Jovan Rajs,[1] *M.D., Ph.D.*

Cardiovascular Abnormalities in Children: A Ten-Year Forensic Pathologic Study

REFERENCE: Rajs, J., **"Cardiovascular Abnormalities in Children: A Ten-Year Forensic Pathologic Study,"** *Journal of Forensic Sciences*, JFSCA, Vol. 30, No. 4, Oct. 1985, pp. 1157-1178.

ABSTRACT: In order to obtain information on types, incidence, and significance of cardiovascular abnormalities in children, a total of 104 consecutive medicolegal autopsies of children aged 8 days to 16 years during a 10-year period from May 1974 to April 1984 were studied. Extensive histological examination of the hearts was performed in 92 out of 104 cases and complemented with chemical and microbiological analyses. In the natural death group consisting of 53 children, 26 (49%) showed abnormalities: 7 (13%) malformations, 11 (21%) cardiomyopathies, 5 (9%) idiopathic subaortic hypertrophy, and 3 (7%) a heart weight only 50% of the expected weight. In the violent death ("control") group, abnormalities were found in 8 of 39 cases (21%), all of which were cardiomyopathy. Only 5 of 34 cardiovascular abnormalities (every 7th case), all complex malformations, were clinically recognized. In 14 (15%) of the total 92 examined cases the cardiovascular abnormality was the only apparent cause of death, and in 12 (13%) a contributing cause of sudden unexpected natural death, while in 3 (3%) it was related to a fatal accidental injury. In 5 (13%) of the 39 cases of violent death, cardiomyopathy was an incidental finding without any connection to the circumstances or cause of death. The causes of cardiovascular abnormalities were associated with bacterial and viral infections, respiratory disorders, phenytoin sensitivity, or were unknown. Because of the differences in diagnostic criteria employed by previous investigators, it cannot be determined whether the incidence of the cardiovascular abnormalities and sudden cardiac death in children found in this material was higher than in other studies.

KEYWORDS: pathology and biology, children, cardiovascular system, postmortem examinations, cardiovascular abnormalities

Authors of previous physical and pathoanatomical studies differ in their opinion concerning the types and frequencies of cardiovascular disease in children. Akman et al [*1*] diagnosed by detailed (clinical) examination cardiac abnormalities, mostly congenital malformations, in 25 (0.6%) of 4074 children, 5 to 17 years of age. Norén et al [*2*] found myocarditis and also cases of extensive myocardial fibrosis, endocardial fibroelastosis, and patent ductus arteriosus in 17 (12.3%) of 138 cases, and Saphir et al [*3*] found similar abnormalities in 97 (6.83%) of 1420 histologically reviewed autopsies of children through the age of 16 years. The frequency of asymptomatic myocarditis as an incidental finding in autopsies of persons who died of violence has been reported to be 3 to 5% [*2,4-6*]. The types and relative frequency of cardiovascular abnormalities causing sudden unexpected death in children aged 1 to 21 years were thoroughly analysed by Lambert et al [*7*] in an international cooperative study. The authors stressed the necessity of information on the absolute frequency of the various cardiovascular abnormalities to permit an estimation of the risk for the individual patient.

The morphological criteria employed for the diagnosis of myocarditis are varied, particularly the quantitative ones, concerning the number of inflammatory cells in a single focus as

Received for publication 18 Dec. 1984; accepted for publication 7 Jan. 1985.
[1]Department of Forensic Medicine, Karolinska Institutet, Stockholm, Sweden.

well as the number of foci and investigated tissue blocks [2,4-6]. Consequently, the opinions about the significance of myocarditis are oscillating between "fatal" and "only of academic rather than clinical interest" [8,9]. There are also discrepancies concerning the criteria used to define cardiomyopathies [10], but much less so for cardiovascular malformations.

The forensic pathologic (medico-legal) autopsies comprising fatalities as a result of natural as well as violent causes have previously been used as a suitable basis for evaluation of cardiovascular abnormalities, with cases of violent death serving as "controls" in comparison with the fatalities as a result of natural causes [2,11]. However, a histological examination of the heart was performed by these authors in only 117 of 1378, and 138 of 329 autopsies, respectively.

The aim of this study was to use information collected from forensic pathologic autopsies to document more accurately the actual types and frequencies of fatal and asymptomatic cardiovascular abnormalities in children.

Methods

A total of 3250 nonselected deaths were investigated by the author during a 10-year period, from May 1974 to April 1984. Of these, 104 deaths (3.2%) occurred in children aged between 8 days and 16 years. Fifty-five children (53%) died suddenly of natural causes outside the hospital. Forty-nine (47%) died of violence; forty-two (41%) in accidents, three (3%) committed suicide, and three (3%) were murdered. In twelve cases (12%) no histological examination of the macroscopically normal heart was performed (eleven males, one female; nine victims of accidents, one suicide, and two natural deaths). Of the remaining 53 children who died naturally, 32 were boys and 21 girls; 36 of them were under the age of 1 year. Of the remaining 39 children who died of violence, 24 were boys and 15 girls; among these only 4 were under the age of 1 year.

The majority of the children resided in the Stockholm area. Patient histories and information about circumstances of death were obtained from the medical and police records as well as from surviving relatives of the children. Before autopsy, the bodies were kept in a refrigerated mortuary near a temperature of +4°C. Autopsy was performed one to six days after death and was completed with histological examination of the heart and other organs, as well as with toxicological and, in cases of nonviolent death, bacteriological and virological analyses. The intact hearts were separated above the atria and pulmonary and aortic valves, weighed, and the ratio of actual versus expected heart weight was calculated with regard to age [12]. Samples for microscopic examination were taken from the atrial and ventricular septa; the anterior and posterior wall of the left ventricle, including both papillary muscles; and the anterior wall of the right ventricle. Sections from the left ventricle were in the majority of cases oriented parallel to the longitudinal axis of the ventricle. Depending on the size of the heart, 5 to 15 tissue blocks per case were examined.

All tissue blocks were submitted to routine histologic staining methods. The myocardial sections were also stained with phosphotungstic acid hematoxylin (PTAH), hematoxylin-basic fuchsin-picric acid (HBFP), periodic acid-Schiff reaction (PAS), Congo red, and Weigert's resorcin fuchsin elastic stain, and in some instances, with toluidine blue. Sections from the lungs were also stained with Perl's blue stain in order to visualize "heart-failure" cells [13,14].

Criteria

Cardiomyopathy as a general term is used to denote intrinsic disease of the myocardium, which is not caused by shunts or valvular disease [15]. In cases exhibiting predominantly acute, subacute, or chronic inflammatory lesions the cardiomyopathy is referred to as "myocarditis." Chronic cardiomyopathies, hypertrophic or nonhypertrophic, in which myocardial fibrosis with minimal inflammatory reaction was found are called fibrotic cardiomyopathies [10]. The classification of the cardiomyopathy, whether primary or secondary to other sys-

temic disease, or to diseases of other organs, was evaluated. The term primary endocardial fibroelastosis is used according to McCormick [*16*].

The minimal alterations taken into consideration were those found by light microscopic examination consisting of one or more areas of inflammation, characterized by infiltrates of at least 20 inflammatory cells, with or without associated necrosis or fibrosis, as proposed by Norén et al [*2*]. Degenerative alterations characterized by a lack of inflammatory reaction were not considered. Thus, the finding of the proliferative cellular reactive phase of the process called myofibrillar degeneration [*17*] was a prerequisite to the diagnosis myocarditis, but neither the early features of the process—contraction bands, nor the late phase of stromal condensation. The following were not recorded when found in nonhypertrophic hearts:

small, acellular fibrous scars in the myocardium;
calcifications in the apices of the papillary muscles;
increased amounts of interstitial fat;
bizarely shaped and disorganized myofibers [*18–20*]; or
mononuclear leukocytes adjacent to singular vascular branches and nerves in the subepicardial adipose tissue.

If intensive medical or surgical care had been given immediately before death, only those obvious myocardial alterations older than the condition which motivated the treatment were reported in this study. This implies that findings of fragmentation of the myofibers or recent interstitial hemorrhages which might have developed agonally were not reported.

Results

The findings of the present study are outlined in Tables I through VIII. Individual cases of cardiovascular abnormalities are listed by a roman numeral indicating the table number and an arabic numeral indicating the position in the table.

Congenital Malformations

In seven children, autopsy disclosed congenital malformation of the heart, that is, in 7% of the total of 104 autopsies or 13% of the 55 natural deaths (Table I). In five instances the malformation had been previously recognized, which comprised the only clinically diagnosed cardiovascular diseases in this series. Four of these malformations were complex; one child had only an isolated coarctation of the aorta (Fig. 1). Three of these five children died suddenly at different intervals after cardiac surgery (Cases I/1, I/3, and I/6) and two other children died before planned surgery (Cases I/4 and I/7). In the cases of isolated atrial or ventricular septal defect (Fig. 2), the malformation had not been previously diagnosed (Cases I/2 and I/5).

Cardiomyopathies

Among the total of 92 autopsies investigated histologically, 19 (21%) showed cardiomyopathy. In no case was this condition diagnosed before death. The occurrence of the various cardiomyopathies in the natural and violent death groups is shown in Table II, and the distribution according to sex in Table III.

Myocarditis—Nine children (10%) had myocarditis. In five (5%) the lesions were nonspecific nongranulomatous, focal myocarditis (Figs. 3 to 5). In four (4%) other cases, myofibrillar degeneration was observed (Fig. 6). In four instances inflammatory and necrotic lesions were associated with fibrosis.

The past history and the findings are shown in Table IV. In five of the nine cases the myocarditis was an isolated pathological finding, while in four it coincided with other organ alterations. Endocarditis did not occur in this series.

TABLE I—*Age, sex, past history, and postmortem findings of seven children with congenital heart malformation.*

Patient	Age and Sex	Past History	Postmortem Findings	Ratio Heart Weight / Expected Heart Weight
1	3.5 months, female	Transposition of the great vessels. Mild respiratory infection one day before found dead in crib.	Surgically corrected transposition of the great vessels.	2.2
2	2 months, female	No history of previous illness. Mild respiratory infection one day before found dead in crib.	Atrial septal defect at the fossa ovalis.	1.0
3	8 years, male	Transposition of the great vessels. Instantaneous death during meal.	Surgically corrected transposition of the great vessels. Minor branches of pulmonary arteries with thickened wall or obliterated lumina.	3.4
4	1.5 months, female	Coarctation of the aorta. Crib death.	Coarctation of the aorta. Obliterated ductus arteriosus. Thickening of the minor branches of the pulmonary arteries.	4.0
5	3 months, male	No history of previous illness. Crib death.	Central muscular ventricular septal defect. Aspiration of gastric content. Staphylococcus aureus in heart blood.	2.0
6	14 years, male	Noonan's syndrome with clinically diagnosed atresia of the tricuspid valve. Temporary attacks of tachycardia. Instantaneous death during walk.	Atresia of the pulmonary trunk. Operative anastomosis between aorta and right pulmonary artery.	1.9
7	1.5 months, female	Vater syndrome with clinically diagnosed patent ductus arteriosus and rectovaginal fistula. Crib death.	Patent ductus arteriosus and atrial septal defect at the fossa ovalis. Rectovaginal fistula. Cake kidneys.	1.2

Chronic Cardiomyopathy—Seven children aged 3 to 15 years (8%) had signs of chronic cardiomyopathy (Table V, Figs. 7 and 8). In two additional children, minute, focal, nonreactive scars were noted microscopically but were not considered significant. Five of the seven children had fibrotic cardiomyopathy, of which four demonstrated predominantly left ventricular hypertrophy and one biventricular hypertrophy. The remaining two children had cor pulmonale (Fig. 9). The chronic cardiomyopathy was an isolated process in four instances and concomitant with chronic respiratory disorder in three other cases (Cases IV/4, V/5, and V/7).

Endocardial Fibroelastosis—In three children (3%), all under the age of two years, endocardial fibroelastosis was found (Table VI and Figs. 10 and 11). The incidence in the total autopsy material was 0.09%.

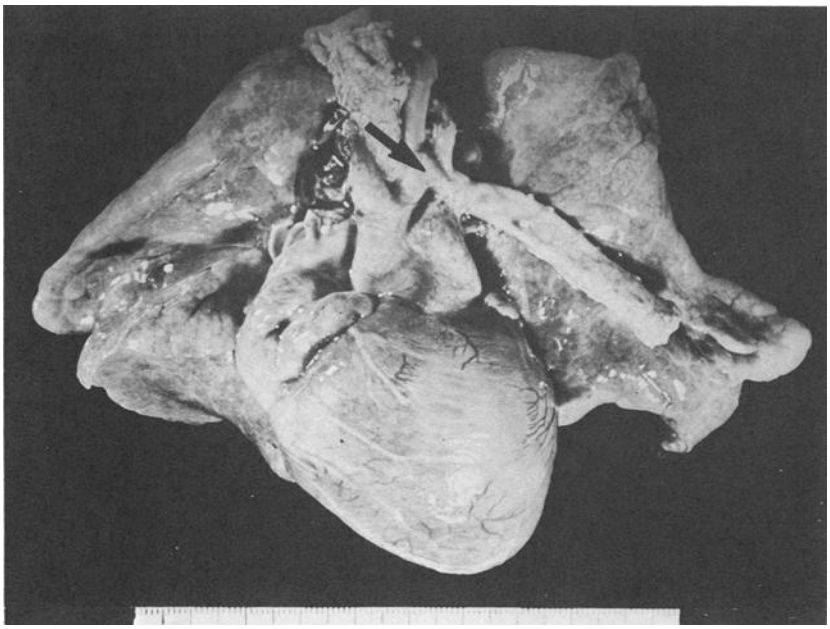

FIG. 1—*Case I/4. Sudden death. Coarctation of the aorta* (arrow) *with obliteration of ductus arteriosus and dilatation of pulmonary trunk. Heart weight 400% of normal.*

Heart Weights

The comparison of the actual heart weights to the age-related expected heart weights showed that the heart weights of the 31 children who died of violence and whose autopsy showed no gross or histological cardiovascular alterations were concentrated in a symmetric, narrow histogram contained within 2 standard deviations (SD) from the mean (Fig. 12*a*). The heart weight of children with cardiomyopathies and heart malformations tended to be shifted to the right, toward higher values (Fig. 12*b* and *c*).

In the remaining group of 35 children who died suddenly and unexpectedly and whose hearts were histologically examined, the heart weight was more than 2 SD above the expected weight in eight cases (Fig. 12*d*). In four boys and one girl aged one and one-half to four and one-half months, the heart weighed 140 to 200% of the expected weight. Massive bronchopneumonia was found in one of them, while in the remaining four, autopsy showed no other pathological findings. According to the past history, a boy with a heart weight 200% of that expected suffered nocturnal attacks of crying and cyanosis, while the past histories of the other four children revealed no information. These large hearts showed a subaortic hypertrophy of the interventricular septum (Fig. 13). No inflammation or fibrosis was noted in these hearts, but in three cases spirally arranged bundles of myofibres were seen in the subaortic area (Fig. 14).

In three children, the heart weighed only 50% of the expected value. Two boys—three and fifteen months old—died suddenly and unexpectedly, one of them with a history of episodes of dyspnea. There was no increased amount of lipofuschin pigment in these small hearts, indicating that the condition was a result of cardiac hypoplasia rather than of atrophy. The third child with a heart weight of only 50% of that expected was a marantic 15-year-old girl with 2 years' history of anorexia nervosa. During the months before death her pulse rate was about 40/min

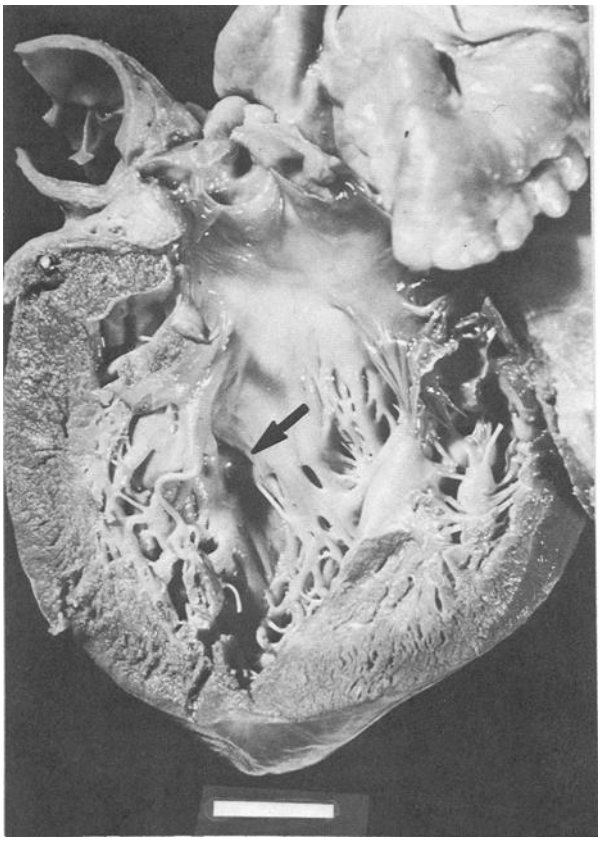

FIG. 2—*Case I/5. Sudden death. Central muscular ventricular septal defect* (arrow) *with secondary fibroelastosis of the endocardium. Heart weight 200% of normal.*

TABLE II—*Incidence of cardiomyopathies found in 92 histologically reviewed forensic pathologic childhood autopsies.*

Type of Death	Reviewed by Histology		Myocarditis		Chronic Cardio-myopathy		Endocardial Fibro-elastosis		Total	
n	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Sudden unexpected 55	53	(100)	5	(9)	5	(9)	1	(2)	11	(21)
Violent 49	39	(100)	4	(10)	2	(5)	2	(5)	8	(21)
Total 104	92	(100)	9	(10)	7	(8)	3	(3)	19	(21)

TABLE III—*Distribution of cardiomyopathies according to the sex of 92 histologically reviewed forensic pathologic childhood autopsies.*

Alterations	Males		Females	
	56	(%)	36	(%)
Myocarditis	4	(7)	5	(14)
Chronic cardiomyopathy	4	(7)	3	(8)
Endocardial fibroelastosis	2	(4)	1	(3)
Total	10	(19)	9	(25)

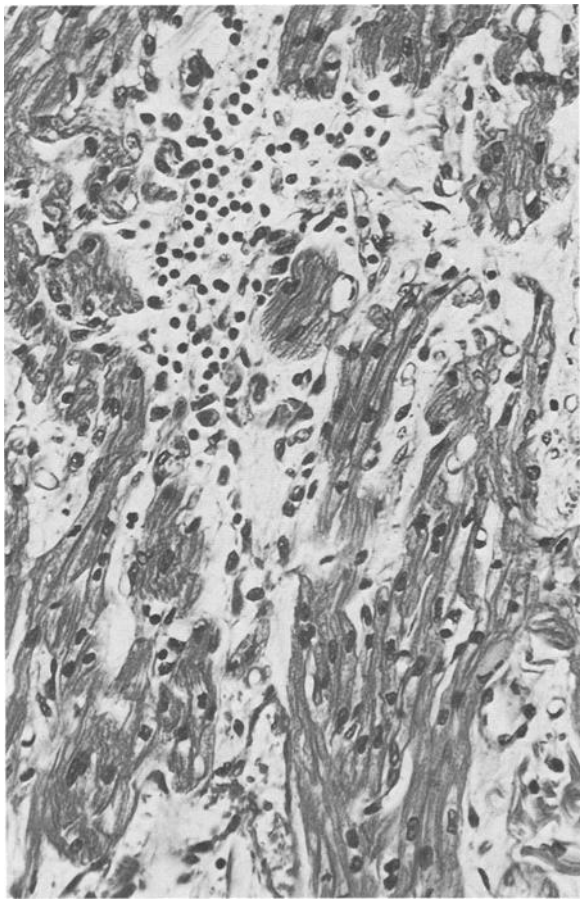

FIG. 3—*Case IV/9. Sudden death. The minimal reported sole alteration in this series: focus consisting of about 70 polymorphonuclear and mononuclear leukocytes in the lower right part of the interatrial septum proximally to the AV mode. Hematoxylin and eosin ×320.*

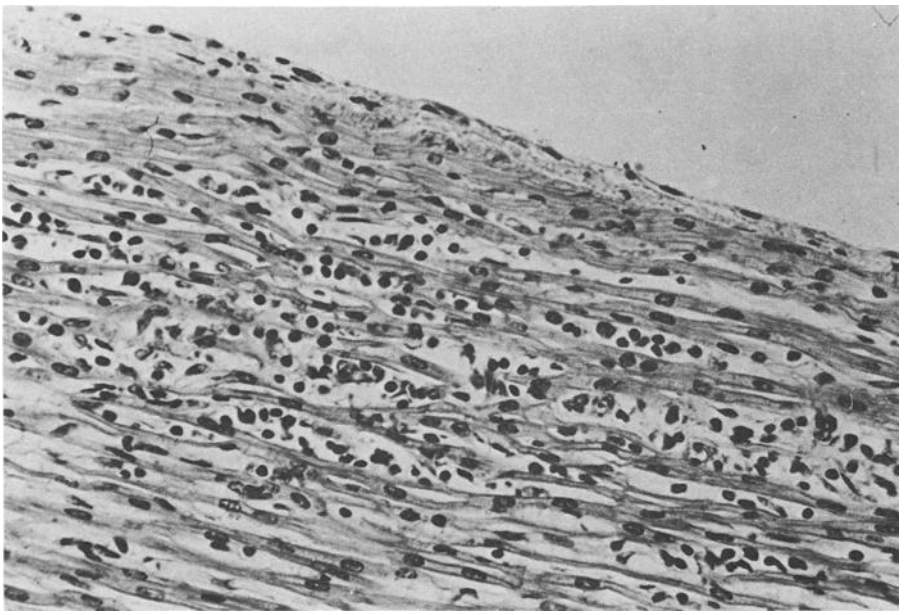

FIG. 4—*Case IV/1. Sudden death. ECHO viremia. Focus of necrotic myofibers and mononuclear leukocytes in the left ventricular subendocardium. Hematoxylin and eosin ×200.*

and the systolic blood pressure 90 to 100 mmHg. Episodes of relative tachycardia with a pulse rate of 100/min were noted. One month before death her electrocardiogram (ECG) showed regular sinus rhythm and repolarization changes, particularly in the left inferior ventricular wall. Severe bronchopneumonia was the immediate cause of death. The myocardium showed atrophic myofibers and increased cellularity of the interstices, but no other alterations.

Thus, a heart weight beyond 2 SD of the expected weight was considered to be pathological and was likely to be associated with functional disturbances such as insufficiency of the cardiac pump function, hypotonia, bradycardia, or subnormal oxygen consumption.

The five children with hypertrophic heart constituted 14%, and the child with hypoplastic heart 3%, of the total of 36 children under the age of 1 year who died suddenly and unexpectedly. The ratios of actual versus expected heart weights as related to various cardiovascular findings are shown in Table VII.

Other Findings

The distribution of the various cardiovascular abnormalities according to the age of the autopsied children is presented in Fig. 15.

About one third of the children under the age of one year exhibited some abnormality, and cardiovascular diseases were the dominant postmortem finding through all ages in the natural death group. The incidence of cardiovascular abnormalities decreased with age in the violent death group (Fig. 16). The incidence of alterations was fairly constant during the ten-year period (data not shown). In this series, no children had a history or evidence of malnutrition, except the cases with operated esophagotracheal fistula and anorexia nervosa. Alcohol or drug abuse, diabetes, and heart diseases did not occur in the families of the children with cardiovascular abnormalities. Apart from the children with a known history of congenital heart malformation, bronchial asthma, and epilepsy, no children had been on continuous drug treatment.

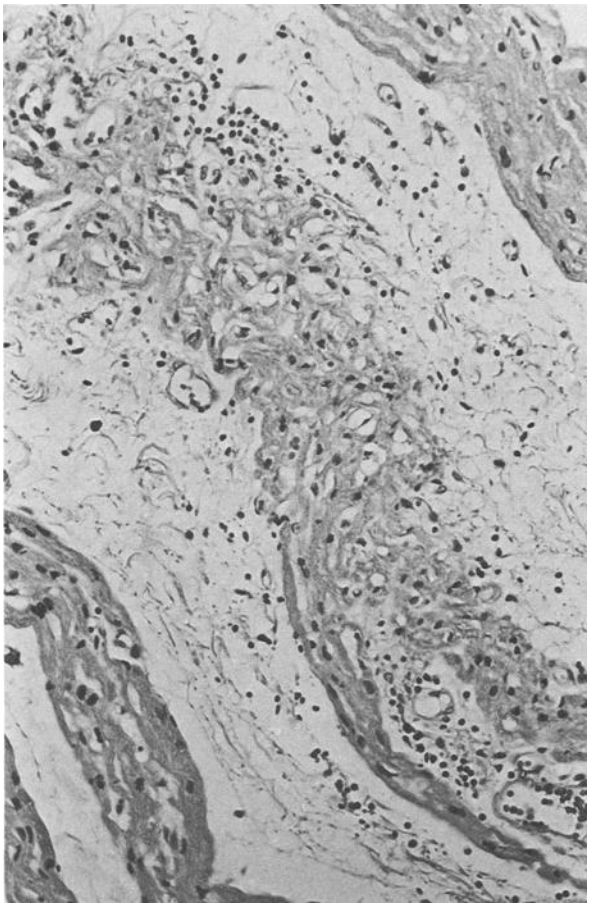

FIG. 5—*Case IV/2. Sudden death. Perivascular mononuclear leukocytes surrounding one of the left branches of the AV bundle. Patient treated for epilepsy with phenytoin and phenobarbital. Hematoxylin and eosin* ×*80.*

The histological techniques failed to disclose abnormal storage of glycogen, mucopolysaccharides, or amyloid. Heart failure cells as indicators of chronic pulmonary congestion were found only in three cases, all with congenital heart malformations.

Cause of Death

Among the 92 children histologically examined following autopsy, 34 (37%) showed cardiovascular abnormalities (that is, malformations, cardiomyopathies, or heart weight aberrations) which needed to be taken into account when evaluating the cause of death. The corresponding figures for the sudden unexpected natural death group were 26/53 (49%) and for the violent death group 8/39 (21%), all 8 being cardiomyopathies. The estimated significance of the cardiovascular abnormalities is shown in Table VIII.

In 5 of 39 (13%) children who died of violence and whose hearts were histologically examined, the cardiomyopathy was an incidental autopsy finding without any plausible connection

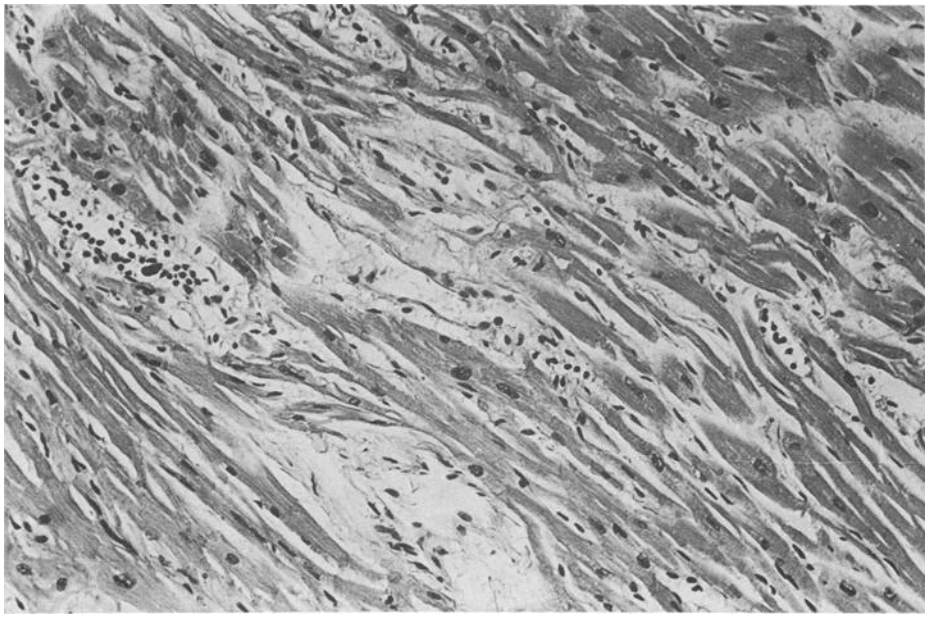

FIG. 6—*Case IV/3. Violent death. Myofibrillar degeneration with foci of endothelial cells, fibroblasts, and monocytes. Condensed stroma with increased amount of collagenous fibers. Hematoxylin and eosin ×200.*

TABLE IV—*Age, sex, past history, and postmortem findings of nine children with myocarditis.*

Patient	Age and Sex	Past History	Postmortem Findings	Ratio Heart Weight / Expected Heart Weight
1	3 months, female	Mild respiratory infection seven days before being found dead in crib.	Numerous foci with more than 100 mononuclears in the left ventricular wall, subendocardium, and interatrial septum. Interstitial pneumonia. Virological evidence of ECHO-virus in the lungs, kidneys, and spleen.	1.0
2	4 years, male	Mental retardation of unknown origin. Epilepsy of grand mal type. Treated with phenytoin and phenobarbital. Found dead.	In the left ventricular subendocardium 3 foci with 15, 20, and 100 mononuclears, 1 focus adjacent to the bifurcation of the AV bundle. Bronchopneumonia. Microcephalia. 3.6 mg/dL phenytoin and traces of phenobarbital in blood.	1.0
3	13 years, female	Mild form of measles and influenza years before death. Suicidal jump from a high tower. Died immediately.	Ventricular myocardium with numerous focal necroses with 15 to 50 mononuclears and mast cells as well as stromal condensation and minute scars.	0.9

TABLE IV—*Continued.*

Patient	Age and Sex	Past History	Postmortem Findings	Ratio Heart Weight / Expected Heart Weight
4	6 years, male	Cerebral paralysis with epileptiform seizures since birth. Treated with phenytoin and phenobarbital. Week before death caught cold and became slow, adynamic, and febrile. Found dead in prostrate position.	Focal necroses in the left ventricular subendocardium with 50 to 100 mononuclears and some mast cells. Areas of stromal condensation and focal scarring. Gliosis of the cerebellum. Purulent bronchopneumonia.	0.7
5	27 months, female	Parotitis at six months. Laryngotracheobronchitis at twelve months. After that episodes of fainting and cyanosis. Found drowned in bathtub.	Five foci of necrosis with 20 to 50 mononuclears in both ventricular walls. Aspiration of gastric content. Lungs as by drowning.	1.6
6	4.5 years, female	No history of preceding illness. Stabbed to death by schizophrenic brother.	Two foci of necrosis with about fifty mononuclears and fibrous scars in the interstices of the left ventricular myocardium. Chronic hepatitis with areas of postnecrotic cirrhosis. Chronic bronchitis.	0.8
7	8.5 months, male	No history of preceding illness. Crib death.	Numerous foci consisting of 20 to 30 mononuclears in the atrial and ventricular myocardium. Virological evidence of cytomegalovirus in the lungs and liver.	1.2
8	7 years, male	Influenza at the age of five with 40°C fever for one week. No symptoms of cardiac disease. Found dead in a boat cabin 1 h after he complained of tiredness and went to sleep. No previous exposition to exhaust gas.	Numerous foci of 50 to 100 mononuclears with necrotic myocytes or fibrosis. Perivascular infiltrates of mononuclears. Blood carbon monoxide only 26%.	1.1
9	4 months, female	No historyof preceding illness. Crib death.	One focus with about seventy polymorphonuclears just proximally to the AV node. Minute foci of bronchopneumonia. Klebsiella pneumoniae in lung tissue and staphylococcus aureus in lungs, blood, and spleen.	1.0

with the circumstances or cause of death (see Cases IV/3, IV/6, V/3, V/6, and VI/1). In the remaining three, the preexisting nonmainfested cardiomyopathy probably triggered the fatal accident (see Cases IV/5 and VI/2) or contributed to the fatal outcome of the accidental injury (see Case IV/8). Since the number of histologically examined autopsies of children who died in accidents 34, the incidence of a "clinically silent" cardiomyopathy as an originating factor could be as high as 9%.

TABLE V—*Age, sex, past history, and postmortem findings of seven children with chronic cardiomyopathy.*

Patient	Age and Sex	Past History	Postmortem Findings	Ratio Heart Weight / Expected Heart Weight
1	15 years, male[a]	Severe cranio-cerebral injury followed by unconsciousness for five days at the age of eight years. Later measles and scarlatina, mild form. Instantaneous death while running.	Myocardial fibrosis with focal necroses and thickening of the wall of the minor branches of the coronary arteries. Residua after cerebral injury.	1.5
2	14 years, male	Encephalitis, laryngotracheobronchitis and gastroenteritis with respiratory insufficiency at the age of 15 months. Viral etiology suspected but not proven. Measles, severe form, at the age of six years. Used to be dyspnoic when eating nuts. Instantaneous death while running.	Myocardial fibrosis and focal necroses with 50 to 100 mononuclears and thickening of the wall of the minor branches of coronary arteries. Mononuclears and recent hemorrhages in the vicinity of the AV bundle.	1.2
3	10.5 years, female	Mental retardation. Epileptic seizures of grand mal type. Treated with phenytoin and phenobarbital for many years. Injured in traffic accident, died two days later.	Pronounced thickening of the wall of the minor branches of the coronary arteries. Focal scars in the myocardium. Diffuse fibrosis of the ventricular septum.	1.3
4	3 years, female	Operated congenital esophageotracheal fistula. Attacks of stridorous breathing. General hypotrophy. Sudden death during a coughing attack.	Biventricular hypertrophy. Patchy myocardial fibrosis, stromal condensation and numerous foci of myocytic necrosis with 25 to 50 mononuclears. Chronic bronchitis and acute broncho-pneumonia.	1.1
5	12 years, male	Severe bronchial asthma since early childhood. Found dead.	Cor pulmonale. No myocardial fibrosis, no inflammation.	1.4
6	8 years, male	Pneumonia caused by *Haemophilus influenzae* at the age of one year. No history of cardiac disease. Run over by truck and died within 2 h of retroperitoneal hemorrhage.	Stromal condensation and 5 foci of 15 to 20 mononuclears with some eosinophils in the ventricular myocardium.	1.6
7	1 year, female	Congenital arthrogryposis. Attacks of dyspnea and cyanosis. Recurrent respiratory infections. Transient systolic murmurs. During the last two weeks of life short periods of apnea. Crib death.	Cor pulmonale. Stromal condensation and numerous foci of up to 30 mononuclears. Bronchopneumonia. Mesenterium commune.	1.4

[a]This case was reported previously [*21*].

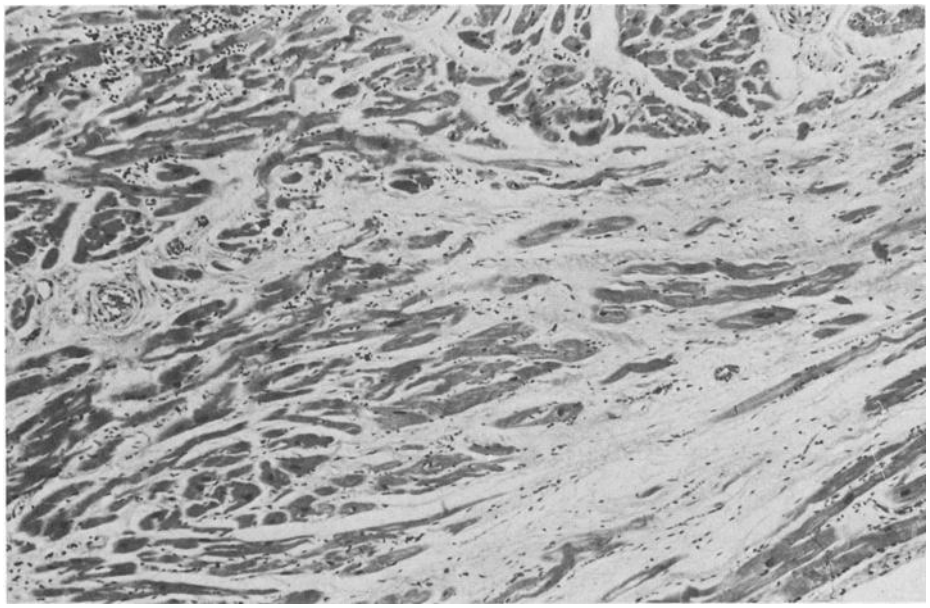

FIG. 7—*Case V/2. Sudden death. Fibrotic cardiomyopathy. Fibrous scar and mononuclear leukocytes in the left ventricular wall. Hematoxylin and eosin ×80.*

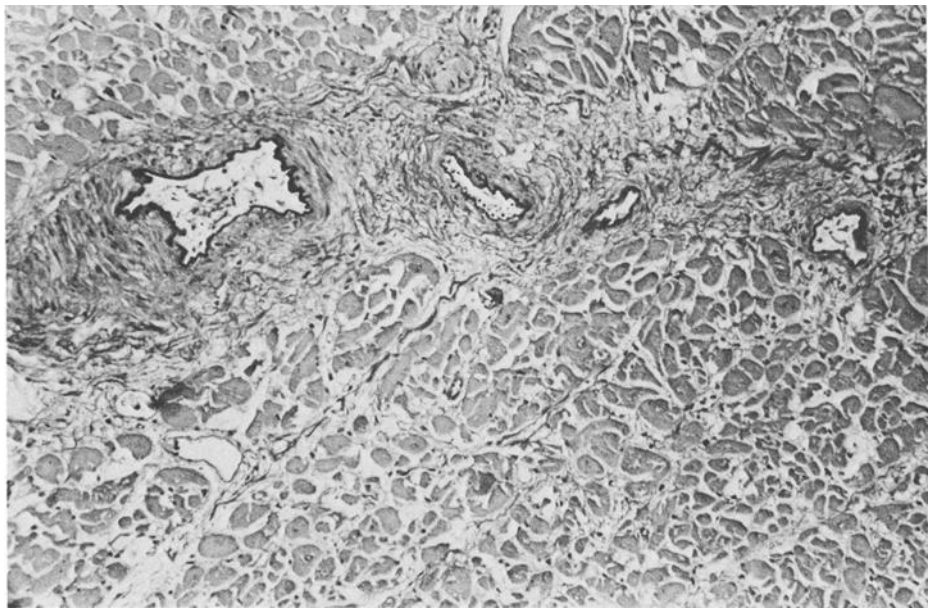

FIG. 8—*Case V/3. Violent death. Fibrotic cardiomyopathy with abundant collagenous tissue perivascularly and in the interstices. Treated for epilepsy with phenytoin and phenobarbital. Weigert's resorcin fuchsin elastic stain ×200.*

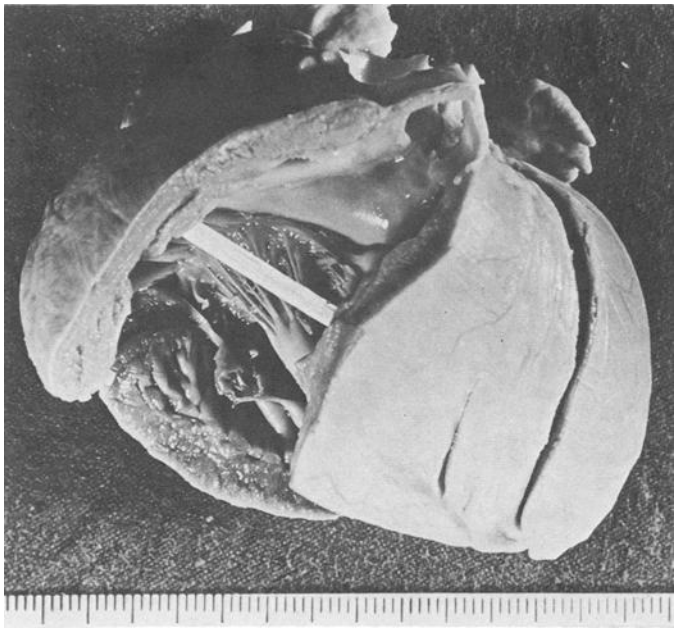

FIG. 9—*Case V/7. Sudden death. Cor pulmonale in a child suffering from arthrogryposis. Heart weight 140% of normal.*

Discussion

The minimal reported inflammatory alteration in this study was the same as that of Norén et al [*2*], that is, less than that of Stevens and Underwood Ground [*6*], 20 instead of 100 cells in a single focus. Rigid morphological criteria are seemingly inadequate when evaluating cardiac alterations in childhood autopsies [*2,22*]. Besides the quantitative criteria, there are functional aspects: small lesions may have great importance if localized within or close to functionally important structures like the conduction system, subendocardium, or papillary muscles [*2,22,23*].

Burch et al [*24*] found no less than 29 instances of interstitial myocarditis among 50 routine autopsies of infants and children up to 4 years; this is the highest frequency of myocarditis in an autopsy series. Saphir et al [*3*] found myocarditis only in 97 (6.83%) of 1420 autopsies of children of the same age as in this study. However, these authors did not include "reparative changes, except in an instance in which such reparative myocarditis was encountered in a patient with diphtheria." Obviously, they did not report all alterations observed.

The present study includes a rather small number of patients but an exhaustive histological review of 88% of nonselected child autopsies during a ten-year period and attempts to cover all cardiovascular abnormalities. This implies that the results are not so exaggerated as they may appear when compared to other studies [*2–6,9,11*]. Moreover, it seems to be realistic that the incidence of cardiovascular abnormalities could be even higher, since the applied morphological criteria have been rather rigid (see Methods section). Thus, alterations of the fibrous body of the aortic valve, minute but impressive with regard to their close relation to the artrioventricular (AV) node and bundle [*22*], as well as anomalies of the AV bundle [*25,26*] were not systematically examined and accordingly not included in this study.

This study shows that congenital malformation is not the most prevalent cardiovascular abnormality in childhood autopsies, which might have been concluded after a total population

TABLE VI—*Age, sex, past history, and postmortem findings of three children with endocardial fibroelastosis.*

Patient	Age and Sex	Past History	Postmortem Findings	Ratio Heart Weight / Expected Heart Weight
1	14 months, male	In the 15th week of pregnancy the mother had pneumonia, treated with penicillin. High fever for several days when seven months old. Occasionally cyanotic lips and cold hands when suckling. Killed in traffic accident.	Endocardial fibroelastosis of the left heart ventricle, chronic type. Three foci of myocytic necrosis in the left ventricular wall (20 to 50 mononuclears).	0.8
2	22 months, male	Always healthy. Got caught and suffocated between two beds.	Endocardial fibroelastosis of the left ventricle, chronic type. Five foci of myocytic necrosis in the left ventricular wall (20 to 30 mononuclears). Aspiration of gastric contents. Subconjunctival hemorrhages.	1.0
3	4.5 months, female	Always healthy. Respiratory infection seven days before being found dead in crib.	Endocardial fibroelastosis of the left ventricle, acute type. Four foci of 30 to 40 mononuclears in the ventricular myocardium as well as mononuclears perivascularly. Atelectatic lungs and bronchopneumonia. Heart blood culture: α-hemolytic streptococci.	2.0

study of children in Bogalusa [*1*]. The postmortem incidence of endocardinal fibroelastosis was less than in McCormick's series [*16*]—0.09% instead of 0.22%—but the estimation is uncertain with regard to the local differences between legal systems and indications for autopsy.

Noteworthy is the high incidence of myocarditis and chronic cardiomyopathies in both the natural and violent death group, particularly in females. These two conditions, which were not always distinguishable from each other, had, according to the past history and microbiological analyses, a multifactorial etiology. Unusual, but previously described [*27,28*], was the case of fatal acute myocarditis during the viremic phase of cytomegalovirus infection. The etiology of the chronic cardiomyopathies was particularly obscure. Not only infections, but other conditions appeared as possible etiologic factors, including craniocerebral injury, epilepsy, and phenytoin sensitivity, as previously pointed out [*21,29,30*], as well as chronic disorders affecting respiratory functions, such as bronchial asthma, tracheobronchial fistula, and arthrogryposis.

Since it is unclear whether the incidence of cardiomyopathies in this study is higher or only more realistic than in other reports cited, there seems to be little reason to discuss the causes of a possibly increased incidence. However, it is worth noting that Sweden is relatively selenium poor [*31*], as well as that the selenium concentration in the myocardium of the Swedish population is also relatively low. The described cardiomyopathies were mostly nonspecific and might well be associated with a latent type of Keshan cardiomyopathy [*32-34*], or imply that selenium deficiency could result in higher vulnerability of the myocardium to other ubiquitous noxious factors.

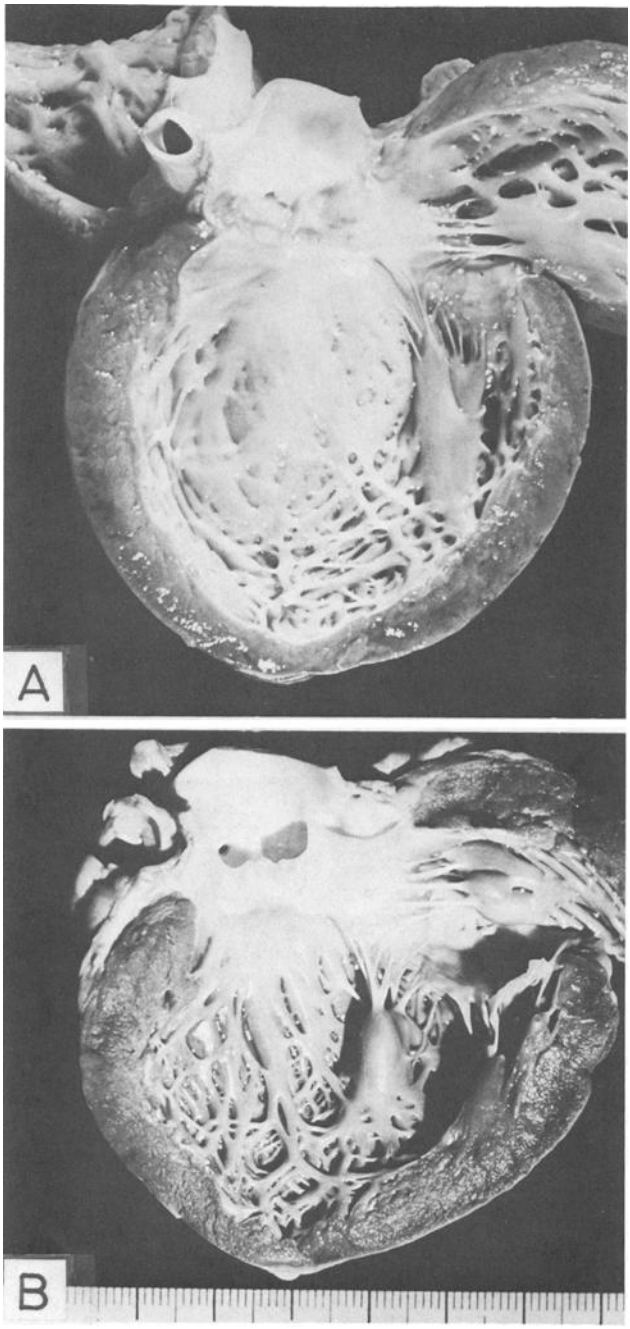

FIG. 10—*Primary endocardial fibroelastosis.* (a) *Case VI/3. Acute type. Sudden death. Heart weight 200% of normal.* (b) *Case VI/2. Chronic type. Violent death. Heart weight normal.*

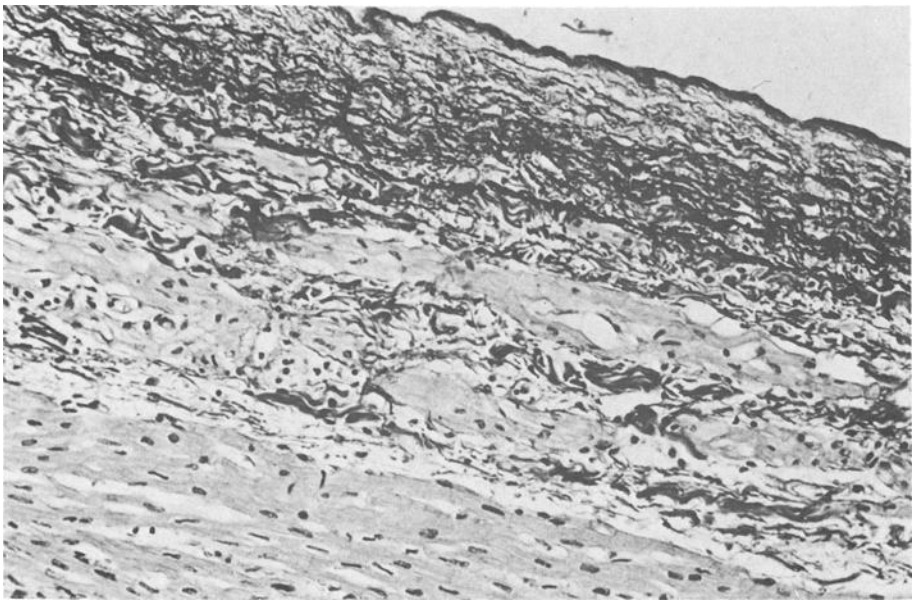

FIG. 11—*Same case as in Fig. 10b. Increase of elastic and collagenous fibers in the endocardium* (upper part) *and of collagenous fibers and mononuclear leukocytes between the atypical cardiac myocytes* (middle part). *Weigert's resorcin fuchsin elastic stain* ×*200.*

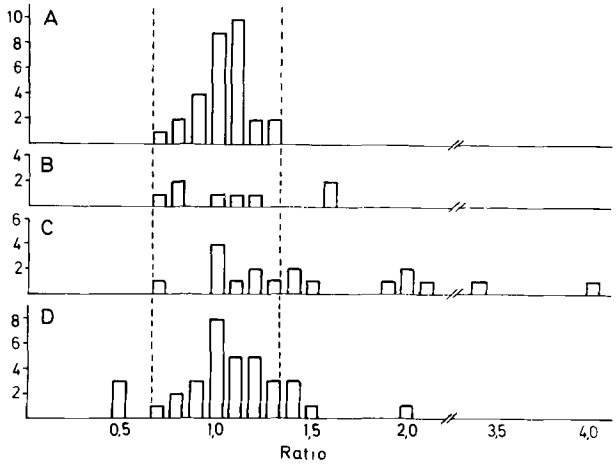

FIG. 12—*Ratio actual: expected heart weight in 31 children who died of violence, with no cardiovascular abnormalities* (a), *8 children who died of violence* (b), *18 children who died naturally and whose autopsy showed cardiomyopathy or heart malformation* (c), *and of the remaining 35 children who died naturally* (d). *The hatched frame denotes 2 SD of the heart weight of the children in* (a).

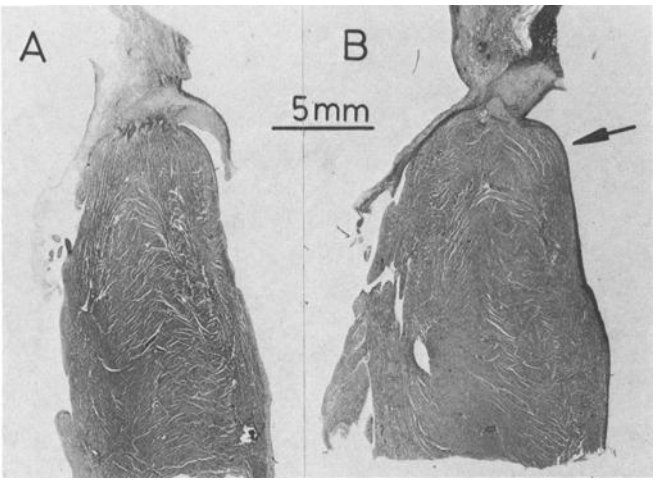

FIG. 13—*Frontal section through the ventricular septum of the heart of a three-month-old boy who died of otitis media and sepsis* (a), *and of a boy of the same age who was found dead in his crib* (b). *The ratio actual: expected heart weight was in* (a) *1.0 and in* (b) *1.4. Note increased thickness of the septum and outbulging of the subaortic area* (arrow) *with thickening of the elastic layer of the subendocardium in* (b). *Weigert's resorcin fuchsin elastic stain.*

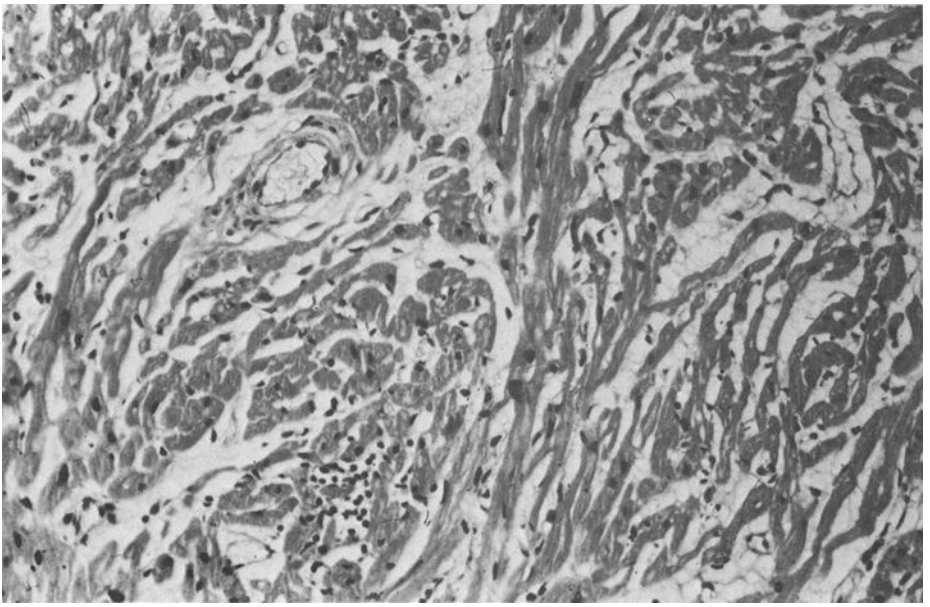

FIG. 14—*Area of disorganized myofibers with a focus consisting of about 20 mononuclear leukocytes in the upper part of the interventricular septum. Same case as in Fig. 14*b. *Hematoxylin and eosin* ×*200.*

TABLE VII—*Ratio actual: expected heart weight of 92 children with histologically reviewed cardiovascular findings.*

Finding	*n*	Ratio	
		Mean	(Range)
No abnormality, violent death	31	1.03	(0.7-1.3)
Malformation	7	2.25	(1.0-4.0)
Myocarditis	9	1.01	(0.7-1.6)
Chronic cardiomyopathy	7	1.35	(1.1-1.6)
Endocardial fibroelastosis	3	1.26	(0.8-2.0)
Other nonviolent deaths	35	1.07	(0.5-2.0)

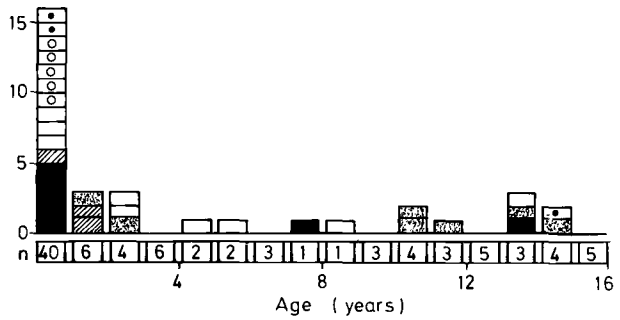

FIG. 15—*Age distribution of children with cardiovascular abnormalities in relation to the total of histologically reviewed autopsies of children of the same age* (n). ■ *Malformations.* □ *Myocarditis.* ⊞ *Chronic cardiomyopathy.* ▨ *Endocardial fibroelastosis. Heart weight* ⊙ *over and* ◉ *under 2 SD.*

Other interesting findings in this study are the heart weight aberrations, which may easily be overlooked at autopsy. That a heart weight beyond 2 SD of the expected value indicates a pathological condition is suggestive from Reiner's tables [*12*], in which SD never exceeds 30% of the mean heart weight of children below the age of 15 years. Potter and Craig [*35*] are still more explicit and consider hearts weighing ≥ 120% of the expected weight to be hypertrophic. The cases of heart hypertrophy in this study may be classed as idiopathic hypertrophic subaortic stenosis as described by Harris and Nghiem [*15*].

Heart hypoplasia, on the other hand, is not mentioned in major text books of cardiac pathology. Its clinical significance may be the same as that of cardiac atrophy in patients suffering from anorexia nervosa, which is known as a reversible condition [*36,37*], but which may also be regarded as potentially life-threatening.

The incidence of the total of cardiovascular abnormalities in this study is high for both the natural and the violent death group: 49 and 21%, respectively. Particularly, the share of cardiovascular abnormalities is high among children who died of natural diseases, indicating that the cause of sudden unexpected death in children is dominated by cardiovascular abnormalities (see Fig. 16 and Table VIII). This series suggests that, in addition to the widely recognized complex malformations, there is a high incidence of cardiovascular abnormalities in children, which are asymptomatic but may be instantaneously fatal, or which may heal or become chronic and then, asymptomatic or not, either heal or be fatal per se or give rise to accidental injury. All these conditions have a high turnover on an asymptomatic level, are seldom observed clinically, and are easily overlooked pathoanatomically.

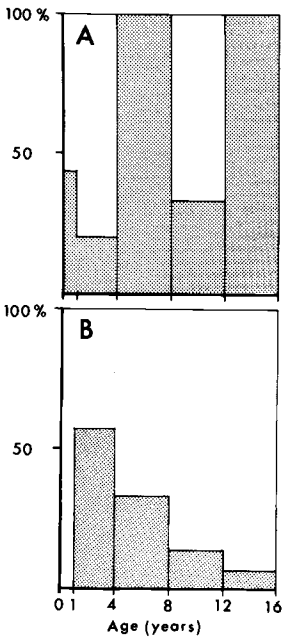

FIG. 16—*Percentage of children with cardiovascular abnormalities in the total of children who died naturally* (a) *and of violence* (b).

TABLE VIII—*Estimated significance of cardiovascular abnormalities for the cause of death in 92 histologically reviewed forensic pathologic childhood autopsies.*

Cardiac Alterations	Relation to the Cause of Death							
	Sole Cause		Presumably Sole Cause		Associated with Other Conditions		No Relation	
n %	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Malformation 7 (7)	4	(4)	0		3	(3)	0	
Myocarditis 9 (10)	2	(2)	0		5	(5)	2	(2)
Chronic cardiomyopathy 7 (7)	2	(2)	0		3	(3)	2	(2)
Endocardial fibroelastosis 3 (3)	0		0		2	(2)	1	(1)
Idiopathic hypertrophic subaortic stenosis 5 (5)	4	(4)	0		1	(1)	0	
Cardiac hypoplasia or atrophy 3 (3)	0		2	(2)	1	(1)	0	
Total 34 (37)	12	(13)	2	(2)	15	(16)	5	(5)

References

[1] Akman, D., Berenson, G. S., Blonde, C. V., et al, "Heart Disease in a Total Population of Children: The Bogalusa Heart Study," *Southern Medicine Journal*, Vol. 75, No. 10, Oct. 1982, pp. 1177-1181.

[2] Noren, G. R., Staley, N. A., Bandt, C. M., and Kaplan, E. L., "Occurrence of Myocarditis in Sudden Death in Children," *Journal of Forensic Sciences*, Vol. 22, No. 1, Jan. 1977, pp. 188-196.

[3] Saphir, O., Wile, S. A., and Reingold, I. M., "Myocarditis in Children," *American Journal of Diseases of Children*, Vol. 67, 1944, pp. 294-312.

[4] Sopher, I. M., "Myocarditis and the Aircraft Accident," *Aerospace Medicine*, Vol. 45, No. 8, Aug. 1974, pp. 963-967.

[5] Saphir, O., "Myocarditis: General Review with Analysis of 240 Cases," *Archives of Pathology*, Vol. 33, 1942, pp. 88-137.

[6] Stevens, P. J. and Underwood Ground, K. E., "Occurrence and Significance of Myocarditis in Trauma," *Aerospace Medicine*, Vol. 41, No. 7, July 1970, pp. 776-780.

[7] Lambert, E. C., Menon, V. A., Wagner, H. R., et al, "Sudden Unexpected Death from Cardiovascular Diseases in Children," *American Journal of Cardiology*, Vol. 34, July 1974, pp. 89-96.

[8] House, R. K., "Diffuse Interstitial Myocarditis in Children," *American Journal of Pathology*, Vol. 24, 1948, pp. 1235-1248.

[9] Gore, I. and Saphir, O., "Myocarditis. A Classification of 1402 Cases," *American Heart Journal*, Vol. 34, No. 6, 1947, pp. 827-830.

[10] Hudson, R. E. B., "The Cardiomyopathies: Order From Chaos," *American Journal of Cardiology*, Vol. 25, Jan. 1970, pp. 70-77.

[11] Gormsen, H., "Sudden Unexpected Death Due to Myocarditis," *Acta Pathologica Microbiologica Scandinavica, Supplement*, Vol. 105, 1955, pp. 30-48.

[12] Reiner, L., "Gross Examination of the Heart," in *Pathology of the Heart and Blood Vessels*, third ed., S. E. Gould, Ed., Charles C Thomas, Springfield, IL, 1968, pp. 1111-1149.

[13] Armed Forces Institute of Pathology, *Manual of Histological and Special Technique*, 2nd ed., McGraw-Hill, New York, 1970.

[14] Lie, J. T., Holley, K. E., Kampa, W. R., et al, "New Histochemical Method for Morphologic Diagnosis of Myocardial Ischemia," *Mayo Clinic Proceedings*, Vol. 46, 1971, pp. 319-327.

[15] Harris, L. C. and Ngheim, Q. X., "Cardiomyopathies in Infants and Children," *Progress in Cardiovascular Diseases*, Vol. 15, No. 3, 1972, pp. 255-287.

[16] McCormick, W. F., "Endocardial Fibroelastosis: A Summary of the Literature and a Review of 24 New Cases," *Southern Medicine Journal*, Vol. 51, Oct. 1958, pp. 1232-1240.

[17] Reichenbach, D. and Benditt, E. P., "Myofibrillar Degeneration: A Common Form of Cardiac Muscle Injury," *Annals of the New York Academy of Sciences*, Vol. 156, 1970, pp. 164-176.

[18] Teare, D., "Asymmetrical Hypertrophy of the Heart in Young Adults," *British Heart Journal*, Vol. 20, 1958, pp. 1-8.

[19] Maron, B. J. and Fisher, R. S., "Sudden Infant Death Syndrome (SIDS): Cardiac Pathologic Observations in Infants with SIDS," *American Heart Journal*, Vol. 93, No. 1, June 1977, pp. 762-766.

[20] Maron, B. J., "Myocardial Disorganisation in Hypertrophic Cardiomyopathy. Another Point of View," *British Heart Journal*, Vol. 50, 1983, pp. 1-3.

[21] Rajs, J., "Relation Between Craniocerebral Injury and Subsequent Myocardial Fibrosis and Heart Failure. Report of 3 Cases," *British Heart Journal*, Vol. 37, No. 4, April 1976, pp. 396-402.

[22] James, T. N., "Sudden Death in Babies: New Observations in the Heart," *American Journal of Cardiology*, Vol. 22, 1968, pp. 479-506.

[23] Sevy, S., Kelly, J., and Ernst, H., "Fatal Paroxysmal Tachycardia Associated with Focal Myocarditis of the Purkinje System in a 14-Month-Old Girl," *Journal of Pediatrics*, Vol. 72, No. 6, June 1968, pp. 796-800.

[24] Burch, G. E., Sun, S.-C., and Chu, K.-C., "Interstitial and Coxsackie-virus B Myocarditis in Infants and Children. A Comparative Histologic and Immunofluorescent Study of 50 Autopsied Hearts," *Journal of the American Medical Association*, Vol. 203, 1968, pp. 55-62.

[25] Lie, T. J., Rosenberg, H., and Erickson, E., "Histopathology of the Conduction System in the Sudden Infant Death Syndrome," *Circulation*, Vol. 53, 1976, pp. 3-8.

[26] Sturner, W. Q., Lipsitt, L. P., Oh, W., et al, "Abnormal Heart Rate Response During Newborn Sucking Behavior Study: Subsequent Sudden Infant Death Syndrome with Cardiac Conduction Abnormality," *Forensic Science International*, Vol. 16, 1980, pp. 201-212.

[27] Bergman, A. B., Beckwith, M. B., and Ray, C. G., Eds, *Proceedings of the Second International Conference on Causes of Sudden Death in Infants*, University of Washington Press, Seattle, 1970, p. 95.

[28] Sun, C.-C. J. and Smith, T., "Sudden Infant Death with Congenital Cytomegalic Inclusion Disease," *American Journal of Forensic Medicine and Pathology*, Vol. 5, No. 1, March 1984, pp. 65-67.

[29] Falconer, B. and Rajs, J., "Postmortem Findings of Cardiac Lesions in Epileptics: A Preliminary Report," *Forensic Sciences*, Vol. 8, 1976, pp. 63-71.
[30] Haruda, F., "Phenytoin Hypersensitivity: 38 Cases," *Neurology*, Vol. 29, Nov. 1979, pp. 1480-1485.
[31] Casey, C. E., Guthrie, B. E., Friend, G. M., et al, "Selenium in Human Tissues from New Zealand," *Archives of Environmental Health*, Vol. 37, 1982, pp. 133-135.
[32] Keshan disease research group of the Chinese Academy of Medical Sciences, Beijing, *Chinese Medical Journal*, Vol. 92, 1979, pp. 477-482.
[33] Wei-Han, Y., "A Study of Nutritional and Bio-geochemical Factors in the Occurrence and Development of Keshan Disease," *Japanese Circulation Journal*, Vol. 46, No. 11, Nov., pp. 1201-1207.
[34] "Selenium in the Heart of China," Editorial, *The Lancet*, Vol. 27, Oct. 1979, pp. 2-3.
[35] Potter, E. L. and Craig, J. M., *Pathology of the Fetus and the Infant*, third ed., A Year Book Medical Publishers, Inc., Lloyd-Luke (Medical Books), London, 1976, p. 247.
[36] Gottdiener, J. S., Gross, H. A., Henry, W. L., et al, "Effects of Self-Induced Starvation on Cardiac Size and Function in Anorexia Nervosa," *Circulation*, Vol. 58, 1978, pp. 425-433.
[37] Gould, L., Reddy, C. V., Singh, B. K., et al, "Evaluation of Cardiac Conduction in Anorexia Nervosa," *PACE*, Vol. 3, 1980, pp. 660-665.

Address requests for reprints or additional information to
Dr. Jovan Rajs
Department of Forensic Medicine
Karolinska Institutet
Box 60400
S-104 01 Stockholm, Sweden