Natural History of Ventricular Septal Defect
A Study Involving 790 Cases

PIERRE CORONE, M.D., FRANÇOISE DOYON, STATISTICIAN, SERGE GAudeau, M.D., FRANÇOIS GuÉRIN, M.D., PIERRE VERNANT, M.D., HENRI DUCAM, M.D., CLAUDE Rumeau-ROUquette, M.D., and PATRICK GAUDEUL, M.D.

SUMMARY The development of 790 untreated patients affected by ventricular septal defect (VSD) has been the object of a 25-year study. Of these patients, 72% had had at least one catheterization; 13% had several. The mean observation interval is six years, and the average age at the latest data is 19.5 years. This study covers 4717 patient-years.

For the entire population, the incidence rate of aortic regurgitation is 6.3% (4.3 for 1000 patient-years) and that of bacterial endocarditis is 3.7% (2.4 for 1000 patient-years). Twenty-five patients died, 15 of them between the ages of one and 39.

Of the 499 cases with several clinical examinations, 71% remained stable. In 21%, changes suggesting some level of closure developed; in 7%, infundibular stenosis began to evolve and in 1% pulmonary vascular disease began to appear or became accentuated.

These different rates are studied and discussed in relation to patients' age, VSD type, and various follow-up characteristics.

THE EVOLUTION OF THE VENTRICULAR SEPTAL DEFECT (VSD) in the first years of life has been the focus of several studies. These have shown that large septal defects are particularly serious during the early years but that spontaneous closure occurs in about one third of all cases.1 4

The development of patients who are older than one year and affected by VSD has not been studied extensively.5 7 One is generally astonished by the frequency of VSDs noticed at birth (about two out of 1000 living children) and even at school age (one out of 1000 children) and the rare observation of this abnormality in adults.8-11 Late mortality, the possibility of late closure, or transformation into cyanotic diseases (tetralogy of Fallot or the Eisenmenger complex) have been offered as explanations.12 13 In addition, a certain number of patients affected by VSD and free of all symptoms may not be recognized or may avoid seeing physicians, and thus escape medical statistics.14

This study endeavors to give further information about this late evolution. A relatively older population (469 subjects out of 790 were more than four years old when they entered the study) was followed by the same medical team for a long period.

Materials and Methods

This study involves 790 cases of VSD, 272 of which were initially examined as outpatients at the Hôpital des Enfants Malades, while 518 of them were examined at a cardiology service of a university hospital (Broussais, La Pitié and Henri Mondor in Paris).

Patients with an associated stenosis of the pulmonary tract (excluding all those with cyanosis) or aortic regurgitation were included in this study, along with patients with isolated VSD. Patients with minor malformations that would not affect prognosis were also included (140 [18%], see table 1). Neither patients with complex cardiopathies

From the University Hospital Centers (C.H.U.) Pitie-Salpétreire, Henri Mondor and Enfants y Malades, Departments of Pediatric Cardiology, Paris, France, With the help of the Groupe de Recherches Epidémiologiques sur la Mere et l'Enfant (I.N.S.E.R.M.).
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Address for reprints: Dr. P. Corone, C.H.U. Pitie-Salpétreire, 83, Boulevard de l'Hôpital, 75634 Paris Cedex 13, France.
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(tetralogy of Fallot, transposition or corrected transposition of the great arteries) nor those with orifical or isthmic aortic stenosis were included. In 90 cases (11%), these patients had some extracardiac anomalies: 8 trisomie 21, 2 Turner, 2 Marfan, and 3 complex malformative syndromes.

The population was distributed into four classes:

**Table 1. Description of Cardiovascular Malformations Associated with VSDs**

<table>
<thead>
<tr>
<th>Malformations</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSD isolated*</td>
<td>640</td>
</tr>
<tr>
<td>VSD associated with</td>
<td>140†</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>49</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>31</td>
</tr>
<tr>
<td>Mitral insufficiency</td>
<td>8</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>58</td>
</tr>
<tr>
<td>Pulmonary insufficiency</td>
<td>10</td>
</tr>
<tr>
<td>Tricuspid insufficiency</td>
<td>6</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>19</td>
</tr>
<tr>
<td>Partial pulmonary venous abnormal return</td>
<td>3</td>
</tr>
<tr>
<td>Superior vena cava anomaly</td>
<td>14</td>
</tr>
<tr>
<td>Pulmonary artery branch stenosis</td>
<td>6</td>
</tr>
</tbody>
</table>

*Included in this group are VSDs coexisting with pulmonary stenosis (defining group IV) and those which coexist with aortic regurgitation (considered as a complication of a VSD).
†Some patients had more than one associated malformation.

A) 183 (23%) were examined once. One hundred and ten of these had not yet had operations and four have since died.
B) 108 (14%) were examined once before their operation.
C) 114 (14%) were examined at least twice and then had operations. The evolution of the defect was studied up to the last presurgical examination.
D) 385 (49%) were examined at least twice and have not been operated on so far.

The main characteristics of each of these categories are indicated in table 2.

The follow-up period is more than five years for 435 patients, over ten years for 196, and over 15 years for 67. The average period of this follow-up is 7.8 years for categories C and D. The distribution of age at the first examination and the distribution of age when last heard of (table 3) illustrate the disparity among cases in this respect.

The statistical analysis of the results was made on the INSERM computer, in collaboration with the Epidemiological Research Team on Mother and Child.

**Results**

**Population Characteristics**

At the first examination, made by a member of our team which determined the patient’s entrance into the survey, 53%
of the population were boys and 47% girls. This population was older than that of previous studies: only 19% of the patients were under one year, 59% over 5 years, and 17% over 15 years. The age at our first examination was not the age of discovery of heart disease: 69% were diagnosed in their first year and 90% were under 5 when the defect was detected. Some were discovered very late: 12 VSDs were detected after the age of 20.

Clinical Features

Seventy percent of the patients were free of any symptoms and in class I of the New York Heart Association (NYHA) classification; 25% were in Class II; 4%, in Class III; and three patients were in Class IV. A systolic murmur was present in all cases, with a thrill in 86% of them. The heart volume was judged normal or slightly increased in 70% of the cases, and greatly augmented in 30%.

Hemodynamic Features

Five hundred sixty-two patients (72%) have had at least one catheterization. In the remainder, the diagnosis was assessed on clinical data alone. There is no doubt that catheterization is theoretically necessary to categorize a VSD at the first examination, and to follow its evolution. Nevertheless, an extrapolation seemed justified by the excellent concordance between clinical and hemodynamic data. Each case was put into one of the five following categories, based on the classification of Fyler et al.15, 16

Group I included patients with a small VSD of the "Maladie de Roger" type. No functional disorders, cardiomegaly, nor increase of pulmonary pressure was present in this group.

Group II included patients with large VSDs and cardiomegaly with a large left-to-right shunt. An increase of pulmonary arterial pressure was present and classified as either moderate (group IIa), or accentuated (group IIb) which defined pressure greater than 70% of systemic pressure.

Group III included patients with VSDs with associated pulmonary vascular disease (pulmonary vascular resistances/systemic resistances > 0.70) which reflected high pulmonary hypertension (close to systemic pressure) and reduction of the shunt.

Group IV included patients with VSDs associated with an infundibular or orificial obstruction in the pulmonary outflow tract; in these, a pressure gradient between the right ventricle and the pulmonary artery of at least 25 mm Hg was present which provided protection of the pulmonary circulation.

The grouping of the 790 cases thus established is described in table 2. One can see that group I (Maladie de Roger) represents 38% of the population. Among 89 catheterized group IV VSDs, 32% have a right ventricle-pulmonary artery gradient between 25 and 39 mm Hg; 37%, a gradient between 40 and 69; 31%, a gradient greater than or equal to 70.

Ventricular septal defects with associated trisomie 21 were severe. Out of the eight cases observed with this association, five were of group IIb (three of them have been operated on), one of group III, and two of group IV. No trisomie 21 was found in groups I and IIa. A patent ductus arteriosus was in three cases associated with the VSD.

Evolution

Functional Behavior

For patients examined at least twice (categories C and D), functional status proved to be remarkably stable, and in nearly all of them, remained excellent or at least, good (table 4).

Hemodynamic Behavior

For the 499 cases seen at least twice (249 of which had one catheterization, 85 had two, and 14 had three), the majority of VSDs remained stable (355 cases, 71%) (table 5). They occupy a diagonal on the chart. One hundred and three of the patients (21%) showed evolution toward a closure (area a); 69 (14%) of which closed completely; and 26% had one catheterization and 6% had several.

<table>
<thead>
<tr>
<th>Class</th>
<th>First Examination</th>
<th>Last Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>327 (71%)</td>
<td>348 (72%)</td>
</tr>
<tr>
<td>II</td>
<td>118 (26%)</td>
<td>116 (24%)</td>
</tr>
<tr>
<td>III</td>
<td>14 (3%)</td>
<td>18 (4%)</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>461</td>
<td>484</td>
</tr>
</tbody>
</table>

*It was possible to appraise the functional status in 92% of all cases at the first examination and in 97% at the last examination.
Seven cases seem to evolve toward an increase of pulmonary vascular resistance (area b), five of them ultimately developing the Eisenmenger syndrome. Three of the seven cases of VSD were in group IIb: the first had three catheterizations, at 14, 16, and 21 years. At these three examinations, pulmonary arterial pressures were respectively 100/40, 100/40, and 140/75 and the pulmonary vascular/systemic resistance ratios were 0.33, 0.50 and 1. The second had hemodynamic studies when he was three and five years old. Pulmonary arterial pressures were 80/40 and 100/50 and resistance ratios were 0.41 and 0.82. The third, whose defect evolved into Eisenmenger’s complex, was catheterized at 19 months and 14 years. His pulmonary arterial pressures were 72/32 and 80/40, with calculated resistance ratios of 0.59 and 1.81. At the time of his second examination, peripheral saturation was 83.5%. Such an evolution was never observed in the VSDs in groups I, IIa, or IV.

In 34 patients (7%) an infundibular stenosis evolved (area c). In five of these the stenosis was so severe that a tetralogy of Fallot was produced.

Spontaneous closure was observed; however, this study does not permit any evaluation of its absolute frequency, as one would have had to follow an entire population from birth to death. Nor could a true appraisal of the closure's frequency with age be made from our data: the time elapsed between two successive examinations varied widely and in some the interval was very long and prevented any reasonable estimate of the age when spontaneous closure took place.

The age characteristics of patients with spontaneous closure were looked at. The age at which the defect was first seen open was evaluated (table 6). This analysis will underestimate the age of closure, but may help in determining the chances a child of a particular age has of spontaneous closure. It appears that the younger the child, the greater his chances. Two of the VSDs did close relatively late, after the ages of 16 and 17.

The size of the VSD plays a part in determining the chances of closure. While smaller VSDs are more likely to close, larger VSDs may also follow the same course: 58 out of the 215 VSDs in group I (27%) closed completely; 37 out of 133 VSDs in IIa (28%) closed completely (10 cases) or partially (27 cases); eight out of 82 VSDs in group IIb (10%) closed completely (one case proved by two catheterizations) or partially (seven cases). We have observed no closures among the VSDs in groups III and IV.

### Complications

There are three main complications which threaten patients affected by VSD: aortic regurgitation, bacterial endocarditis, and congestive heart failure. The first two are exceptional in infancy. Heart failure is peculiar to infants, and when it occurs later it is usually secondary to either aortic regurgitation or bacterial endocarditis or both.

Aortic regurgitation was found in 50 cases. The cause of aortic regurgitation was thought to be bacterial endocarditis in five cases, streptococcic infection in four cases (three acute rheumatic fevers and one scarlet fever), and probably prolapse of the right anterior aortic valve (Laubry-Pezzi syndrome) in 38 cases. In three cases, the origin could not be determined accurately.

The time of occurrence of aortic regurgitation can easily be determined in cases of endocarditis and streptococcic infection. In other cases the best estimate is the interval between an examination in which no diastolic murmur was observed and the one in which the murmur is noted for the first time. The accuracy of this method of dating depends on the quality and frequency of the examinations. In many of our cases, the VSD was complicated by an aortic regurgitation at our first examination. For the 38 cases regarded as Laubry-Pezzi syndromes (table 7), the age at which aortic regurgitation was first diagnosed was used. For 35 of these 38, aortic regurgitation was present at the first examination.

The population of each age group represents the number of patients actually examined in this age group, with the exception of those known as already having been affected by this complication.

Bacterial endocarditis (table 8) affected 29 cases and congestive cardiac failure 84 cases (table 9). The two complications are so serious that they are unmistakable. Even years later, it is possible to make a highly probable retrospective diagnosis, and to date them approximately. We took these complications into account even if they occurred before their entry into the study. Therefore, the rate of these

### Table 6. Chances of Spontaneous Closure According to Age and to VSD Group

<table>
<thead>
<tr>
<th>Age bracket (in years)</th>
<th>Group I</th>
<th>Group IIa</th>
<th>Group IIb</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>29/88 (34%)</td>
<td>7/88 (8%)</td>
<td>1/44 (2%)</td>
<td>37/218 (17%)</td>
</tr>
<tr>
<td>5-9</td>
<td>16/91 (15%)</td>
<td>1/77 (1%)</td>
<td>0/47 (0%)</td>
<td>17/215 (8%)</td>
</tr>
<tr>
<td>10-14</td>
<td>11/97 (11%)</td>
<td>2/30 (5%)</td>
<td>0/34 (0%)</td>
<td>13/170 (8%)</td>
</tr>
<tr>
<td>15-19</td>
<td>2/97 (4%)</td>
<td>0/18 (0%)</td>
<td>0/10 (0%)</td>
<td>279 (3%)</td>
</tr>
<tr>
<td>≥ 20</td>
<td>0/47 (0%)</td>
<td>0/14 (0%)</td>
<td>0/13 (0%)</td>
<td>0/74 (0%)</td>
</tr>
</tbody>
</table>

*Group III and IV VSDs have never been observed, in this population, evolving toward closure.

†The age brackets are those during which the VSDs that closed themselves were observed still opened for the last time.
complications was calculated for our patients, as if all of them had been followed since birth. The population of each age group represents the number of patients who reached this age with the exception of those who had been affected by bacterial endocarditis at an earlier age. This explains why the number of cases in each age bracket differs in the three tables.

The incidence rate according to hemodynamic groups is represented in Table 10.

The incidence of congestive heart failure appears to be higher when an ASD is associated with VSD: heart failure was thus observed in nine cases out of 49, four of them before the age of one. We observed no instances of heart failure before one year old in patients in hemodynamic group III.

Mortality

Table 11 shows the assessment of the 25 deceased, according to the VSD hemodynamic group, the age at death, and the complications that could have affected the VSD.

Discussion

Certain characteristics of the population must be kept in mind in interpreting our results: these include the low percentage of infants; the relatively high percentage of adolescent and adult patients, which distinguishes this study from many others; the fact that the spontaneous course was interrupted by surgery in part of our population; the special orientation of the Hôpital Broussais, where a great number of patients coming from the provinces and abroad were hospitalized because of the gravity of their condition and the hope of being improved by surgery; the observation period, extending over ten years for nearly 200 patients and exceeding 20 years in 12 cases; the different frequency of examination from one patient to another; the low number of repeated catheterizations.

The foregoing comments point up the weaknesses of this study and all similar attempts. The generalizations drawn in this discussion must be made with prudence.

Aortic Regurgitation

Fifty cases (6.3%) of VSDs studied here were complicated by aortic regurgitation during the course of their evolution; that is, an incidence of 4.3 for 1000 patient-years. The figure of 6.3% is close to those of Nadas (5%) and Plauth (6.6%).

In a few of the cases the origin of the complication could not be determined and in others aortic regurgitation was present at the first examination. Within these limitations of our data, we can say that aortic regurgitation is never found before the age of two, is only rarely observed between two and four years old, and that its incidence is greatest in children between the ages of 5 and 9. This corroborates the data of Halloran9 (selective age: 6 years old), Plauth18 (between 4 and 7) and Nadas19 (between 3 and 8).

Aortic regurgitation worsens the patients’ condition in three-quarters of all cases. Bacterial endocarditis (3 cases) and congestive heart failure (10 cases) are possible complications. The mortality rate of these patients is 12% (six cases). Nevertheless, the remaining 25% of cases were remarkably stable based on follow-ups of 4 to 18 years, the mean follow-up for the 50 cases being 7.5 years.

Bacterial Endocarditis

Twenty-nine cases (3.7%) were complicated by certain or very probable bacterial endocarditis, that is, an incidence of 2.4 for 1000 patient-years. In 1966, Shah20 adding his cases to those of the literature, found a rate of 2.1, and in 1971, Keith31 found a rate of 1.3 for 1000 patient-years in 295 patients ranging in age between 13 and 22 years.

The incidence of bacterial endocarditis varies greatly with age.32 In our study, there was not a single case under two years of age; a rate of 1.2 for 1000 patient-years from two to 14 and 7.1 for 1000 patient-years between the ages of 15 and 20. Only one case was observed in a small group followed beyond the age of 30.

Dental portal of entry was, by far, the most frequent. It is conceivable that the absence of bacterial endocarditis under the age of two is explained by the absence of teeth. Parents may have less control over children from age 15 years on and some of the children will stop going to dentists. These developments may explain the increased frequency in young adults.

Table 7. Aortic Regurgitation by Prolapse of the Aortic Valve According to Age of Discovery (38 cases)

<table>
<thead>
<tr>
<th>Age Bracket (in years)</th>
<th>Observed VSDs</th>
<th>N</th>
<th>Aortic Regurgitation N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2</td>
<td>192</td>
<td>0</td>
<td>(0 )</td>
</tr>
<tr>
<td>2-4</td>
<td>188</td>
<td>2</td>
<td>(1.1)</td>
</tr>
<tr>
<td>5-9</td>
<td>322</td>
<td>17</td>
<td>(5.1)</td>
</tr>
<tr>
<td>10-14</td>
<td>261</td>
<td>9</td>
<td>(3.5)</td>
</tr>
<tr>
<td>15-19</td>
<td>135</td>
<td>4</td>
<td>(3.0)</td>
</tr>
<tr>
<td>≥20</td>
<td>137</td>
<td>6</td>
<td>(4.4)</td>
</tr>
</tbody>
</table>

Table 8. Bacterial Endocarditis according to Age of Occurrence (29 cases)

<table>
<thead>
<tr>
<th>Age Bracket (in years)</th>
<th>N of VSDs</th>
<th>N</th>
<th>Bacterial Endocarditis rate for 1000 patient-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>790</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>762</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>2-4</td>
<td>738</td>
<td>3</td>
<td>1.4</td>
</tr>
<tr>
<td>5-9</td>
<td>654</td>
<td>2</td>
<td>0.7</td>
</tr>
<tr>
<td>10-14</td>
<td>516</td>
<td>4</td>
<td>1.9</td>
</tr>
<tr>
<td>15-19</td>
<td>342</td>
<td>6</td>
<td>4.5</td>
</tr>
<tr>
<td>20-29</td>
<td>204</td>
<td>13</td>
<td>8.3</td>
</tr>
<tr>
<td>30-39</td>
<td>63</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>≥40</td>
<td>24</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Table 9. Congestive Heart Failure According to Age (84 cases)

<table>
<thead>
<tr>
<th>Age Bracket (in years)</th>
<th>N of VSDs</th>
<th>N</th>
<th>Congestive Heart Failure rate for 1000 patient-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>790</td>
<td>34</td>
<td>43</td>
</tr>
<tr>
<td>1</td>
<td>731</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>2-4</td>
<td>707</td>
<td>9</td>
<td>4.5</td>
</tr>
<tr>
<td>5-9</td>
<td>662</td>
<td>10</td>
<td>3.4</td>
</tr>
<tr>
<td>10-14</td>
<td>306</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>15-19</td>
<td>341</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>20-29</td>
<td>209</td>
<td>8</td>
<td>5.7</td>
</tr>
<tr>
<td>30-39</td>
<td>72</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>≥40</td>
<td>26</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
The occurrence of bacterial endocarditis seems more frequent in the VSDs of groups I and IV (table 10), possibly because these were not surgically treated and thus the patients had been exposed to the risk for a longer period of time. Johnson argues that patients with small VSDs are at higher risk than others. We found that patients with VSDs complicated by aortic regurgitation are more at risk than the others (three out of 50 cases).

The prognosis of bacterial endocarditis is appraised in various ways. In this study, with a mean follow-up of 7.5 years, the prognosis appears poor. Death ensued in four cases (three of which were VSDs with aortic regurgitation and one was in hemodynamic group III), and the condition worsened in 50% of all cases. The unfavorable course may be influenced by the treatment some of these patients received. Many of our cases (18) occurred more than ten years ago, before advanced antibiotic regimens had been developed. The prognosis is probably better now, at least for those cases that do not develop subsequent to surgery.

Five cases of bacterial endocarditis were observed in patients who had had operations. One child was operated on for repair of VSD and correction of aortic regurgitation which needed insertion of a Starr prosthesis. Three of the others were of group IIA and one of group IV. The bacterial endocarditis occurred five months, 15 months, 18 months, and three years after operation. One of these children had a postoperative catheterization with normal findings; two other children had no murmur at all and were considered as having a normal heart. The last had a 2/6 systolic murmur. One of these five children died following the endocarditis. We have no recorded cases of bacterial endocarditis following spontaneous closure.

**Congestive Heart Failure**

Three distinct categories of patients may be distinguished according to age.

Under the age of one, congestive heart failure is frequent and complicates nearly all the patients with large shunts (group IIb). It is seldom observed in those of group IIA and almost always spares those of groups I, III and IV (table 10). The incidence varies greatly at this age from one study to another, according to the population of different types of VSD included therein. The calculated rate in our work (43 for 1000 patient-years) is certainly underestimated, considering our recruitment. In children who survive, congestive heart failure has a tendency to disappear about the age of two and does not compromise any subsequent prognosis.

Between one to 39 years of age we observed 45 cases of congestive heart failure, or a calculated rate of 4.1 for 1000 patient-years. In this age bracket, heart failure is generally observed in VSDs which had been complicated by bacterial endocarditis, aortic regurgitation (10 cases) or rheumatic fever (one case). The prognosis is poorer in patients who develop heart failure. Twelve percent of the patients died.

### Table 10. Percentage of Different Complications according to VSD Group

<table>
<thead>
<tr>
<th>VSD group</th>
<th>N</th>
<th>Aortic Regurgitation</th>
<th>Bacterial Endocarditis</th>
<th>Congestive Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>302</td>
<td>6</td>
<td>4</td>
<td>1*</td>
</tr>
<tr>
<td>II a</td>
<td>220</td>
<td>8</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>II b</td>
<td>137</td>
<td>3</td>
<td>2</td>
<td>31</td>
</tr>
<tr>
<td>III</td>
<td>30</td>
<td>0</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>IV</td>
<td>101</td>
<td>10</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

*This patient had VSD with aortic regurgitation.

### Table 11. Spontaneous Deaths According to the VSD Hemodynamic Class, Age at Death and VSD Complications

<table>
<thead>
<tr>
<th>VSD class</th>
<th>VSD N</th>
<th>Deaths N</th>
<th>Age at Death</th>
<th>VSD Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;1 year (in months)</td>
<td>1 to 30 (in years)</td>
</tr>
<tr>
<td>I</td>
<td>302</td>
<td>3</td>
<td>33*</td>
<td>35</td>
</tr>
<tr>
<td>II a</td>
<td>220</td>
<td>4</td>
<td>3</td>
<td>9</td>
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<tr>
<td>II b</td>
<td>137</td>
<td>9</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>30</td>
<td>6</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>IV</td>
<td>101</td>
<td>3</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>790</td>
<td>25</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

*This patient presented with supraventricular paroxysmal tachycardia.
Beyond the age of 40, we observed five patients with heart failure out of 26 patients. Many of these patients came to be examined — and thus entered the study — only because they had manifestations of cardiac failure. Four of these five patients were over 40 when they came for their first consultation.

Mortality

Mortality rate is difficult to assess within the terms of this study for two reasons. 1) The majority of patients entered the study only after the age of one. Most of those children who died in their first year are excluded. 2) Two hundred and twenty-two of our patients had been operated on. A certain number of these (in particular VSD IIb) would perhaps have died had they not had any surgery.

Twenty-five deaths (3%) were registered: three occurred before the age of one and seven after the age of 40. Six of these seven patients were followed for a short period and were only hospitalized in view of their serious condition. Among the 15 deaths that occurred between the ages of one and 39, five were not attributable to VSD (three were accidental, one secondary to encephalitis, and one to a renal disease).

Of the ten deaths possibly related to cardiopathy, seven involved VSDs with bacterial endocarditis and/or aortic regurgitation, one VSD I with paroxysmal arrhythmias (deceased at 33), and two VSD IIb (deceased at 17 and 25 years of age).

All investigators emphasize the low mortality of patients with VSDs once their first birthday has been reached. Campbell (with a population with large VSDs) found 21 per 1000; Kachaner: 7.6; Keith: 6.9; and Mitchell: 10.5. We find a slightly higher figure — 19 for 1000 — for the one-to-40 age group.

Spontaneous Closure

The spontaneous closure is one of the most exciting aspects of the natural history of ventricular septal defect. All data in the literature point to its frequency, which had been underestimated for a long time. However, this frequency varies greatly from one study to another, depending on the population-age studied, criteria for inclusion in the patient population, follow-up period, and the percentage of different types of VSD. The following figures have been reported: Bonham-Carter: 63% (out of 144 VSDs); Hoffman: 33%; Keith: 21%; Mitchell: 35% (under 6 months); Yokoyama: 90% (in an assessment resulting from the comparison of the VSD rate found in 22,444 outpatients and 56,582 autopsy records.

While this study includes only a few patients in their first year of life and therefore does not take into account the closures which occurred at this age, this restriction only gives greater weight to the figures we found. Of the VSD group followed and not operated upon (385 cases of category D), we observed 14% complete closures and 7% partial closures. This means an overall figure of 21% partial or total occlusion. It is very likely that the real rate of closure is far higher than this.

Out of 4000 adult autopsies performed at C.H.U. Pitié-Salpêtrière (Prof. Guy Chomette), only two isolated VSDs were found: one was a muscular, very tiny VSD (2 mm) in a woman of 83, who died following a cholecystectomy; the other was in a woman of 23 affected by VSD in hemodynamic group III (followed by one of us), who died 24 hours after she had given birth. This assessment is close to Yokoyama's findings, in which only one VSD over 40 years of age was observed in 4700 deaths.

Pulmonary Pressures and Resistances

In our experience, VSDs in groups I, IIa or IV do not worsen because of increasing pulmonary pressure and resistances, a finding corroborated in the literature (Keith, 1971).

In VSD III, pulmonary resistances can increase to the point of reversing their shunt, thus becoming Eisenmenger syndromes. We observed this in four patients with VSD III. This finding does not contribute to clinical decisions about these patients as this type of VSD contraindicates any surgery.

The VSD patients in hemodynamic group IIb do not follow a clear pattern. Out of the 82 cases in this group, we observed only three whose clinical features suggest that pulmonary resistances increased. One of those developed into an inversion of the shunt. In the studied population, therefore, this unfortunate possibility is rare: below 4% for the VSDs IIb as a whole and 10% of the 32 cases followed up for more than five years. Campbell found such an evolution more frequently — 19 out of 43 cases — followed for an average of six years. Keith found that 22% of the infants with characteristics that correspond approximately to our group IIb developed Eisenmenger's syndrome.

The relative scarcity in our study of an evolution toward increased pulmonary resistance can be explained by the fact that most of the VSD IIb cases were operated at a fairly young age. The statistics would have been quite different if these cases had been allowed to evolve over a longer period.

Stenosis of the Pulmonary Tract

Infundibular, orifical or mixed, stenosis of the pulmonary tract was found associated with VSD in 13% of our cases at the first examination. Increasing the pressures in the right ventricle, it diminishes the shunt through the VSD and so tends to "protect the lungs." Of the 499 cases followed, 7% moved into hemodynamic group IV: 23 of the 133 VSDs in hemodynamic group IIa and six from the hemodynamic group IIb. Moreover, the ratio of VSDs in group IV increases with age: it is 21% in the group over 30 years of age whereas it is rare in childhood. Kachaner finds only 6% of group IV VSDs in 341 infants. However, Rudolph only rarely encountered infants with no measurable pressure difference who then went on to develop significant muscle hypertrophy of the outflow region.

Once present, infundibular stenosis may increase. Repeated catheterizations in several of our patients show that the degree of infundibular stenosis may increase with age. In five cases (1% of all followed cases), the development of infundibular stenosis was sufficient to reverse the shunt through the VSD, producing cyanosis and a clinical picture close to, if not identical with tetralogy of Fallot. Two of these cases were in VSD group IIb (2.5% of the 82 cases of this group) and three were VSD group IV (6% of the 42 cases of the group).
Conclusion

The characteristics of the studied population and those of the survey allow the appraisal of the spontaneous evolution of VSDs between the ages of one and 40. The prognosis, on the whole, is excellent. In ten patients with VSD, it is possible to project that seven will remain stable, two will have a tendency to close their VSD, and one will develop infundibular stenosis. The evolution toward a pulmonary vascular disease is observed only in some cases of VSD with large left-to-right shunts and pulmonary hypertension (VSD group IIb).

Death is rarely caused by isolated VSD. Mortality is usually linked to associated complications such as aortic regurgitation and/or bacterial endocarditis. The possibility that these complications may develop justifies a close observation of patients affected by VSD and constant care to avoid or cure any infection.

Only patients with VSDs associated high pulmonary hypertension and large left-to-right shunts and those complicated by recent aortic regurgitation require surgery. In our opinion, the great majority of patients with VSDs who live beyond one year of age will not need operations.

It is quite clear that the decreased number of VSDs in adults is not the consequence of persons with this defect having died in childhood. It is highly probable that spontaneous closure occurs in many persons born with this defect.

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