. W., Sobin, S., and Thomas, W. C. (1957). Aneurysms of the coronary arteries. Report of three cases in infants and review of literature. *Amer. J. Path.*, **33**, 819.
- De la Chapelle, C. E., and Kossmann, C. E. (1954). Myocarditis. *Circulation*, **10**, 747.
- Dimond, E. G., and Lin, T. K. (1954). The clinical picture of pulmonary stenosis. *Ann. intern. Med.*, **40**, 1108.
- Doherty, J. E., and Dood, K. (1957). Electrocardiographic changes resembling myocardial infarction in a young child. *Amer. Heart J.*, **54**, 782.
- Doll, E. (1955). EKG Veränderungen im Sinne eines lateralen Herzinfarktes bei einem an Encephalomyelitis erkrankten Kinde. *Ann. paediat. (Basel)*, **185**, 321.

- Dominguez, P., Lendrum, B. L., and Pick, A. (1959). False "coronary patterns" in the infant electrocardiogram. *Circulation*, **19**, 409.
- Dufek, V. (1957). *Infarkty myokardu u mladých lidí. (Myocardial Infarcts in Young People.)* SZN, Prague.
- Edmonds, H. W., and Seelye, W. B. (1951). Endocardial sclerosis. *Pediatrics*, **7**, 651.
- Ellis, R. W. B. (1935). Infarcts and aneurysm of the heart in an infant of nine months. *Proc. roy. Soc. Med.*, **28**, 1333.
- Engle, M. A., and Glenn, F. (1955). Primary malignant tumor of the heart in infancy. Case report and review of the subject. *Pediatrics*, **15**, 562.
- Fager, D. B., Bigler, J. A., and Simonds, J. P. (1951). Polyarteritis nodosa in infancy and childhood. *J. Pediat.*, **39**, 65.
- Fangman, R. J., and Hellwig, C. A. (1947). Histology of coronary arteries in newborn infants. *Amer. J. Path.*, **23**, 901.
- Forrer, H. (1930). *Ausgedehnte Gefäßverkalkung im frühen Kindesalter.* Inaugural dissertation. J. H. Meier, Zürich.
- Fowler, N. O., Gueron, M., and Rowlands, D. T., Jr. (1961). Primary myocardial disease. *Circulation*, **23**, 498.
- Friedberg, C. K., and Horn, H. (1939). Acute myocardial infarction not due to coronary artery occlusion. *J. Amer. med. Ass.*, **112**, 1675.
- Gault, M. H., and Usher, R. (1960). Coronary thrombosis with myocardial infarction in a newborn infant. Clinical, electrocardiographic and post-mortem findings. *New Engl. J. Med.*, **263**, 379.
- Goldman, A. M. (1962). Acute myocarditis simulating myocardial infarction. *Dis. Chest*, **41**, 61.
- Goormaghtigh, N., de Vos, L., and Blanquaert, A. (1955). Ostial stenosis of coronary arteries in a 9-year-old girl. *Arch. intern. Med.*, **95**, 341.
- Grant, R. P., and Estes, E. H., Jr. (1951). *Spatial Vector Electrocardiography*, 2nd ed. Blakiston, Philadelphia.
- Gross, L., Kugel, M. A., and Epstein, E. Z. (1935). Lesions of the coronary arteries and their branches in rheumatic fever. *Amer. J. Path.*, **11**, 253.
- Grossman, L. A., and Adams, C. W. (1964). Diminutive coronary artery syndrome. *J. Amer. med. Ass.*, **188**, 1111.
- Gruenewald, P. (1949). Necrosis in the coronary arteries of newborn infants. *Amer. Heart J.*, **38**, 889.
- Guild, H. G., Kindell, F. B., and Gibson, T. A. (1938). Arteriolosclerosis in childhood. *Bull. Johns Hopk. Hosp.*, **62**, 159.
- Hadorn, W. (1961). Seltene Herzkrankheiten unbekannter Genese. *Med. Klin.*, **56**, 653.
- Hastreiter, A. R., and Miller, R. A. (1964). Management of primary endomyocardial disease. *Pediatr. Clin. N. Amer.*, **11**, 401.
- Hogg, G. R. (1962). Cardiac lesions in hemolytic disease of the newborn. *J. Pediat.*, **60**, 352.
- House, R. K. (1948). Diffuse interstitial myocarditis in children. *Amer. J. Path.*, **24**, 1235.
- Hughes, F. W. T., and Perry, C. B. (1929). Senile arterial changes in a child aged seven weeks. *Bristol med.-chir. J.*, **46**, 219.
- Huttmann, A., and Cimpoeșu, M. J. (1958). Vortäuschung eines Myokardinfarktes durch interstitielle Myokarditis. *Z. Kreisl.-Forsch.*, **47**, 1107.
- James, T. N. (1962). Observations on the cardiovascular involvement, including the cardiac conduction system, in progressive muscular dystrophy. *Amer. Heart J.*, **63**, 48.
- (1964). An etiologic concept concerning the obscure myocardiopathies. *Progr. cardiovasc. Dis.*, **7**, 43.
- , and Fisch, C. (1963). Observations on the cardiovascular involvement in Friedrich's ataxia. *Amer. Heart J.*, **66**, 164.
- Jokl, E., and Greenstein, J. (1944). Fatal coronary sclerosis in a boy of ten years. *Lancet*, **2**, 269.
- Kambolis, K. P., Lebhar, N. F., and Barnett, R. N. (1958). Coronary thrombosis and myocardial infarction in a 4½-year-old boy. *Pediatrics*, **22**, 135.
- Kaplan, H. M. (1958). Immunologic studies of heart tissue. *J. Immunol.*, **80**, 254.
- Keay, A. J., Oliver, M. F., and Boyd, G. S. (1955). Progeria and atherosclerosis. *Arch. Dis. Childh.*, **30**, 410.
- Keith, J. D. (1959). The anomalous origin of the left coronary artery from the pulmonary artery. *Brit. Heart J.*, **21**, 149.
- , Rowe, R. D., and Vlad, P. (1958). *Heart Disease in Infancy and Childhood.* MacMillan, New York.
- Keizer, D. P. R., and Rochet, R. R. (1952). Anomalous origin of left coronary artery. *Amer. J. Dis. Child.*, **83**, 769.
- Kempton, J. J. (1951). Calcified aneurysms of the coronary arteries. *Proc. roy. Soc. Med.*, **44**, 733.
- Kline, I. K. (1961). Myocardial alterations associated with pheochromocytomas. *Amer. J. Path.*, **38**, 539.
- Klinefelter, H. F. (1942). The heart in sickle cell anemia. *Amer. J. med. Sci.*, **203**, 34.
- Koch, F., Schmidt, G. W., and Doll, E. (1957). Beitrag zur Agammaglobulinämie im Kindesalter. *Mshr. Kinderheilk.*, **105**, 211.
- Kremer, D. N. (1936). Medullary tumor of the adrenal glands with hypertension and juvenile arteriosclerosis. *Arch. intern. Med.*, **57**, 999.
- Lambert, E. C., and Vlad, P. (1958). Primary endomyocardial disease. *Pediatr. Clin. N. Amer.*, **5**, 1057.
- Lasser, R. P., and Jenkins, G. (1957). Chest pain in patients with isolated pulmonic stenosis. *Circulation*, **15**, 258.
- Leach, W. B. (1955). Calcific arteriosclerosis of infancy. *Canad. med. Ass. J.*, **73**, 733.
- Lightwood, R. (1932). A case of dwarfism and calcinosis associated with widespread arterial degeneration. *Arch. Dis. Childh.*, **7**, 193.
- Lindo, C. L., and Doctor, L. R. (1955). The electrocardiogram in sickle-cell anemia. *Amer. Heart J.*, **50**, 218.
- Lindsay, S. (1950). The cardiovascular system in gargoylism. *Brit. Heart J.*, **12**, 17.
- Lipman, B. C., Rosenthal, I. M., and Lowenburg, H., Jr. (1951). Arteriosclerosis in infancy. *Amer. J. Dis. Child.*, **82**, 561.
- McCormick, W. F. (1958). Endocardial fibroelastosis: a summary of the literature and review of 24 new cases. *Sth. med. J. (Bgham, Ala.)*, **51**, 1232.
- McDonald, S., Jr. (1932). Congenital syphilitic mesaortitis associated with acute yellow atrophy of the liver. *Brit. J. vener. Dis.*, **8**, 263.
- McMichael, J. (1929). Extensive visceral endarteritis obliterans in a young child. *Arch. Dis. Childh.*, **4**, 165.
- Martelle, R. R. (1955). Coronary thrombosis in a five-month-old infant. *J. Pediat.*, **46**, 322.
- Mehrizi, A., Rosenstein, B. J., Pusch, A., Askin, J. A., and Taussig, H. B. (1964). Myocardial infarction and endocardial fibroelastosis in children with polycystic kidneys. *Bull. Johns Hopk. Hosp.*, **115**, 92.
- Minkowski, W. L. (1947). The coronary arteries of infants. *Amer. J. med. Sci.*, **214**, 623.
- Moon, H. D. (1957). Coronary arteries in fetuses, infants, and juveniles. *Circulation*, **16**, 263.
- Moragues, V., Bawell, M. B., and Shrader, E. L. (1950). Coronary embolism: review of the literature and report of a unique case. *ibid.*, **2**, 434.
- Munro-Faure, H. (1959). Necrotizing arteritis of the coronary vessels in infancy. Case report and review of the literature. *Pediatrics*, **23**, 914.
- Nadas, A. S. (1963). *Pediatric Cardiology*, 2nd ed. Saunders, Philadelphia.
- , Alimurung, M. M., and Sieracki, L. A. (1951). Cardiac manifestations of Friedrich's ataxia. *New Engl. J. Med.*, **244**, 239.
- , Gamboa, R., and Hugenholtz, P. G. (1964). Anomalous left coronary artery originating from the pulmonary artery. Report of two surgically treated cases with a proposal of hemodynamic and therapeutic classification. *Circulation*, **29**, 167.
- Nelson, W. E. (1959). *Textbook of Pediatrics*, 7th ed. Saunders, Philadelphia.
- Neubauer, C. (1944). Myocarditis in acute infective diseases. A review of 200 cases. *Arch. Dis. Childh.*, **19**, 178.
- Noren, G. R., Raghib, G., Moller, J. H., Amplatz, K., Adams, P., Jr., and Edwards, J. E. (1964). Anomalous origin of the left coronary artery from the pulmonary trunk with special reference to the occurrence of mitral insufficiency. *Circulation*, **30**, 171.
- Norris, R. F. (1935). Syphilitic aortitis in childhood and youth. Report of 2 cases with sudden death. *Bull. Johns Hopk. Hosp.*, **57**, 206.
- Otero, E. A., del Zar, L., and Hojman, D. (1956). Embolia coronaria en una niña de 14 años con insuficiencia mitral, reumática sin endocarditis bacteriana. *Rev. argent. cardiol.*, **23**, 23. (French abstract, *Arch. Mal. Coeur*, **49**, 1164).
- Parrott, R. H., Joseph, L. G., and Nesbit, R. R. (1951). Left ventricular hypertrophy in infantile polycystic kidney disease. *J. Amer. med. Ass.*, **147**, 648.

- Pickard, C. M., Owen, J. G., and Dammin, G. J. (1947) Aneurysms of the coronary arteries due to polyarteritis nodosa occurring in an infant: report of a case with coronary artery thrombosis and myocardial infarction. *J. Lab. clin. Med.*, **32**, 1513.
- Prescott, R., Quinn, J. S., and Littmann, D. (1963). Electrocardiographic changes in hypertrophic subaortic stenosis which simulate myocardial infarction. *Amer. Heart J.*, **66**, 42.
- Pruitt, R. D., Curd, G. W., Jr., and Leachman, R. (1962). Simulation of electrocardiogram of apicolateral myocardial infarction by myocardial destructive lesion of obscure etiology (myocardiopathy). *Circulation*, **25**, 506.
- , Dennis, E. W., and Kinard, S. A. (1963). The difficult electrocardiographic diagnosis in myocardial infarction. *Progr. cardiovasc. Dis.*, **6**, 85.
- Rae, M. V. (1937). Coronary aneurysms with thrombosis in rheumatic carditis. *Arch. Path.*, **24**, 369.
- Ramsay, R. E., and Crumrine, R. M. (1931). Coronary thrombosis in an infant aged 4 months. *Amer. J. Dis. Child.*, **42**, 107.
- Ravich, R. M., and Rosenblatt, P. (1947). Myocardial infarction in the newborn infant. *J. Pediat.*, **31**, 266.
- Rossi, E. (1954). *Herzkrankheiten im Säuglingsalter*. G. Thieme, Stuttgart.
- Ruttenberg, H. D., Jue, K. L., Elliott, L. P., Anderson, R. C., and Edwards, J. E. (1964). Cardiac myopathy, probably of congenital origin. A case simulating anomalous origin of the left coronary artery from the pulmonary trunk. *Circulation*, **29**, 768.
- Sabiston, D. C., Jr., Neill, C. A., and Taussig, H. B. (1960a). The direction of blood flow in anomalous left coronary artery arising from the pulmonary artery. *ibid.*, **22**, 591.
- , Pelargonio, S., and Taussig, H. B. (1960b). Myocardial infarction in infancy. The surgical management of a complication of congenital origin of the left coronary artery from the pulmonary artery. *J. thorac. cardiovasc. Surg.*, **40**, 321.
- , Ross, R. S., Criley, J. M., Gaertner, R. A., Neill, C. A., and Taussig, H. B. (1963). Surgical management of congenital lesions of the coronary circulation. *Ann. Surg.*, **157**, 908.
- Sanghvi, L. M., Misra, S. N., Bannerji, K., and Gupta, K. D. (1958). Electrocardiogram in chronic severe anemia. *Amer. Heart J.*, **56**, 79.
- Saphir, O. (1959). Nonrheumatic inflammatory diseases of the heart, p. 696; Myocarditis p. 779. In *Pathology of the Heart*, 2nd ed. Ed. by J. E. Gould, C. C. Thomas, Springfield, Illinois.
- , and Cohen, N. A. (1957). Myocarditis in infancy. *Arch. Path.*, **64**, 446.
- , and Field, M. (1954). Complications of myocarditis in children. *J. Pediat.*, **45**, 457.
- Scholer, H. (1961). Ueber eine infarktähnliche EKG-Manifestation einer akuten Myokarditis (Pseudo-Epicard-Syndrom). *Cardiologia (Basel)*, **38**, 66.
- Schornagel, H. E. (1956). Intimal thickening in the coronary arteries in infants. *Arch. Path.*, **62**, 427.
- Schott, J., Jacobi, M., and Wald, M. A. (1955). Electrocardiographic patterns in the differential diagnosis of progressive muscular dystrophy. *Amer. J. med. Sci.*, **229**, 517.
- Scott, E. P., and Miller, A. J. (1946). Coronary thrombosis. Report of a case in an infant 11 months of age. *J. Pediat.*, **28**, 478.
- Scott, J. M. (1961). Fatty change in the myocardium of the newborn. *Brit. med. J.*, **2**, 1746.
- Shivelhood, E. K. (1948). Myocardial infarction in a 12-year-old boy with diabetes. *Amer. Heart J.*, **35**, 655.
- Shrader, E. L., Bawell, M. B., and Moragues, V. (1956). Coronary embolism. *Circulation*, **14**, 1159.
- Siegenthaler, W. (1958). Die cardiovasculären Veränderungen beim viszeralen Lupus erythematosus. *Cardiologia (Basel)*, **32**, 161.
- Sinclair, W., Jr., and Nitsch, E. (1949). Polyarteritis nodosa of the coronary arteries. *Amer. Heart J.*, **38**, 898.
- Spach, M. S., Howell, D. A., and Harris, J. S. (1963). Myocardial infarction and multiple thrombosis in a child with primary thrombocytosis. *Pediatrics*, **31**, 268.
- Sprague, H. B., and Orgain, E. S. (1935). Electrocardiographic study of cases of coronary occlusion proved at autopsy at the Massachusetts General Hospital 1914-34. *New Engl. J. Med.*, **212**, 903.
- Strauss, L., and Platt, R. (1957). Endocardial sclerosis in infancy associated with abnormal storage (gargoylism). *J. Mt Sinai Hosp.*, **24**, 1258.
- Stryker, W. A. (1946a). Coronary occlusive disease in infants and in children. *Amer. J. Dis. Child.*, **71**, 280.
- (1946b). Arterial calcification in infancy with special reference to the coronary arteries. *Amer. J. Path.*, **22**, 1007.
- Talbot, N. B., Butler, A. M., Pratt, E. L., MacLachlan, E. A., and Tannheimer, J. (1945). Progeria. Clinical, metabolic and pathologic studies on a patient. *Amer. J. Dis. Child.*, **69**, 267.
- Tedeschi, C. G., and Stevenson, T. D., Jr. (1951). Interstitial myocarditis in children. *New Engl. J. Med.*, **244**, 352.
- Thomas, W. A., Lee, K. T., McGavran, M. H., and Rabin, E. R. (1956). Endocardial fibroelastosis in infants associated with thrombosis and calcification of arteries and myocardial infarcts. *ibid.*, **255**, 464.
- Thorén C. (1964). Cardiomyopathy in Friedreich's ataxia with studies of cardiovascular and respiratory function. *Acta paediat. (Uppsala)*, **53**, Suppl., 153.
- Traisman, H. S., Limperis, N. M., and Traisman, A. S. (1956). Myocardial infarction due to calcification of the arteries in infants. *Amer. J. Dis. Child.*, **91**, 34.
- Van Creveld, S., and De Jager, H. (1956). Myocarditis in newborns caused by coxsackie virus. Clinical and pathological data. *Ann. paediat. (Basel)*, **187**, 100.
- Vlad, P., Rowe, R. D., and Keith, J. D. (1955). The electrocardiogram in primary endocardial fibroelastosis. *Brit. Heart J.*, **17**, 189.
- Watson, D. G., and Keith, J. D. (1962). The Q wave in lead V₆ in heart disease of infancy and childhood, with special reference to diastolic loading. *Amer. Heart J.*, **63**, 629.
- Wegelius, O., and von Knorring, J. (1964). Severe disseminated myocardial fibrosis in man without coronary involvement. The result of an autoimmune process? *Acta. med. scand.*, **412**, Suppl., 239.
- Weisenfeld, S., and Messinger, W. J. (1952). Cardiac involvement in progressive muscular dystrophy. *Amer. Heart J.*, **43**, 170.
- Williams, H., O'Reilly, R. N., and Williams, A. (1953). Fourteen cases of idiopathic myocarditis in infants and children. *Arch. Dis. Child.*, **28**, 271.
- Ziegler, R. F. (1951). *Electrocardiographic Studies in Normal Infants and Children*. C. C. Thomas, Springfield, Illinois.

Corrigendum

Control of Enuresis with Imipramine, by D. Shaffer, A. J. Costello, and I. D. Hill.

Page 667. 6 lines from bottom of right-hand column. For 'one of the 3 patterns: Placebo, Low, Placebo; Placebo, High, Placebo; Low, Placebo, Low' read—'one of the 4 patterns: Placebo, Low, Placebo; Placebo, High, Placebo; Low, Placebo, Low; High, Placebo, High'.