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THE NATURAL HISTORY OF VENTRICULAR SEPTAL DEFECTS

HELEN NANOVIC PETERS

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THE NATURAL HISTORY OF
VENTRICULAR SEPTAL DEFECTS

by

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INTRODUCTION

The natural history of the isolated ventricular septal defect is variable and as yet incompletely defined. The purpose of this thesis is to review specific aspects of the natural history of this defect as reflected in patterns of growth and development in infancy and childhood and to correlate the clinical course of the lesion with the hemodynamic data and available anatomic detail.

The small ventricular septal defect may be completely asymptomatic and is often not discovered until adult life. Certain children who are diagnosed as having a ventricular septal defect because of a typical murmur will frequently follow a benign, uncomplicated course. The same group will be threatened more seriously by bacterial endocarditis than by the increased work of the heart imposed by their abnormal intracardiac shunt. Still another group is composed of those children who, as infants, are consistently unable to compensate for their large left-to-right shunt. At the University of Minnesota (1), infants with isolated ventricular septal defects and congestive heart failure prior to six months of age, suffered a twenty-five per cent mortality in the first two years of life when treated medically. These are only two examples of the range of clinical courses which a ventricular septal defect may follow.

The first description of the clinical findings and pathology of the ventricular septal defect was written by Roger in 1879 (2). Today, the

term "maladie de Roger" is used to describe the small membranous defect with a characteristic murmur which gives rise to few if any symptoms. Further description of one of the complications of the ventricular septal defect was made by Eisenmenger in 1897 (3). He referred to an adult with a ventricular septal defect who developed cyanosis. This change is now recognized to be due to the progression of pulmonary vascular resistance to such an extent that the shunt reverses and becomes predominantly right-to-left.

Since that time, numerous papers have been published describing the defects, clinical findings, and hemodynamics. Certainly the most controversy has surrounded the attempts to outline the natural history of ventricular septal defects. Zacharioudakis (4) reports twenty-three cases of isolated ventricular septal defect, all of whom died under fifteen months of age. The size of the defects ranged from three to nineteen millimeters. The conclusion reached was that no apparent relationship existed between the size of the defect and the time of death. Four other patients with similar clinical findings, electrocardiograms, and cardiac catheterization data who survived congestive heart failure in infancy later appeared to be improved between the ages of two to four years. In another series by Morgan (5) of one hundred and twenty-five patients with ventricular septal defects, seventeen developed congestive heart failure between one and six months of age. Ten of these seventeen

patients died and had defects which measured between four and fifteen millimeters in diameter. No clinical findings or laboratory data were felt to be of prognostic significance in reference to this group. In contrast, spontaneous closure of ventricular septal defects in which a left-to-right shunt had been previously proven by cardiac catheterization was documented in thirty patients in a study by Evans (6). These patients were asymptomatic and had originally been referred for the evaluation of a murmur.

Surgical correction of ventricular septal defects has evolved rapidly in the past several years. In 1954, Kay and Zimmerman (7) sutured the defect blindly through the wall of the right ventricle. Lillehei (8) and Kirklin (9) in 1955 used the pump-oxygenator for extracorporeal circulation and achieved direct repair of the defect. Studies compiled by Cooley (10) in 1960 reflected the high mortality of open-heart surgery in infancy. Thirty-nine per cent of forty-one cases of ventricular septal defect less than two years of age did not survive surgery. However, in the age range from two through fifteen years, the mortality was only seven per cent in one hundred and eleven cases. Banding of the pulmonary artery was first used successfully by Muller and Dammann (11) as a temporary means of controlling a large left-to-right shunt. This technique has been used with very good results in a group of thirteen symptomatic children, ages three to twenty-two months, all of whom were improved and free of heart failure after banding (12).

Pathology:

In utero, the fetus is unaffected by the presence of a ventricular septal defect since the shunt is merely another means by which the lungs are bypassed. The structural changes which occur after birth vary according to the size of the defect. For purposes of this discussion, a small defect is one which permits a differential in pressures to exist between the two ventricles; whereas a large defect may function as a single ventricle with little pressure differential. The structural changes described by Edwards (13), which occur in a small ventricular septal defect, include slight enlargement of the left ventricle with normal thickness of both ventricles.

The most common type of ventricular septal defect is the membranous defect which is usually located in the outflow portion of the ventricular septum. It is found immediately posterior and inferior to the crista supraventricularis, under the tricuspid valve. Less commonly, the defect may occur immediately below the pulmonary valve or it may consist of multiple defects. The muscular type of defect occurs in the apical area of the septum, posterior to the membranous portion of the ventricular septum. The conduction tissue of the heart lies in close proximity to the membranous defects. The main bundle of His is found in the postero-inferior portion of the defect and the beginning of the right branch lies parellel to the inferior edge. Thus, trauma during surgery

to tissue in these areas may cause prolonged heart block or ventricular asystole.

The structural changes which develop in the lung secondary to increased pulmonary pressure and flow occur in the muscular arteries and arterioles. These changes have been described by Edwards (14) as type I: high-resistence, high-reserve system and type II: high-resistence, low-reserve system. The normal fetal vasculature is an example of type I. Type I is also seen in most patients with a ventricular septal defect when they are less than two years of age. Microscopically, the muscular medial layers are thickened, with an increased elastic layer. The first portion of the arterioles is usually affected most by the medial hypertrophy and the narrowing of the lumen. There are few, if any, fibrous intimal lesions in the arterioles. By contrast, the type II: high-resistence, low-reserve system shows the characteristic obliterative intimal lesions in the large muscular arteries. The configuration of the narrowed lumen is quite irregular, even suggesting the picture of an organized thrombus. Beyond the obstructed areas, the small arteries and arterioles are dilated with thin walls.

In a group of autopsies performed on fifty children with ventricular septal defects collected by Wagenvoort (15), intimal proliferation was uncommon in those less than one year of age, but above that age it was almost invariably present. Two infants, eleven and twenty-seven days

old, were found to have intimal proliferation at autopsy. Whether these changes are due to the persistence of the fetal type of pulmonary vasculature or if the vessels were normal for a short interval following birth and then hypertrophied has not yet been determined.

Incidence:

The approximate incidence of congenital heart disease is six per thousand live births. Ventricular septal defects comprise twenty-two per cent of the total group of children with heart defects in a series from the Toronto Heart Registry and the Hospital for Sick Children (16). Males and females appear to be equally afflicted with ventricular septal defects.

Clinical Findings:

The typical auscultatory finding in a small ventricular septal defect is a loud, harsh, pansystolic murmur heard best in the third or fourth left intercostal space at the sternal border. There is usually an accompanying systolic thrill. The murmur begins as soon as isometric contraction increases left ventricular pressure above right ventricular pressure. During inspiration, the murmur diminishes in intensity due to increased right ventricular filling. The second heart sound is often difficult to hear because of the length of the murmur; however, the second sound in the pulmonic area is frequently widely split. The pulmonic component of the second sound becomes accentuated with increased

pulmonary artery resistance and may eventually assume a banging or snapping quality. A short, rumbling, apical diastolic murmur is commonly heard due to increased mitral blood flow during the phase of rapid filling. A third heart sound may be quite loud. In a series by Hauwaert (17) of twenty-one asymptomatic patients with small, proven ventricular septal defects, fifty per cent had the typical pan-systolic, plateau-shaped murmur and thirty per cent had diamond-shaped murmurs as recorded by phonocardiography. The diamond-shaped murmur was felt to be comparable to a murmur created by a stenosed valve, which reaches its maximum intensity in mid-systole. Only one of the twenty-one had a mitral diastolic flow murmur. In large ventricular septal defects, the systolic murmur is sometimes of low intensity and relatively short, since most of the shunting will occur in early systole. The thrill may frequently not be present in these cases.

Appearance and Activity:

Children with small, asymptomatic ventricular septal defects are normal in growth and development. With a large left-to-right shunt or pulmonary hypertension, the patients are usually underweight and may have a prominent precordium. Exercise tolerance is usually near-normal, dyspnea occurring only with vigorous activity. Even those children with

large defects have good exercise tolerance until the oxygen saturation is lowered by a right-to-left shunt with effort.

Radiological Examination:

The heart size and shape are normal or almost normal in small defects. Moderate and large septal defects are associated with hearts which are generally enlarged with a bulging pulmonary artery and pulsating hilar shadows. By fluoroscopy, both ventricles may be enlarged. The left atrium is often enlarged due to increased blood flow. The degree of hilar pulsation may be regarded as an indication of increased pulmonary artery pressure and blood flow. Pulsations which extend to the periphery of the lung fields also indicate a high pulmonary blood flow. However, with the development of increased pulmonary vascular resistance, the peripheral portions of the lung fields are cleared and the central pulsations become more forceful near the hilum.

Electrocardiography:

A normal electrocardiogram in a patient with a ventricular septal defect usually indicates a small left-to-right shunt without pulmonary hypertension. Most patients who have moderate to large defects show hypertrophy or loading of both ventricles. However, in infants, especially those less than seven months of age, a normal electrocardiogram may be present in spite of a moderate to large defect (18). Right ventricular

hypertrophy alone is not common in isolated ventricular septal defects and is present only with marked pulmonary hypertension or with hypertrophy of the right ventricular outflow tract. Left ventricular hypertrophy is likewise uncommon and would suggest a very large left-to-right shunt. Right incomplete bundle branch block is not a reliable guide to the size or severity of the defect and may occur in the absence of right ventricular hypertrophy. Signs of right or left atrial enlargement are frequently present. Disorders of rhythm are not common in ventricular septal defects.

Vince and Keith (19) analyzed one hundred and nineteen cases of isolated ventricular septal defects and found a normal pattern in fourteen per cent. Right ventricular loading was present in still another fourteen per cent and was defined by the following criteria: voltage of R in V_1, voltage of S in V_6, and the R/S ratio in V_1 greater than the maximum normal for the age; positive T in V_1 after the third day of life when the R/S ratio is greater than 1.0 and a qR pattern in V_1. Left ventricular loading occurred in eleven per cent of their patients as defined by the voltage of R in V_6 and the voltage of S in V_1 being greater than the maximum normal for the age, the R/S ratio in V_1 being less than the minimum normal for the age, secondary T inversion in V_5 and/or V_6, and a deep Q over the left precordium of four millimeters or greater. Sixty-one per cent of the group had combined ventricular overloading

which embodied the signs of right and left overloading plus direct signs of right ventricular hypertrophy with the following signs in the left chest leads: (a) q wave of one millimeter or more and (b) T_6 inversion after a positive T in the right chest leads. They felt that the best evidence of increased left atrial pressure and left atrial enlargement was notching and broadening of the P wave in standard lead I or II. Since these findings are the result of an increased flow, they give an indirect indication of pulmonary vascular resistance. Broadening of the P wave or late inversion of the P in V_1 associated with broadening are similar evidence. Significant broadening was regarded as a P wave greater than 0.09 second in the pediatric age group. In their series, thirty per cent had significant notching of P in I or II. Forty per cent showed a right incomplete bundle branch block pattern which was interpreted as diastolic loading of the right ventricle. They found no qR patterns in V_1, but occasionally in RV_3 or further to the right. A qRs pattern was present in V_1 in two cases and both had enlarged hearts with right ventricular pressure at systemic levels. Sixty per cent of the cases showed a q wave in V_6 of two millimeters or more; it was three millimeters or more in forty per cent.

Hemodynamics:

During catheterization, the diagnosis of ventricular septal defect depends upon an increase in oxygen content of at least one volume per

cent above that of the right atrium or an increase in oxygen saturation of five per cent or more. The right ventricular pressure reflects the degree of pulmonary hypertension or of obstruction, such as would be created by hypertrophy of the outflow tract. The average normal range of pressure in the right ventricle is fifteen to thirty millimeters of mercury in systole and two to five millimeters of mercury in diastole. The systemic and pulmonary blood flows, and, therefore, the size of the shunt, can be calculated from the oxygen content of systemic and pulmonary arterial and venous samples taken while the patient is breathing one hundred per cent oxygen. The diagnosis of ventricular septal defect has, on rare occasions, been confirmed by actually passing the catheter through the defect and into the left ventricle or by passing the catheter through a patent foramen ovale and injecting radio-opaque dye which would show filling of the right ventricle via the defect.

The actual size of the defect is less important than its ratio to the heart size (cardiac diameter) as a factor in altering cardiac dynamics (20). No correlation has been found between cardiac catheterization data and the location of the defect. An increase of right ventricular systolic pressure to between thirty-five and eighty millimeters of mercury is due mainly to the increased blood flow of the left-to-right shunt, and at these pressures the pulmonary resistance usually has remained normal (21). However, right ventricular systolic pressures above eighty millimeters

of mercury were always found to be associated with an abnormally elevated pulmonary resistance in the hemodynamic studies done by Garcia (21).

MATERIALS AND METHODS

From the records of the Grace-New Haven Community Hospital and the Pediatric Cardiac Clinic, over three hundred case histories of patients who had or were thought to have a ventricular septal defect were reviewed. For purposes of this investigation, forty-eight patients were selected on the basis of the following criteria:

1) that the patient had been seen in this hospital for the first time when less than one year of age,
2) that a ventricular septal defect had been proven by cardiac catheterization, surgical observation, or post-mortem examination in addition to the clinical impression, and
3) that there be no other hemodynamically significant cardiac anomalies.

The analysis of these records was terminated as of September, 1962.

RESULTS

The group was composed of twenty-nine female and nineteen male children. The pregnancy history of the mother at the time of the birth of the patient revealed four instances of first trimester vaginal bleeding. One of the mothers was given an unknown quantity of stilbesterol for three weeks because of the bleeding. There were two cases of bleeding in the fourth month of pregnancy. One mother was subjected to general anesthesia during the first month of pregnancy for the removal of an ovarian cyst. The mothers of five patients had previously had miscarriages or abortions and one of these mothers had delivered a stillborn infant. The ages of the parents were in the twenties and thirties except one mother who was forty and three fathers who were forty-one, forty-five, and forty-nine years old at the time of the child's birth. The offspring with ventricular septal defects ranged from the first-born to the eighth-born in the family.

Three of the patients had non-cardiac problems of interest: M. Si. had webbing between the third and fourth toes and pyloric or duodenal obstruction requiring gastroenterostomy at five days of age; the other two had severe and progressive neurological disease, one had a Werdnig-Hoffman-type syndrome and the other a progressive degenerative central nervous system disease which remains incompletely diagnosed even after thorough post-mortem study. There was a single

instance of congenital heart disease occurring in a sibling, the sister of T. H. has a murmur typical of a ventricular septal defect which has not yet been proven by catheterization. No other patient revealed a documented history of congenital heart disease in a relative. Non-cardiac congenital anomalies occurred in the families of two patients: a sibling of J. K. died of hydrocephalus and a sibling of J. A. died of complications of spina bifida.

The age of the patients at the time the first sign of congenital heart disease was discovered and also the age when they were first seen in the Grace-New Haven Community Hospital are shown in Tables I and II. All but one of the patients had the first sign of congenital heart disease prior to six months of age and thirty of the patients had the first sign prior to three months of age. Thirty patients were seen for the first time when under six months of age. Twenty-nine of the forty-eight patients developed congestive heart failure. Seventeen of these patients were first seen at approximately the same time as the onset of the congestive failure as shown in Table IV.

Clinical Findings:

On physical examination, all of the children had the classical, harsh pansystolic murmur of a ventricular septal defect; whereas only forty-two had a palpable thrill. Only one patient in this group showed a change in the murmur while under clinical observation. K. L. showed

TABLE I

Nineteen Patients Who Did NOT Develop Congestive Heart Failure

Patient	Age at First Sign* of Congenital Heart Disease	Age When First Seen at G-NHCH
C. M.	birth	9 months
R. Wil.	birth	12 months
M. Si.	1 week	2 months
P. Cav.	2 weeks	6 months
R. G.	3 weeks	5 months
T. S.	3 weeks	12 months
G. C.	5 weeks	10 months
S. E.	6 weeks	2 months
E. E.	6 weeks	3 months
L. M.	6 weeks	11 months
R. G.	2 months	5 months
T. H.	2 1/2 months	5 months
L. R.	3 months	4 months
F. R.	3 months	5 months
K. H.	3 months	8 months
R. S.	3 months	9 months
E. D.	4 months	6 months
G. L.	5 months	9 months
J. Ch.	6 months	7 months

* The first sign was a murmur in these patients.

TABLE II

Twenty-Nine Patients Who Developed Congestive Heart Failure

Patient	Age at First Sign* of Congenital Heart Disease	Age When First Seen at G-NHCH	Age at Onset of Congestive Heart Failure
T. C.	birth	1 1/2 months	5 1/2 weeks
B. C.	birth	3 months	3 months
R. Wid.	birth**	5 months	5 months
P. B.	birth	5 1/2 months	5 1/2 months
W. B.	birth	8 months	8 months
P. Cas.	3 days	6 weeks	2 months
R. B.	3 days	5 months	5 1/2 months
S. L.	3 days	6 months	7 months
W. C.	8 days	birth	4 1/2 years
B. D.	10 days***	3 months	7 months
J. Co.	15 days	3 months	15 days
S. G.	3 weeks	3 months	2 months
D. M.	4 weeks	2 1/2 months	2 1/2 months
J. A.	4 weeks	3 months	5 weeks
K. L.	4 weeks	4 months	4 months
R. F.	4 weeks	6 months	8 weeks
S. M.	4 weeks	7 months	7 months
S. Wi.	6 weeks	2 months	10 weeks
L. K.	2 months	6 months	7 months
M. Se.	3 months	3 months	3 months
B. T.	3 months	5 months	4 months
R. Wh.	3 months	5 months	3 months
E. W.	3 months	5 months	4 months
F. C.	4 months	4 months	4 months
Y. C.	4 months	4 months	4 months
S. Wu.	4 months	8 months	5 months
D. A.	4 1/2 months	4 1/2 months	4 1/2 months
J. K.	5 months	5 months	5 1/2 months
D. G.	9 months	11 months	2 1/2 years

* The first sign was a murmur in all but two cases.

** R. Wid. presented with cyanosis at birth.

*** B. D. presented with dyspnea at ten days of age.

TABLE III

Age at First Sign of Congenital Heart Disease versus Onset of Congestive Heart Failure in Twenty-Nine Patients

Age at First Sign of Congenital Heart Disease	Age at Onset of Congestive Heart Failure						
	Birth	1 day to 6 weeks	7 weeks to 3 months	4 months to 6 months	7 months to 1 year	Over 1 year	Totals
Birth	0	1	1	2	1	0	5
1 day to 6 weeks	0	2	5	2	3	1	13
7 weeks to 3 months	0	0	3	1	1	0	5
4 months to 6 months	0	0	0	5	0	0	5
7 months to 1 year	0	0	0	0	0	1	1
Totals	0	3	9	10	5	2	29

TABLE IV

Age When First Seen at Grace-New Haven Community Hospital versus Onset of Congestive Heart Failure in Twenty-Nine Patients

Age When First Seen at Grace-New Haven Community Hospital	Age at Onset of Congestive Heart Failure						
	Birth	1 day to 6 weeks	7 weeks to 3 months	4 months to 6 months	7 months to 1 year	Over 1 year	Totals
Birth	0	0	0	0	0	1	1
1 day to 6 weeks	0	1	1	0	0	0	2
7 weeks to 3 months	0	2	5	0	1	0	8
4 months to 6 months	0	0	3	9	2	0	14
7 months to 1 year	0	0	0	1	2	1	4
Totals	0	3	9	10	5	2	29

TABLE V

Twenty-Nine Patients Who Developed Congestive Heart Failure

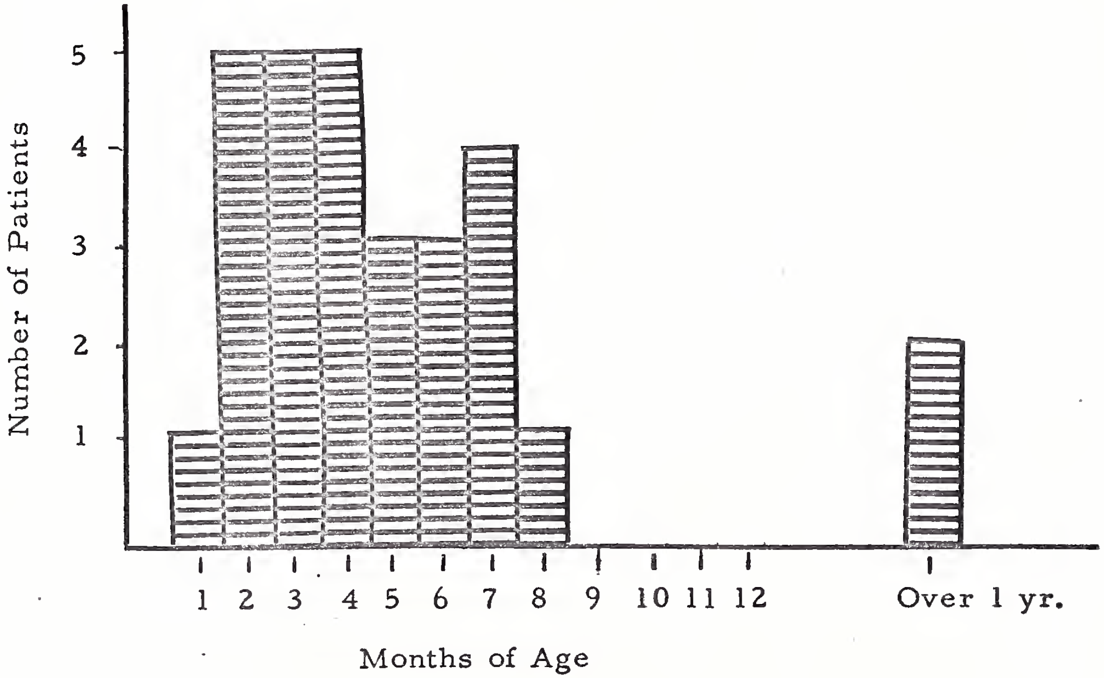
Patient	Age at Onset CHF	Size of Defect	Shunt*
J. Co.	15 days	1 cm. **	
J. A.	5 weeks		23% R-L
T. C.	5 1/2 weeks	1.4 cm. **	
R. F.	8 weeks		
P. Cas.	2 months	.7 cm. **	
S. G.	2 months		5.0
S. Wi.	10 weeks		3-3.5
D. M.	2 1/2 months		
R. Wh.	3 months	2 cm. **	1.5 plus 10% R-L
B. C.	3 months		
M. Se.	3 months		
E. W.	4 months	1 cm.	1.5-2.3
B. T.	4 months		2.75
Y. C.	4 months		1.8
F. C.	4 months		2.25
K. L.	4 months		1.2 plus 28% R-L
D. A.	4 1/2 months	2 cm.	2-2.5
R. Wid.	5 months	1 cm. **	
S. Wu.	5 months	2 cm. **	
R. B.	5 1/2 months		
J. K.	5 1/2 months		2.0
P. B.	5 1/2 months	1 cm. **	
L. K.	7 months		4.0
S. L.	7 months		
S. M.	7 months		
B. D.	7 months		
W. B.	8 months	1.5 cm.	4.0
D. G.	2 1/2 years		25% R-L
W. C.	4 1/2 years	2.5 cm.	2.5-4

* Unless otherwise specified, the figure under Shunt refers to the increase of pulmonic flow over systemic flow.

** Size of defect at post-mortem examination.

Figure 1

Age at Onset of Congestive Heart Failure
in Twenty-Nine Patients



a disappearance of the thrill and of the murmur to the point where it could be recorded only by phonocardiography. This change, which occurred at ten years of age, was associated with an increase in the intensity of the second sound at the pulmonic area and the appearance of slight cyanosis. She also had a decrease in the number of respiratory infections. An apical, rumbling, diastolic murmur was heard in thirty-one cases. The second sound in the pulmonic area was described as being accentuated in thirty-six cases.

Cyanosis was not observed at rest in any case; however, thirteen out of the forty-eight reportedly had episodes of cyanosis with crying or with upper respiratory infections.

Early feeding problems, such as slowness or gagging, were reported in twenty-five cases.

Congestive Heart Failure:

Twenty-nine of the forty-eight patients developed congestive heart failure. The onset of congestive heart failure occurred prior to six months of age in twenty-two patients and only three infants developed failure before six weeks of age. These findings are shown in Tables II, III, and IV, as well as Figure 1, and are consistent with the experiences of all others. The age at onset did not appear to correlate with either the size of the defect nor the size of the shunt when known, as shown in Table V. The predominant symptoms of congestive heart failure were

tachypnea and hepatomegaly. Peripheral edema was seen in only one patient, S. Wu., in the terminal phase of her illness.

Growth and Development:

The weight of thirty-five of the forty-eight patients was followed from birth to six years of age and recorded in Table IX. A total of twenty-six of these children were below the third percentile at six months of age. Twelve of these patients subsequently gained to over the third percentile by six years of age as shown in Table IX, B; in fact, this increase was attained by two years of age. The improvement in weight in these children had occurred prior to surgical correction of their defects. Fourteen children always remained below the third percentile as in Table IX, C.

The age and weight of the patients at the time of cardiac catheterization are shown in Table X. Only one out of six patients who had a pulmonary flow less than twice the systemic flow was under the third percentile in weight at the time of catheterization; whereas, four out of nine patients whose pulmonary flow was twice to four times the systemic flow were below the third percentile in weight at the time of catheterization. With pulmonary flows four and five times the systemic flow, four out of five patients were below the third percentile in weight.

Twenty-eight out of twenty-nine patients who developed congestive heart failure were below the third percentile in weight before six months.

Only seven of these twenty-eight had improved to over the third percentile by two years of age. Ten patients still remained below the third percentile at six years of age.

Eleven out of twenty patients who were never in congestive heart failure were below the third percentile in weight before six months of age; whereas, eight patients appeared to have normal growth and development. Six of the eleven patients had improved to over the third percentile in weight by six years of age. The exception in this group, G. C., began to develop normally, but later showed poor growth as a result of a progressive central nervous system disease from which she died at the age of seven years.

Radiological Examination:

Repeated x-ray examinations were performed in the Cardiac Clinic on all the patients. Definite increase in pulmonary vasculature was observed in forty-one cases, while the remainder showed a questionable increase. Prominence of the main pulmonary artery was evident in thirty-six of those children with an increased pulmonary vasculature. In only four cases did narrowing of the peripheral pulmonary vasculature develop. These changes occurred at ages five years, seven years, and thirteen years. Left atrial enlargement, as shown by barium swallow, was present in forty of the cases with increased

TABLE VI

Serial Cardiac Catheterizations*

		Systolic Pressures(mm. Hg.)			Arterial Oxygen Saturation Breathing		
Patient	Age	RVP	PAP	FAP**	Oxygen	Air	Shunt***
A. No Change of Pressure							
P. Cav.	7 years	45	35	100		94%	1. 5-1. 75
	10 years	45	45				less than 2. 0
S. G.	8 months	87				90%	
	7 years	90	55	105	100%	95%	5. 0
B. Increase of Pressure							
J. A.	2 years	66		120		82%	
	7 years	110	113	140	97%	81%	23% R-L
E. W.	2 years	70		80		92%	
	6 years	90	90	90		93%	1. 5-2. 3

* Including patients who did not undergo surgery and patients who had two catheterizations prior to closure of their defects.

** RVP = right ventricular pressure; PAP = pulmonary artery pressure; FAP = femoral artery pressure.

*** Shunt as defined in Table V.

TABLE VI - Continued

		Systolic Pressures(mm. Hg.)			Arterial Oxygen Saturation Breathing		
Patient	Age	RVP	PAP	FAP	Oxygen	Air	Shunt
D. A.	3 years	78	90				
	5 years	90	80		100%	89%	2-2.5
D. G.	4 years	110	115			91%	
	8 years				95%	88%	25% R-L
C. Decrease of Pressure							
L. R.	8 years	45	35	100	100%	95%	2.5-5
	10 years	35	36	95			
R. Gr.	6 months	55			100%	94%	
	7 years	45	35	130		95%	
K. H.	3 years	57	64	102		94%	
	5 years	40	45				
Y. C.	1 year	60		75		90%	
	6 years	40	40		100%	95%	1.8
B. D.	5 years	67	63			94%	
	15 years	49	29				2.0

TABLE VI - Continued

Patient	Age	Systolic Pressures(mm. Hg.)			Arterial Oxygen Saturation Breathing		Shunt
		RVP	PAP	FAP	Oxygen	Air	
J. Ch.	11 years	75	90		100%	98%	
	20 years	60	60		100%	94%	4. 0
W. B.	2 years	88	86	110		86%	
	7 years	75	70	110	100%	94%	4. 0
P. B.	7 years	90	85	120		93%	
	12 years	75	75	105			
E. E.	1 year	95		118		85%	
	6 years	85	80	97	98%	90%	
R. Ga.	1 year	120			100%	92%	
	7 years	60	50	115		92%	

TABLE VII

Serial Pressure Recordings in Surgical Patients

			Systolic Pressures(mm. Hg.)			
Patient		Age	RVP	PAP	FAP	Size of Defect
D. M.	Immediately before and after banding of pulmonary artery	3 months		65 23	70 98	Unknown.
K. H.	Immediately before and after closure of defect	5 years	40 20	45		1. 5 cm.
L. R.	Immediately before and after closure of defect	10 years	35 25	36 25	95	1 cm.
P. B.	Immediately before and after closure of defect	12 years	75 40	75	105	1 cm.
T. H.	2 months before surgery 1 year after surgery	5 years 6 years	40 27	28 20	68	.5 cm.
E. E.	At surgery 2 months after surgery	6 years 6 years	85 55	80 50	97	Size not described. Closure incomplete.
L. M.	3 months before surgery 2 years after surgery	4 years 6 years	75 40	80	117	1. 5 cm. Closure incomplete.

TABLE VIII

FATALITIES

Patient	Age at Death	Size of Defect	CHF*	Cause of Death
P. Cas	3 months	.7 cm.	yes	Congestive heart failure
T. C.	4 months	1.4 cm.	yes	Postop. cardiac arrest**
J. Co.	4 months	1 cm.	yes	Congestive heart failure
R. Wid.	5 months	1 cm.	yes	Pneumococcal pneumonia
S. Wu.	3 years	2 cm.	yes	Werdnig-Hoffman disease
G. C.	7 years	unknown	no	Undiagnosed CNS disease
D. A.	7 years	2 cm.	yes	Postop. cardiac arrest**
P. B.	12 years	1 cm.	yes	Auto accident

* Seven of these patients developed congestive heart failure during life.
** Congestive heart failure present at time of surgery.

TABLE IX

Patients Listed According to their Weight Curve from Birth to Six Years of Age

A. Patients ALWAYS ABOVE the third percentile.

Patient	CHF	Size of Defect	Shunt
R. Wil.	never		1. 5
F. R.	never		1. 25
J. K.	5 1/2 months		2. 0
P. Cav.	never		1. 5-1. 75
G. L.	never		2-2. 5
E. D.	never		30% R-L
K. H.	never	1. 5 cm.	
S. E.	never		1. 5
L. R.	never	1 cm.	2. 5-5

B. Patients BELOW the third percentile at six months who rose to ABOVE the third percentile before six years.

Patient	CHF	Size of Defect	Shunt
C. M.	never		
S. L.	7 months		
S. M.	7 months		
T. S.	never		
B. C.	3 months		
D. M.	2 1/2 months		
T. H.	never	. 5 cm.	
R. Ga.	never	2 cm.	
E. W.	4 months	2 cm.	1. 5-2. 3
R. S.	never		2-2. 5
W. B.	8 months	1. 5 cm.	4. 0
L. M.	never	1. 5 cm.	

TABLE IX - Continued

C. Patients ALWAYS BELOW the third percentile.

Patient	CHF	Size of Defect	Shunt
R. B.	5 1/2 months		
J. A.	5 weeks		23% R-L
D. G.	2 1/2 years		25% R-L
B. D.	7 months		
E. E.	never		4.0
Y. C.	4 months		1.8
K. L.	4 months		1.2 L-R 28% R-L
M. Si.	never	1 cm.	
S. G.	2 months		5.0
R. Wh.	3 months	2 cm.	1.5 L-R 10% R-L
R. Gr.	never		
J. Ch.	never	2 cm.	4.0
P. B.	5 1/2 months	1 cm.	
D. A.	4 1/2 months	2 cm.	2-2.5

The remaining thirteen patients had not yet reached the age of six years or had died before six years of age.

TABLE X

Status of Patient at Time of Cardiac Catheterization

Patient	Age	Shunt*	Weight**
A. Left-to-Right Shunt			
F. R.	13 years	1.25	no
S. E.	6 years	1.5	no
R. Wi.	8 years	1.5	no
P. Cav.	7 years	1.5-1.75	no
E. W.	6 years	1.5-2.3	no
Y. C.	6 years	1.8	yes
J. K.	14 years	2.0	no
D. A.	5 years	2-2.5	yes
R. S.	5 years	2-2.5	no
G. L.	7 years	2-2.5	no
F. C.	6 months	2.25	yes
B. T.	3 years	2.75	yes
L. R.	8 years	2.5-4	no
W. C.	15 years	2.5-5	no
S. W.	6 months	3-3.5	yes
L. K.	6 months	4	yes
E. E.	6 years	4	yes
W. B.	7 years	4	no
J. Ch.	20 years	4	yes
S. G.	7 years	5	yes
B. Right-to-Left Shunt			
R. Wh.	10 years	10%	yes
J. A.	7 years	23%	yes
K. L.	12 years	28%	yes
E. D.	3 years	30%	no

* Shunt - A. as defined in Table V.
- B. the per cent of systemic venous return which bypasses the lungs.

** Weight - "yes" indicates below the third percentile in weight at time of catheterization; "no" indicates above the third percentile according to Stuart growth curve.

pulmonary vasculature. Thirty patients gave radiologic evidence of combined ventricular enlargement, fourteen of right ventricular enlargement, and four of left ventricular enlargement. In those patients who underwent surgical correction of their ventricular septal defect, four out of sixteen showed a definite decrease of pulmonary engorgement.

Hemodynamics:

Forty-six of the forty-eight patients were subjected to cardiac catheterization. Sixteen of these patients were catheterized twice and included patients who did not undergo surgery and patients who had two catheterizations prior to closure of their defects. The results of these sixteen serial cardiac catheterizations are shown in Table VI. The right ventricular systolic pressures remained similar in one patient over a period of three years and in another over a six-year period. Three patients showed an increase in right ventricular systolic pressure: during a five-year interval, J. A. demonstrated a rise from sixty-six to one hundred and ten millimeters of mercury; E. W. had an increase from seventy to ninety millimeters of mercury during a four-year period; and, in two years, the pressure rose from seventy-eight to ninety millimeters of mercury in D. A. D. G. had an incomplete second catheterization, but showed the development of arterial unsaturation and a right-to-left shunt. Ten patients exhibited a decrease of pressures over periods

of two to nine years. The greatest decrease was from one hundred and twenty to sixty millimeters of mercury occurring in R. Ga. probably due to improvement in the "steady" or basal state of the patient. The majority showed a decline of ten to twenty millimeters of mercury at the time of the second catheterization.

Electrocardiography:

Serial electrocardiography of forty-seven patients revealed a normal pattern in two cases, left ventricular hypertrophy in twelve cases, right ventricular hypertrophy in fourteen cases, and combined ventricular hypertrophy in nineteen cases. The P wave was greater than 0.09 second in three cases and showed notching in two cases. There were two cases in which a qR pattern was present in V_1. A total of twenty-five patients showed a q wave in V_6 of two millimeters or more; it was three millimeters or more in eighteen of these cases.

Results of Surgery:

One patient, D. M., underwent banding of the pulmonary artery at the age of three months because of intractable heart failure. Pressure recordings in the pulmonary artery revealed a drop in systolic pressure from sixty-five to twenty-three millimeters of mercury immediately following the banding procedure; whereas, the aortic pressure rose from forty to ninety-five millimeters of mercury upon completion of the surgery.

Fifteen patients, all five years or older, had open-heart surgery to correct their defects which ranged in size from one-half to three centimeters. In two cases the defect was incompletely closed, but the patients have a reduction of pulmonary blood flow and are doing well. Thirteen patients had a successful closure of their defects and are likewise doing well. Two additional patients died of cardiac arrest in the immediate postoperative period: D. A. died at seven years of age after open-heart surgery, while T. C. died at four months of age after an unsuccessful attempt at closed-heart repair in 1956.

Serial pressure recordings were made in six patients pre- and postoperatively as shown in Table VII. Right ventricular systolic pressures recorded immediately before and after closure of the septal defect showed decreased pressures in three patients; from forty to twenty millimeters, from thirty-five to twenty-five millimeters, and from seventy-five to forty millimeters of mercury. Longer follow-up catheterization studies were performed on three additional patients who showed declines in right ventricular systolic pressures from forty to twenty-seven millimeters, from eighty-five to fifty-five millimeters, and from seventy-five to forty millimeters of mercury.

Fatalities:

Congestive heart failure was the primary cause of death in two infants at the age of three months and four months. Congestive heart

failure was a secondary cause of death in R. Wid. who died of pneumonia at five months of age. Postoperative cardiac arrest occurred in two children ages four months and seven years who were in congestive heart failure at the time of surgery. Three deaths were due to non-cardiac causes: S. Wu. died of a Werdnig-Hoffman-type of syndrome at three years of age, G. C. died of an incompletely diagnosed central nervous system disease at three years of age, and P. B. was fatally injured in an automobile accident at twelve years of age after successful surgical closure of her defect. The causes of death are shown in Table VIII of the eight patients in this study who did not survive childhood.

DISCUSSION

This series of only forty-eight proven cases of isolated ventricular septal defect is limited in several respects. Only those cases first seen under one year of age were included in an attempt to obtain a more accurate survey of the true natural history from birth of this particular cardiac defect. However, this limitation significantly excluded a number of asymptomatic children with proven, small ventricular septal defects now being followed in the Clinic who were free of symptoms during infancy and who presented in childhood with the only complaint being that of a murmur.

This particular group of infants showed a predominance of females to males in a ratio of twenty-nine to nineteen. This finding is unusual, since the ratio in other series has uniformly been equally divided between males and females.

This group showed a high relationship to diseases of the nervous system. Two patients were afflicted with incompletely diagnosed central nervous system disease, one resembled Werdnig-Hoffman disease. Furthermore, two siblings of two different patients died of severe congenital defects of the nervous system. No other series of congenital heart disease has reported a similar incidence of central nervous system disease.

As would be expected, all the children showed the classical murmur of a ventricular septal defect on physical examination and the majority also had a palpable thrill. The apical diastolic murmur of increased mitral blood flow was heard in thirty-one patients and included several patients who were considered to have a small defect and a relatively small shunt. The second sound in the pulmonic area was described as being accentuated in thirty-six cases. The pulmonary artery pressure was recorded in eleven of the twelve patients who did not have an accentuated second sound and revealed six patients to have pressures greater than forty millimeters of mercury; one had a pressure of sixty-five at three months and another had a pressure of ninety at four months.

A total of twenty-nine patients developed congestive heart failure, of which twenty-one began to have symptoms when less than six months of age. Two of these patients died of intractable heart failure at two months and at four months of age. The present series showed a very high incidence of congestive failure as might be expected in this age group, but a low mortality from heart failure, as compared to another series by Morgan (5) of one hundred and twenty-five patients with ventricular septal defects of which seventeen developed congestive heart failure when less than six months old. Ten of these seventeen patients died. The decreased mortality in the present series is felt to be due to better diagnosis and management of heart failure in infancy.

The growth and development of these children was strikingly retarded. Thirty-seven infants were below the third percentile in weight at six months of age. Even at six months of age, fourteen were still below the third percentile. Ten of these fourteen patients had developed congestive heart failure; whereas, four were never in failure. In contrast, congestive heart failure developed in only six out of twelve patients who were below the third percentile in weight at six months and rose to above the third percentile by six years of age. The remaining eleven patients who were below the third percentile at six months of age either died before six years of age or have not yet reached that age. Nine children were never below the third percentile at any time in their

development. It is of interest that only one of these nine patients developed congestive heart failure, as shown in Table IX. By contrast, the eighteen patients who were never in heart failure showed below-average development and only one of them reached above the fiftieth percentile in weight.

Serial cardiac catheterizations in sixteen patients revealed a decrease in right ventricular systolic pressure in ten or seventy-five per cent of the cases. By contrast, four of the sixteen showed a significant rise in right ventricular systolic pressure suggestive of increased pulmonary resistance and in two patients the pressures remained approximately the same. These findings would seem to indicate that beyond the period of infancy, the hemodynamics of the lesion tend to stabilize or to improve in the majority of instances, but in this group twenty-five per cent showed progressive changes.

SUMMARY

Forty-eight patients seen under one year of age with proven, isolated ventricular septal defects were reviewed for the purpose of better understanding the natural history of this cardiac malformation in infancy and childhood. It is immediately realized that this age grouping eliminates the asymptomatic infant who would not have been referred by this age in many instances.

The following are the significant findings as a result of this study:

1. The male to female ratio was approximately 2:3 in this series.
2. Sixty per cent of the patients had congestive heart failure, with only two deaths from this cause alone.
3. Growth and development were greatly impaired in the entire group:
    a) All but one of the twenty-nine patients who developed congestive heart failure fell well below the third percentile in weight on the Stuart growth chart.
    b) The nineteen patients who did not develop congestive heart failure fell well below the average growth curve of the fiftieth percentile.

c) The larger the pulmonary blood flow as demonstrated by hemodynamic studies, the poorer was the growth of the patient.

4. The hemodynamic status of many patients remained the same or improved; however, in this series, twenty-five per cent of the sixteen patients who were submitted twice to cardiac catheterization showed progressive changes.

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