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Spontaneous Closure of Ventricular Septal Defect

M. D. LI, M.D., GEORGE COLLINS, M.D.,
ROBERT DISENHOUSE, M.D. and JOHN D. KEITH, M.D., *Toronto*

A THOROUGH knowledge of the natural history of the ventricular septal defect has become increasingly important in recent years since it has been recognized that a large proportion close spontaneously or decrease to an insignificant size, especially in early infancy. Some form of operative therapy or banding of the pulmonary artery may be required to save life, to improve congestive heart failure or to prevent pulmonary vascular disease. However, this approach is accompanied also by a high mortality in the first six months of life and can be used only when it is clearly needed. Fortunately this applies to a minority of cases, probably less than 10%. The remainder can be managed medically or require no treatment at all.

Spontaneous closure of the ventricular septal defect was first mentioned in 1918 by French[1] in a paper entitled "The Possibility of a Loud Congenital Heart Murmur Disappearing When a Child Grows up". The first documented case of diminution in size of the defect (proved by cardiac catheterization) was published by Azevedo *et al.*[2] in 1958. In 1960 Evans, Rowe and Keith[3] first presented evidence that spontaneous closure of a ventricular septal defect may be a frequent occurrence and can be demonstrated by cardiac catheterization. Since then there have been published at least 30 papers dealing with this topic.

The object of our investigation was to determine the frequency of spontaneous closure that may be expected and to attempt to recognize which cases are likely to fall into this category. It is obvious that in such children operative treatment is not needed.

From the Cardiac Department, The Hospital for Sick Children, Toronto, and Department of Pediatrics, University of Toronto, Toronto, Ontario.
Aided by a grant from the Ontario Heart Foundation.
Reprint requests to: Dr. M. D. Li, War Memorial Children's Hospital of Western Ontario, London, Ontario.

Method of Study

All cases of isolated ventricular septal defect registered in the Department of Cardiology at The Hospital for Sick Children in Toronto from 1950 to 1965 have been included in this present study. There is at least a one-year follow-up in all cases; the longest follow-up was 21 years. The total number of children found to have ventricular septal defect as an isolated phenomenon was 1513. Of these, 633 have been catheterized.

Heart specimens preserved in the pathological museum at The Hospital for Sick Children up to April 1968 have been reviewed for any evidence of spontaneous closure of the ventricular septal defect.

Diagnosis by Clinical Examination Alone

From the records of all cases those which satisfied certain clinical criteria were selected. Special attention was given to the description of the heart murmur, electrocardiogram, chest radiograph, overall clinical picture and follow-up examination.

The characteristic murmur is loud, harsh and pansystolic, maximal in the third and fourth left interspace, with or without an associated thrill, in a child who has no cyanosis. The hilar shadows in the chest radiograph may be increased or normal. Cases may be divided into three groups according to the clinical findings: (1) Those with a characteristic harsh systolic murmur over the lower precordium associated with a thrill. Many of these have electrocardiographic and radiographic changes. (2) Patients

with a characteristic murmur as above but without a thrill. Electrocardiographic changes or x-ray evidence of enlargement of the heart or increased hilar shadowing may be present. (3) Those who have a murmur slightly less harsh than those described above: this particular murmur is moderately loud, usually grade II/IV, maximal in the third or fourth intercostal spaces at the left sternal border, and of uniform intensity throughout systole, beginning with the first sound and extending to or stopping short of the second heart sound. A consistent feature[3] is the superficial blowing quality of the murmur, giving the impression of high frequency vibrations arising immediately under the diaphragm of the stethoscope.

In making a diagnosis on clinical aspects alone, the passage of time and repeated observation usually allow exclusion of certain conditions that may simulate the ventricular septal defect, such as pulmonary infundibular stenosis, pulmonary stenosis, subvalvular aortic stenosis, and mitral or tricuspid insufficiency. In many infants and children in whom the characteristic murmur was the only abnormal finding, we have been able to check our clinical diagnosis by cardiac catheterization and/or angiocardiographic techniques at a later date and have found that the clinical diagnosis was correct in approximately 95% of cases so studied.

In making a firm diagnosis of ventricular septal defect, a number of intracardiac techniques are available. A 5% oxygen rise on entering the right ventricle from the right atrium has been accepted as adequate evidence of such defect. Dye curves using Evans blue or Fox green have been used from time to time to demonstrate the shunt. In recent years the left ventricular cineangiogram or pulmonary artery angiogram has proved most helpful in demonstrating small shunts and in proving that the defect has been closed off at a later date. A sound catheter, hydrogen electrode catheter or fiberoptic catheter has been used in a number of isolated cases to confirm the diagnosis. One or other of these methods was used to identify the ventricular septal defect.

Once the catheter data were collected, the cases were divided into the six hemodynamic groups described by Kidd *et al.*[4] in 1965, as follows:

Hemodynamic Classification

I—low flow, low resistance
II—increased flow, low resistance
III—increased flow, slightly increased resistance
IV—increased flow, greater resistance
V—low flow, high resistance
VI—high resistance, reversal of flow

Pathological Evidence of Spontaneous Closure

The 800 heart specimens in the pathological museum at The Hospital for Sick Children collected in the period from 1945 to 1968 were examined carefully for evidence of spontaneous closure of ventricular septal defect.

Definition of Spontaneous Closure of the Ventricular Septal Defect

We considered the defect had closed spontaneously if: (1) there was cardiac catheter and/or angiocardiographic evidence of closure; (2) no murmur was heard on follow-up examinations; (3) an insignificant or functional type of murmur was heard on follow-up examination; (4) pathological evidence of closure was found at autopsy.

RESULTS OF STUDY

Rarely does one have the opportunity to make a diagnosis of a ventricular septal defect during life, confirm it by cardiac catheter and angiogram and at a later date, after the defect has closed spontaneously, demonstrate the site of closure by anatomical dissection.

As an example, the following data are from one of our patients who came under observation at one week of age. Catheter findings were as follows:

	O_2 saturation %			
Site	*Age 1 week*		*Age 6 months*	
Inferior vena cava	44		43	
Right atrium	41	20% diff.	47	5 % diff.
Right ventricle	61		55	
Aorta	59		54	
Left ventricle	98		85	
	(pressure 50/0 mm. Hg)		(pressure 40/0 mm. Hg)	

An RV angiogram demonstrated an RV-LV shunt at ventricular level and also revealed transposition of the great vessels. The murmur disappeared at 1 year of age. The baby died from pneumonia when 20 months old. The site of closure of the ventricular septal defect was clearly seen as a hollow area filled in with a thin membrane of fibrous tissue (Fig. 1). This case is not included in the series of isolated VSD under discussion since there was associated transposition of great vessels, but is presented to illustrate the complete picture of clinical, hemodynamic and anatomic confirmation.

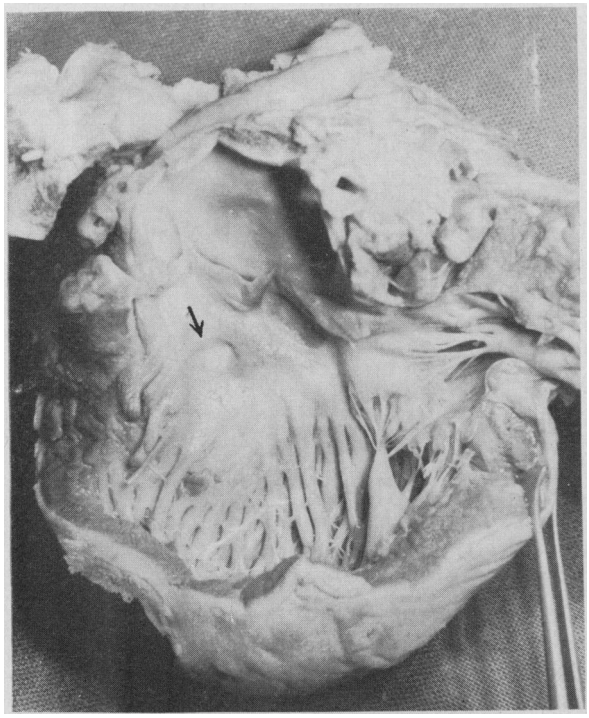

Fig. 1.—Transposition of great vessels with ventricular septal defect. The ventricular septal defect closed spontaneously by fibrous proliferation. Viewed from the right ventricular side.

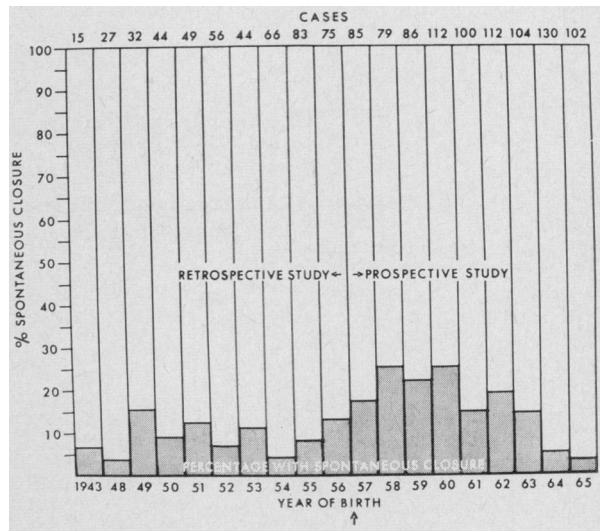

Fig. 2.—Incidence of spontaneous closure of ventricular septal defect arranged by year of birth of the patients. The number at top of each column indicates the number of patients born in that year.

Incidence of Spontaneous Closure of Isolated Ventricular Septal Defect

(a) One of the authors (G.C.) has reviewed 192 infants with isolated VSD in whom the diagnosis was confirmed by catheterization in the first year of life. The majority had the closure proved by catheterization as well. These have all been followed up for five years at least. The incidence of spontaneous closure in early childhood has been 22% by June 1968. In each case the murmur has disappeared. These are unselected cases.

(b) Many older children with an isolated VSD had cardiac catheter studies. A 4% incidence of closure was noted in an earlier group whose defects were larger than those in Group (a).

(c) The remaining 880 cases constitute a group of patients seen in office practice who were diagnosed clinically and followed up for several years. These patients were usually first seen in infancy. Their study covers a period of 15 years; they were seen for a shorter or longer time, depending on whether follow-up was possible. The murmur had disappeared or become insignificant in 165 cases, so that the incidence of closure is 18.8%.

If the above cases, diagnosed clinically or by catheterization, are arranged by year of birth, and the percentage with closure indicated as in Fig. 2, new information comes to light.

Before 1956 less attention was paid to the disappearance of the murmur in patients with ventricular septal defect. After that date we recorded findings with greater care and more precision.

It will be seen that the incidence of closure rose in 1956 and after, reaching a peak of up to 25% in the years 1960 to 1963, in patients born in 1958 and 1960. The curve falls again after that simply because the more recent cases have not been followed up long enough to permit recording those that are closing year by year

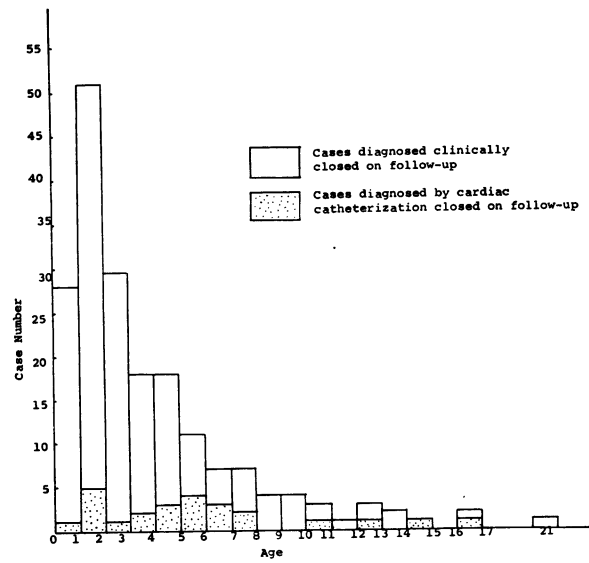

Fig. 3.—Age at first visit following spontaneous closure of ventricular septal defect.

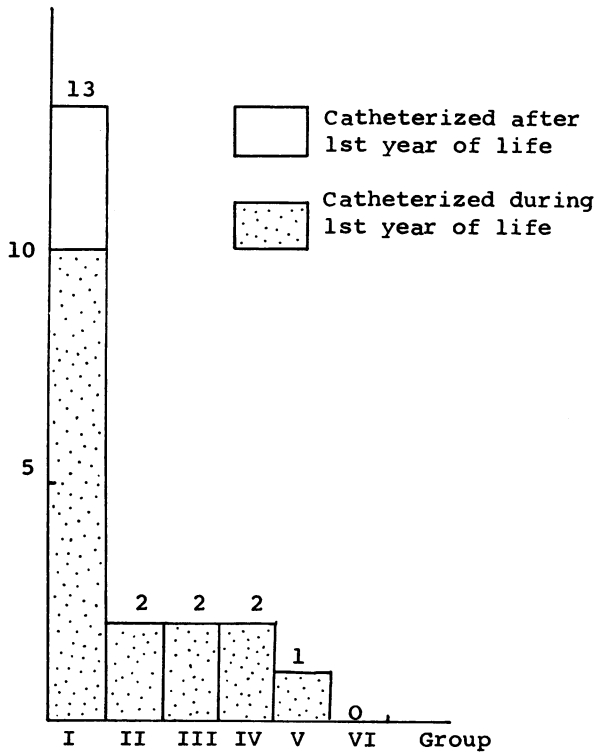

Fig. 4.—Spontaneous closure of ventricular septal defect; hemodynamic groupings of initial catheterization (The Hospital for Sick Children).

in the first eight years of life. With the passage of time it is anticipated that the years from 1963 on will show also an incidence of closure of 25%.

Age of Spontaneous Closure

Of 190 cases that were believed to have closed spontaneously, 109 (57%) did so before 3 years of age and 169 (89%) closed before 8 years of age. Our follow-up is as yet incomplete, but up to 1966 the latest age of closing spontaneously was between 16 and 21 years (Fig. 3).

A further study of patients followed up into adult life is being carried out in our department at the present time and will be reported in the future.

Hemodynamic Grouping

Fig. 4 shows the hemodynamic grouping in infancy of the patients catheterized at The Hospital for Sick Children whose defects ultimately closed. A large majority of the infants were in Group I, which comprises those in whom there was a small shunt and normal pulmonary vascular resistance, as one might expect, since these patients have the smaller defects. However, it is of interest that two patients were in hemodynamic group II, two in III, two in IV, and one in group V, so it is possible for closure to take place even though the defect may be a relatively large one. The three children who were catheterized after the first year of life were all in group I.

Congestive Heart Failure

Among our 190 patients whose defects ultimately closed spontaneously 13 (7%) were in congestive heart failure at some time during infancy. All responded promptly to digitalis and did not present a problem in medical management. None were in failure after their first birthday.

Anatomical Evidence of Spontaneous Closure

Heart specimens of infants and children who had died from various cardiac defects at The Hospital for Sick Children were examined. It was possible to identify 11 specimens that showed evidence of spontaneous closure of an isolated ventricular septal defect. The mechanisms of closure are listed in Table I. The most common of these was by fibrous proliferation, and the second most common was by adhesion of the medial leaflet of the tricuspid valve to the defect. In the closure specimens, with one exception, the defects were located at the membranous portion of the ventricular septum. It is quite possible that closure can occur when the defect is located in the muscular septum, but it is impossible to recognize the site subsequently. If, in fact, 25% of cases do close spontaneously and the site is difficult to recognize post mortem, it may well be that the majority close by muscular hypertrophy (Figs. 5, 6 and 7).

TABLE I.—MECHANISMS OF SPONTANEOUS CLOSURE OF VENTRICULAR SEPTAL DEFECTS AS SHOWN BY SPECIMENS KEPT IN THE PATHOLOGICAL MUSEUM, THE HOSPITAL FOR SICK CHILDREN (1935-1966)

Mechanism of closure	*Number*	
Isolated ventricular septal defect		
Adhesion of medial leaflet of tricuspid valve	4	
Fibrous tract (incomplete closure)	5	
Fibrous patch	1	
Aneurysm of membranous septum	1	11
Associated cardiac defects		
Transposition of great vessels		
Fibrous patch	5	
Fibrous pouch	1	
Adhesion of medial leaflet of tricuspid valve	1	
Pulmonary stenosis		
Fibrous patch	1	
Double inlet left ventricle		
Fibrous patch	1	9
Total		20

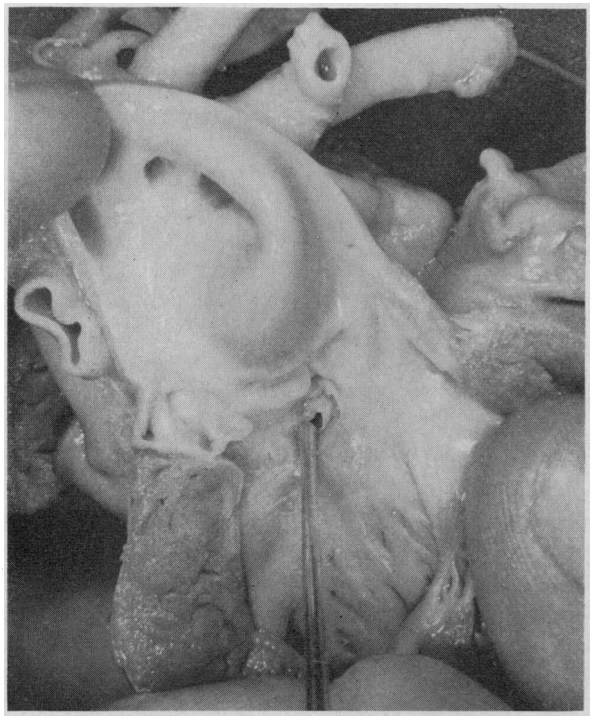

Fig. 5.—Ventricular septal defect which was closing by fibrous proliferation around the defect. The patient was two months old at autopsy.

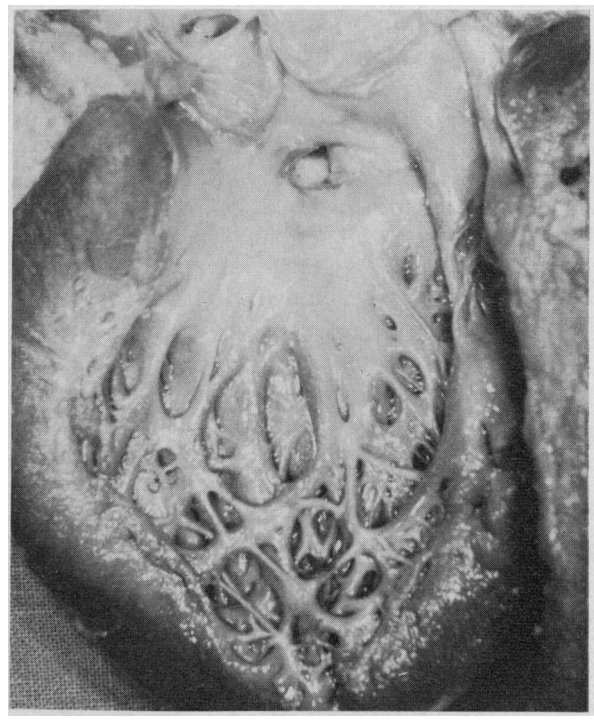

Fig. 6.—Ventricular septal defect closed by adhesion of medial leaflet of tricuspid valve to the defect, as viewed from the left ventricular side.

Spontaneous Closure of Ventricular Septal Defect in Presence of Associated Cardiac Lesions

A ventricular septal defect may close when associated with another cardiac lesion such as transposition of the great vessels,[29] tricuspid atresia,[31] pulmonary stenosis, patent ductus arteriosus, coarctation of the aorta and double inlet left ventricle.

We have had seven cases of spontaneous closure of ventricular septal defect associated with transposition of the great vessels; all were proved at autopsy. Three of them were proved before death by cardiac catheterization. One of them had cardiac catheterization performed when 5 days old; transposition of the great vessels and a small ventricular septal defect were found and atrial septostomy was performed. The patient died at 10 months of age and at autopsy the septal defect had been closed off completely by fibrous proliferation, which formed a pouch when viewed from the left ventricular side.

DISCUSSION

Two hundred and thirty-seven cases of spontaneous closure of ventricular septal defect were reported in the literature up to 1967.[5-28] In the majority (129) closure was assumed from the disappearance of the murmur. Catheter evidence of closure was obtained in 43, and angiocardiographic evidence in 29. Seventy-two in whom the diagnosis was made initially by cardiac

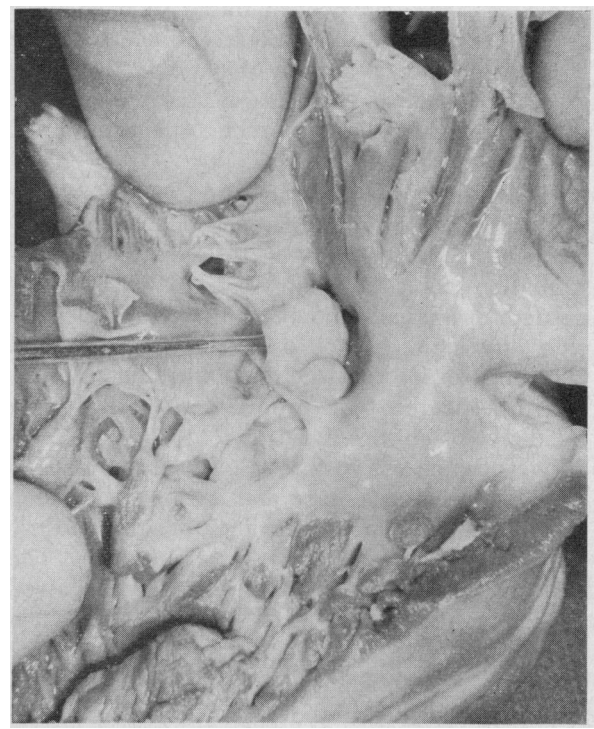

Fig. 7.—Ventricular septal defect closed by aneurysm of membranous ventricular septum. Viewed from the right ventricular side.

catheterization and/or angiocardiography, subsequently were proved by similar techniques or by pathological evidence to have closed spontaneously. Thirty-nine were studied as pathological specimens, and the closed defect was demonstrated. We have added 190 cases, increasing the total seen to 427. Thus, there is abundant evidence that spontaneous closure of the isolated ventricular septal defect is common in the pediatric age group.

In spite of the fact that an anomalous hole in the septum is a common congenital heart lesion, it is difficult to determine accurately the number and percentage of those that close spontaneously. The true incidence of spontaneous closure will take several years yet to determine more precisely, since it is difficult to obtain data for the adult age group. A large number of unselected cases followed up for many years is needed to provide adequate information. Hoffman and Rudolph[8] and Ash[22] record incidence figures and relate them to the general population figures. The former noted spontaneous closure in 15 out of 62 (24%). In Ash's series, 165 infants were followed up for a minimum of two years; 25 cases (15%) closed spontaneously.

In the present series if we take into account only those patients who were seen initially in the first year of life and who also had a cardiac catheterization and were followed up for at least five years, 22% have been found to have their defect close during that interval. Since we have had a liberal cross-section of cases in this category,[4] we believe that this is a representative group and that the incidence of closure must be at least 22%.

However, if one pays attention to the year of birth in each patient with ventricular septal defect in the total group of 1513 cases, new information comes to light. Up to 1955-56 we carried out what amounted to a retrospective study by looking back over our old cases and checking to see in which patients the murmur had disappeared. This produces a relatively low incidence of closure, from 4 to 15%. After 1955-56 we became aware that many of these defects were undergoing closure and we began to keep track of all our cases; the incidence of closure after that date rose to as high as 25%. The children born after 1960 have not been followed up long enough for us to determine the final figure.

The age at which closure takes place has aroused considerable interest. Hoffman and Rudolph[8] demonstrated that it frequently occurred between 6 and 12 months of age. Of 83 cases in the literature where the age of closure was mentioned, in 22% this was under 12 months, in 53% it was before 4 years and in 84% the age of closure was 8 years or less.

These findings are similar to our own reported from The Hospital for Sick Children; 89% of those which underwent closure did so by the end of the eighth year of life. Our closure time was more commonly in the first two to three years of life and fell off progressively after that.

Spontaneous closure of interventricular septal defect is uncommon after the individual has reached adult years. Our oldest case closed between 16 and 21 years of age. In the literature there are three documented cases in which closure occurred in adult life.[14, 18, 25]

Spontaneous closure of a ventricular septal defect associated with transposition of great vessels was first reported by Shaher *et al.*[29] in 1965. Our autopsy and clinical material indicates that this may occur with considerable regularity. Seven such cases have now been identified at The Hospital for Sick Children. This number is likely to increase, since survival of these infants is aided by modern medical and surgical techniques.

The most common mechanism of spontaneous closure of the ventricular septal defect demonstrated at autopsy is adhesion of the medial leaflet of the tricuspid valve to the defect.[15, 25] Fibrous proliferation is not so readily recognized in routine opening of the heart. Other mechanisms of closure have been identified and include: aneurysm of the membranous ventricular septum,[30] muscular hypertrophy, differential growth (size of defect *vs.* size of heart), growth of septum, sinus of valsalva aneurysm "plugging", trauma by high flow leading to fibrous proliferation, diminished flow the result of muscular contraction and localized fibrosis following bacterial endocarditis.

CONCLUSIONS

The incidence of spontaneous closure of a ventricular septal defect appears to be as high as 25% in infancy and childhood. Spontaneous closure occurs chiefly in the first eight years (90%) and is uncommon in the adult. Most defects that close spontaneously are small initially—probably less than 5 or 6 mm. in diameter.

Summary Cases of isolated ventricular septal defect registered in the Department of Cardiology at The Hospital for Sick Children in Toronto from 1950 to 1965 and heart specimens preserved up to April 1968 were reviewed for evi-

dence of spontaneous closure of the ventricular septal defect. The conclusions are: (1) the incidence of spontaneous closure appears to be approximately 25% in infancy and childhood; (2) it occurs chiefly in the first eight years (90%); (3) spontaneous closure appears to be relatively uncommon in the adult; (4) most defects that close spontaneously are small initially, and (5) spontaneous closure of ventricular septal defect in patients with transposition of great vessels may occur in a significant number of cases.

Résumé Nous avons passé en revue les cas isolés de défaut du septum ventriculaire qui sont passés au Service de cardiologie au Hospital for Sick Children de Toronto de 1950 à 1965 et avons réexaminé les pièces cardiaques conservées jusqu'en avril 1968. Nous avions en vue de rechercher les signes de fermeture spontanée dans cette anomalie cardiaque. Voici nos conclusions: 1) la fréquence de la fermeture spontanée est d'environ 25% durant la première enfance et l'enfance; 2) elle survient principalement au cours des huit premières années de la vie (90%); 3) ce phénomène est relativement rare chez l'adulte; 4) la majorité des défauts qui se ferment spontanément sont à l'origine de petite dimension et 5) cette fermeture spontanée se produit dans un nombre considérable de cas chez les malades qui présentent une transposition des grands vaisseaux.

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