Ventricular Septal Defect
with Aortic Regurgitation

Medical and Pathologic Aspects

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The original description of the association of ventricular septal defect with aortic regurgitation is commonly attributed to Breccia. He described a patient without clinical evidence of heart disease but who had, as incidental autopsy findings, a small membranous ventricular septal defect obstructed by proliferative fibrous tissue, and a fibrotic, partially calcified right aortic cusp with a slit-perforation close to its insertion on the aortic wall. None of the aortic cusps had prolapsed. Since this aortic lesion was probably the sequel to an inflammatory process and was, furthermore, clinically silent, Breccia's case does not belong to the syndrome of ventricular septal defect with aortic regurgitation as it is discussed in this paper. Documentation of this syndrome dates back to Laubry and Pezzi's publication in 1921. Since then, close to 100 cases have been reported in the literature.

A review of our experience with this syndrome seemed worth while for several reasons. First, this report represents the largest single group of cases, permitting a uniform description. Second, most of our patients were children, giving us an opportunity to describe the clinical and pathologic picture in this age group and to contrast it with the reports in the literature, which pertain mostly to adults. Third, by careful follow-up of our patients, we were able to trace the natural history of this congenital deformity.

Material and Methods

All patients with the diagnosis of ventricular septal defect and aortic regurgitation found in the files of the medical service of the Children's Hospital Medical Center between the years 1948 and 1962 have been reviewed. In 31 of 34 patients, the clinical diagnosis of ventricular septal defect with aortic regurgitation was confirmed by cardiac catheterization with adequate cineangiographic proof, by operation, and by autopsy. The three remaining patients were catheterized prior to the development of aortic regurgitation and were found to have a ventricular septal defect only. The subsequent appearance of a typical murmur of aortic regurgitation and wide pulse pressure at a typical age without a history of rheumatic fever makes the diagnosis of ventricular septal defect with aortic regurgitation highly probable.

Physical examination by members of the cardiology service, radiograms, cardiac fluoroscopy, 12-lead electrocardiograms, and routine right heart catheterization studies are available on all patients. Left heart catheterization has been performed in 24 patients, in all but two via the retrograde arterial approach. Cineangiograms demonstrating aortic regurgitation are available in all of these patients. In seven others, the diagnosis of aortic regurgitation was confirmed by surgery or autopsy. Repeat and third catheterizations, 2 to 12 years after the first study, were performed on 13 patients. Seven hearts have been examined at autopsy.

Results

History (Table 1)

Thirty-four patients, ranging from 2 months to 18 years at the time of their first examination, 3 to 29 years at present, fulfilled the criteria of ventricular septal defect with aortic regurgitation. This represents slightly less than 5 per cent of the 756 cases of ventricular septal defect studied in our institution between 1948 and 1962. Twenty-four patients were male and 10 female. The discovery of a murmur, usually at less than 1 year of age, led to the diagnosis of heart disease in all patients. Less than one third of

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the patients had symptoms such as tachypnea, excessive perspiration, or slow weight gain, attributed to their heart disease, during infancy. Subsequently, the patients remained asymptomatic until moderate to marked aortic regurgitation had developed.

**Physical Examination (Table 2)**

Approximately one third of the patients were at or below the third percentile on the H. C. Stuart growth chart for height and weight and two thirds of them fell below the fiftieth percentile.

A systolic murmur, usually grade IV (scale of VI) or louder was heard at the left sternal border in all instances. Although it was maximal at the lower left sternal border, where it had the quality of a murmur of ventricular septal defect, in many instances it was transmitted very well to the pulmonary area, where it assumed a stenotic character.

A protodiastolic murmur of aortic regurgitation was present, by definition, in every case, although in many instances, as is discussed later, this was not heard until some years after the discovery of the systolic murmur. In contrast to the loud systolic murmur, the aortic blow was usually of grade-III intensity, or less, and seldom lasted throughout diastole. A continuous murmur with maximal intensity just before the second heart sound as heard in patients with a patent ductus arteriosus was never observed. Rather, the systolic murmur was loudest in mid-systole, decreased toward the second sound, and was then followed with increased intensity by the protodiastolic murmur (fig. 1). Thus, there appeared to be a hiatus between systolic and protodiastolic murmur, resulting in a to-and-fro character.

A mid-diastolic rumble, resembling an Austin Flint murmur, probably caused by increased mitral valve flow, was heard in 22 patients.

The heart sounds were difficult to judge be-

<p>| Table 1 |</p>
<table>
<thead>
<tr>
<th>Ages of Patients at Time of Catheterization and Discovery of Murmur</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
</tr>
<tr>
<td>1 cath.</td>
</tr>
<tr>
<td>2 cath.</td>
</tr>
<tr>
<td>3 cath.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Murmur first noted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 month</td>
<td>12</td>
</tr>
<tr>
<td>Less than 1 year</td>
<td>26</td>
</tr>
<tr>
<td>Less than 5 years</td>
<td>32</td>
</tr>
<tr>
<td>Less than 10 years</td>
<td>34</td>
</tr>
</tbody>
</table>

<p>| Table 2 |</p>
<table>
<thead>
<tr>
<th>Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Murmurs</th>
<th>Total no. of patients</th>
<th>Murmur</th>
<th>Grade III or less</th>
<th>Grade IV or less</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>Systolic</td>
<td>4</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>Protodiastolic</td>
<td>24</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Apical mid-diastolic rumble</td>
<td>22</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Pulse pressures by cuff in mm. Hg at the time of first catheterization

<table>
<thead>
<tr>
<th>Less than 50</th>
<th>50-75</th>
<th>76-100</th>
<th>More than 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>6</td>
<td>17</td>
<td>6</td>
</tr>
</tbody>
</table>

*Circulation, Volume XXIX, June 1964*
cause of the loud murmurs accompanying most of the cardiac cycle. Occasionally, a constant ejection click was heard at the apex. A systolic thrill was present at the mid and lower left sternal border in practically all instances. The cardiac impulse was hyperkinetic and involved principally, but not exclusively, the left ventricle. Left chest prominence was noted frequently, particularly in the older children with marked aortic regurgitation.

At the time of catheterization, when the auscultatory evidence of aortic regurgitation was usually clear-cut, a wide pulse pressure was a common finding; only six patients had a pulse pressure of less than 50. Associated with this significant aortic run-off were bounding carotid pulses with a low dicrotic notch, and a pistol-shot sound was heard over the femoral artery.

**Laboratory Data**

Radiologic examination at the time of the first catheterization (table 3) revealed cardiac enlargement in all but two patients. While the left ventricle was almost uniformly dilated, additional right ventricular enlargement was present in only 13 instances. The pulmonary vessels were within normal limits or only mildly engorged in over two thirds of the patients. In only one instance was there marked vascular engorgement. At cardiac fluoroscopy the aorta was usually hyperactive and prominent, much more so than the pulmonary artery. This and the absence of marked pulmonary vascular engorgement was helpful in differentiating ventricular septal defect with aortic regurgitation from patent ductus arteriosus.

The chest leads of the electrocardiogram at

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*Figure 1*

Phonocardiogram of a patient with ventricular septal defect with aortic regurgitation, demonstrating an injection type of murmur in the second left intercostal space (2LIS); a decrescendo-crescendo sequence of systolic and diastolic murmurs before and after the aortic closure; a rough murmur of ventricular septal defect at the lower left sternal border (4LIS); a good left ventricular rapid filling phase in the apex cardiogram.
the time of catheterization, revealed left ventricular preponderance (table 4). In four cases this was described as normal left ventricular dominance with adult R/S progression. In 27 cases, according to the voltage criteria used in our department, left ventricular hypertrophy was present. Left ventricular hypertrophy with ST and T-wave changes was observed once at the time of catheterization; in three other patients, it developed subsequently. Biventricu-

### Table 3
Radiologic Findings at the Time of the First Catheterization

<table>
<thead>
<tr>
<th>Heart size</th>
<th>Normal</th>
<th>Mild</th>
<th>Cardiomegaly Moderate</th>
<th>Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2</td>
<td>8</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Left ventricular enlargement</td>
<td>32 patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right ventricular enlargement</td>
<td>13 patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial enlargement</td>
<td>4 patients</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary vascular engorgement</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>10</td>
<td>13</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Prominent aorta</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4
Electrocardiographic Findings at the Time of First Catheterization

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Normal</th>
<th>Left ventricular hypertrophy</th>
<th>Left ventricular hypertrophy with strain</th>
<th>Left ventricular hypertrophy and right ventricular hypertrophy</th>
<th>Incomplete right bundle-branch block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean QRS axis</td>
<td>+120 to +91°</td>
<td>+90 to +61°</td>
<td>+60 to +31°</td>
<td>+30 to 0°</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>2</td>
<td>9</td>
<td>17</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5
Catheterization Findings at the Time of First Catheterization

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Pulmonary to systemic flow ratio Less than 2:1</th>
<th>Pulmonary to systemic flow ratio 3:1</th>
<th>Pulmonary to systemic flow ratio 4:1 and more</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean pulmonary artery pressure to mean systemic pressure ratio Less than 0.5</td>
<td>Mean pulmonary artery pressure to mean systemic pressure ratio 0.5 to 0.75</td>
<td>Mean pulmonary artery pressure to mean systemic pressure ratio More than 0.75</td>
</tr>
<tr>
<td>No. of patients</td>
<td>21</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Mean pulmonary capillary pressure (including two patients with left atrial pressure measurements) Less than 10 mm.</td>
<td>Mean pulmonary capillary pressure (including two patients with left atrial pressure measurements) 10-15 mm.</td>
<td>Mean pulmonary capillary pressure (including two patients with left atrial pressure measurements) More than 15 mm.</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>33</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pressure gradient across right ventricular outflow tract in mm. Hg in 11 male and 5 female patients</td>
<td>More than 60</td>
<td>15-20</td>
<td>21-40</td>
</tr>
<tr>
<td>No. of patients</td>
<td>1</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary vascular resistance (units/M.2) Less than 1</td>
<td>Pulmonary vascular resistance (units/M.2) 1-3</td>
<td>Pulmonary vascular resistance (units/M.2) More than 3-5</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>19</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Systemic vascular resistance (units/M.2) Less than 10</td>
<td>Systemic vascular resistance (units/M.2) 10-15</td>
<td>Systemic vascular resistance (units/M.2) More than 10-15</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>3</td>
<td>14</td>
<td>12</td>
</tr>
</tbody>
</table>

* Circulation, Volume XXIX, June 1964
lar hypertrophy was noted twice. The frontal plane mean QRS axis was, in the majority, between +30 and +90°. In an occasional patient, incomplete right bundle-branch block or first-degree atrioventricular block was observed.

A summary of the catheterization findings is presented in Table 5. It may be seen (1) that in almost two thirds of the cases the pulmonary blood flow was less than twice the systemic blood flow, (2) that the pulmonary artery pressure was only once at systemic levels, (3) that the pulmonary wedge pressure was seldom markedly elevated, and (4) that a pressure gradient across the right ventricular outflow tract was present in almost 50 per cent of the patients. The first three points indicate that the left-to-right shunt across the ventricular septal defect was usually not large; we shall discuss later that the size of the defect cannot be judged in this malformation on the basis of shunt size and pressures. The pressure gradient across the right ventricular outflow tract when present, was moderate in most instances. This stenosis was infundibular in 10 patients, infundibular and valvular in 1 patient, and undetermined in 5 patients. The pulmonary vascular resistance was significantly elevated in only one instance. The cineangiograms, demonstrating aortic regurgitation, were a critical part of the diagnosis in that they presented objective evidence of reflux of contrast material from the aortic root into the left ventricle (Fig. 2).

Clinical Course

The natural history of patients with ventricular septal defect with aortic regurgitation deserves special comment. As indicated earlier, a systolic murmur was noted in 26 of the 34 patients under 1 year of age (Table 1). By contrast, in no case was there evidence of aortic regurgitation, either in terms of a wide pulse pressure (more than 50 mm. Hg) or an aortic protodiastolic blow, present under 1 year of age. Table 6 presents the time of appearance of these two manifestations of aortic regurgitation in 18 patients in whom accurate fol-

Figure 2
Cineangiogram shortly after supraavalvular aortic injection of contrast material (Renovist), demonstrating marked regurgitation from the aortic root into the left ventricle. Right anterior oblique view.

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Protodiastolic murmur first noted</th>
<th>Appearance of wide pulse pressure (more than 50 mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st yr.</td>
<td>2nd yr.</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 6
Onset of Aortic Regurgitation as Determined by Appearance of a Protodiastolic Blow or Wide Pulse Pressure in 18 Patients

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low-up examinations are available. The most common time of appearance of aortic regurgitation was between 3 and 8 years of age. Although we have not so far noted the appearance of aortic regurgitation in any patient under 1 year of age or over 10 years of age, three patients developed aortic regurgitation at 2 years, and only two between 8 and 10 years. The anatomic findings as well as the absence of any evidence of rheumatic fever excluded the possibility of rheumatic origin of aortic regurgitation. The progressive nature of the disease was evident, not only by auscultation and by estimation of pulse pressure, but

Figure 3

*Increase in heart size over a 7-year period concomitant with clinical evidence for increasing aortic regurgitation.*

Figure 4

*Development of left ventricular strain in the electrocardiogram concomitant with clinical evidence for increasing severe aortic regurgitation. Chest leads are recorded in one-half standardization unless noted otherwise. Strain pattern was observed first at 13 years of age. Bottom tracing was recorded just prior to surgical intervention.*
Table 7
Radiologic Features: Follow-up Study on 31 Patients over a 2- to 18-Year Period

<table>
<thead>
<tr>
<th>Cardiac enlargement</th>
<th>Pulmonary vascularity</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased 16 patients</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>No change 12 patients</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Decreased 3 patients</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

also on radiologic survey (fig. 3, table 7). Repeat radiograms over 2 to 18 years are available in all but three patients. Abnormal increase in heart size was found in 50 per cent of our follow-up studies and was usually unaccompanied by an increase in pulmonary vascular engorgement. The time of increase in heart size corresponded well with the appearance of aortic regurgitation. While in most patients heart size increased slowly over a 5- to 10-year period after the appearance of aortic regurgitation, in roughly 20 per cent of the patients marked cardiomegaly occurred rapidly over 1 to 3 years. The electrocardiogram showed progression in terms of development of left ventricular strain (fig. 4) in three patients, occurring in one patient between 5 and 7 years of age, in two others between 12 and 13 years.

A history of subacute bacterial endocarditis was present in three of our 34 patients. They were all treated successfully. The organisms identified were Staphylococcus aureus and Beta hemolytic streptococcus. In the third case, no organism was isolated. In none of the cases did subacute bacterial endocarditis produce or alter the clinical evidence of aortic regurgitation.

Repeat cardiac catheterizations, 2 to 10 years after the initial study, are available in 13 patients (table 8). Although these findings indicated essentially unchanged hemodynamics, significant widening of the pulse pressure was observed in approximately 50 per cent of the catheterizations and correlated well with increase in heart size. Finally, among the group of patients with infundibular pulmonic stenosis, the pressure gradient across the pulmonic valve increased significantly in half of the cases. An increase in pressure gradient was, when observed, always associated with increase in pulse pressure. In three of four such observations, no change in the ratio of pulmonic to systemic blood flow occurred, while in one patient the ratio increased.

At this time, 16 patients have been managed conservatively; four of them have died, three in congestive failure and one with sudden severe chest pain and dyspnea. Surgical repair has been undertaken in 16 of our patients (fig. 5). (Two additional patients have been operated upon in other institutions.) The results of surgery will be published separately.

Autopsy Material
In seven cases, it has been possible to ex-

Table 8
Results of 13 Repeat Catheterizations (Excluding Two Patients Restudied Following Surgical Repair)

<table>
<thead>
<tr>
<th>Pulmonary to systemic flow ratio</th>
<th>Increase of more than 50 per cent</th>
<th>Decrease of more than 50 per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Pressure gradient across right ventricular outflow tract</td>
<td>Increase of more than 10 mm.</td>
<td>Decrease of more than 10 mm.</td>
</tr>
<tr>
<td>No change</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Pulmonary capillary pressure</td>
<td>Increase of more than 5 mm.</td>
<td>Decrease of more than 5 mm.</td>
</tr>
<tr>
<td>No change</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

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amine the hearts pathologically, in detail, and
divide them into two groups, determined by
the anatomic location of the septal defect. In
group I (four hearts) the defect involved pri-
marily the membranous septum, but also en-
compased a relatively small portion of the
bulbar musculature as well; in group II (three
hearts) the defect involved the anterior half of
the membranous septum and a good portion of
the anterior, bulbar muscular septum. In this
latter group, the posterior portion of the mem-
branous septum exclusive of the atrial segment
was represented by a fibrous band of variable
width, oriented vertically.

In the hearts in group I (fig. 6), the ven-
tricular septal defect was bounded posteriorly
by the middle (lower pole) of the noncoron-
ary (posterior) aortic cusp; superiorly, by a
point just below the commissure between the
right and noncoronary cusps; anteriorly, by
the middle of the right coronary cusp; and,
inferiorly, by the ridge of the main ventricular
muscular septum. As mentioned before, the
major part of the anterior, muscular septum
was intact in all four hearts. In three of them,
the aortic and pulmonary valves were tri-
cuspid. The prolapse-deformity of the regurgi-
tation involved primarily the right coronary
cusp, and included part of the noncoronary
cusp to a lesser degree. Both great vessels in
the fourth heart were equipped with what
might best be called pseudo-bicuspid valves; a
small, but definite commissural nodule was
present between the two posterior pulmonary
valve cusps, and a more definite fold between
the prolapsing right and noncoronary aortic
cusps. In all four hearts the aortic valve cusps
were minimally to moderately thickened and
rolled, in a somewhat inverse ratio to the de-
gree of ballooning seen in a particular cusp.

In the hearts in group II (fig. 7), the ven-
tricular septal defect was bounded, in distinc-
tion from group I, posteriorly by a point just
below the commissure between the right and
noncoronary cusps (and anterior to the fibrous
remnant of the posterior membranous septum,
mentioned earlier); superiorly, by the lower
pole of the right coronary cusp; anteriorly, by
a point in the bulbar septum near the posterior
pulmonary valve cusp, in two cases immedi-
ately adjoining it, and, in one, approaching it
within 4 mm.; inferiorly, by the ridge on the
main ventricular muscular septum, and, in
right ventricular view, at the superior pole of
the septal band of the crista supraventricularis.
Although occupying a very similar position, in
respect to the crista, the typically deformed
muscular architecture of the tetralogy of
Fallot was not seen.

Figure 5
Progression in heart size in a patient with ventricular septal defect with aortic regurgitation.
Note increase in size prior to surgery, decrease after surgery.
Groups I and II showed certain other features that are of interest and that, by and large, are similar. The degree of overriding of the aorta, while not always easy to estimate, seemed to be about 30 per cent. On the whole, this represents a very modest degree of positional transposition, an effect that may, in part, be due to the continued presence of ventricular membranous and bulbar septal elements that served as a relative anchor for the aortic annulus.

Similarly, the degree of rotation of the aortic annulus (displacement of the cusps in a counterclockwise direction, looking from aorta toward ventricle) was in keeping, not only with the degree of overriding, but also with the extent of the anterior and leftward displacement of the crista supraventricularis; it was estimated to be between 30 and 40°. The coronary arteries were normal in origin and distribution in all seven hearts.

Marked hypertrophy of the crista supraventricularis was not seen in either group I or II. Moderate hypertrophy, especially of the parietal portion of the crista, was seen once in each group; at catheterization these two patients had 23- and 18-mm. Hg pressure gradients between right ventricular body and outflow tract. On the other hand, two patients, one of each group, had pressure gradients of 42- and 50-mm. Hg, respectively, at the infundibular level and yet had little cristal hy-
VENTRICULAR SEPTAL DEFECT

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Hypertrophy at autopsy. In the group-II heart, the obstruction could have been caused by the enormously ballooned right coronary cusp, prolapsing into the right ventricular outflow tract. Such an explanation, however, does not seem probable for the group-I heart. Absence of valvular stenosis in the latter heart was proved both by satisfactory catheterization and at autopsy.

Discussion

The entity described above represents one of the pathways that a ventricular septal defect may follow over the years. Perhaps the most interesting point of this presentation is that ventricular septal defect with aortic regurgitation is not a congenital defect inasmuch as aortic regurgitation is not present at birth or during the first year of life. During this early period the clinical and physiologic picture is that of a ventricular septal defect of small-to-moderate size.

Aortic regurgitation develops at some time between the second to tenth year of life. If this occurs on the basis of a poorly supported aortic valve, the actual site of the ventricular septal defect may be important. The septal defects associated with aortic regurgitation are either primarily in the membranous septum with little muscular involvement, or include the membranous septum and extend high into the right ventricular outflow tract, even to a point at the base of the posterior pulmonary valve cusp. The aortic leaflet most commonly prolapsing into the ventricular septal defect, thus causing aortic regurgitation as well as partial obstruction of the right ventricular outflow tract, is thus the right coronary cusp. The noncoronary cusp is almost always involved to a lesser degree, while the left coronary cusp is rarely deformed to any appreciable extent.

In only two previously reported series have specific attempts been made to define the anatomic location of the ventricular septal defect. In the two hearts, examined by Keck et al. at autopsy, the findings were in accord with our cases in group I. The ventricular septal defects were low, involving primarily the membranous septum. In half of Keck's cases, which were studied only at the time of surgical repair, anatomic evidence for pulmonary infundibular stenosis (Keck's group B) was noted: slight in two, moderate in six, severe in one patient. As noted before, only mild infundibular stenosis was found in two of our seven hearts, although two other patients had moderately severe pressure gradients across a nonhypertrophiied right ventricular outflow tract. This difference in observation may be due, at least in part, to the fact that eight of the nine "group-B" hearts of Keck's were examined only at the operating table.

The ventricular septal defect in at least two hearts of Keck's "group-A" patients (no infundibular stenosis), and in one of "group B" (with infundibular stenosis), was located in that area of the septum that we have described as characteristic of group II. This location would militate against Keck's description of such ventricular septal defects as purely membranous.

Ellis et al., reporting on the surgical aspects of the same series as Keck et al., observed that four patients had ventricular septal defects located directly under the pulmonary valve. This is in agreement with the patients in our group II, and with Bialostozky et al.

These observations indicate that the presence or absence of infundibular stenosis is not related to the location (group I or II) of the ventricular septal defect. Likewise, it was not possible to define at autopsy with certainty the anatomic substrate of obstruction in some patients who had pressure gradients across the right ventricular outflow tract at catheterization.

At present, there is no clear-cut answer to the question of why such an anatomic lesion as ballooning and prolapse of aortic and pulmonary valve cusps should occur in some hearts with ventricular septal defects, and not occur in others in which the fundamental anatomic and embryologic lesion appears to be the same. More sophisticated attempts to clarify the morphologic anatomy and embryology of septal defects, in membranous and bulbar areas, and of the musculature of the

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anterior bulbar septum may be helpful in this regard. Studies are in progress here at the present time that attempt to evaluate the histologic appearance and characteristics of the aortic valve annulus, cusps, and muscular adjuncts in a variety of hearts with ventricular septal defect and other associated anomalies.

From the point of view of experimental embryology, in a personal communication, Dr. M. V. de la Cruz (Instituto Nacional de Cardiología de Mexico) indicates that newborn chicks in whom a ventricular septal defect had been created experimentally may develop prolapse of the right coronary cusp if the defect is in a high anterior location, corresponding to the site of some of the ventricular septal defects in human subjects with the described entity.

The clinical features of developing aortic regurgitation are characterized on the one hand by the appearance of a protodiastolic murmur, wide pulse pressure, hyperkinetic left ventricular impulse, and increasing heart size. On the other hand, a prolapsing aortic cusp may, by partially obstructing the ventricular septal defect, diminish pulmonary blood flow and may cause, either by itself or with a hypoprophied crista supraventricularis, a pressure gradient across the right ventricular outflow tract.

The optimal time to attempt surgical correction in patients with ventricular septal defect with aortic regurgitation is, currently, most difficult to determine. Clearly, patients with gross cardiomegaly and electrocardiographic evidence of left ventricular strain, represent almost inoperable situations. The overstretched and fibrosed myocardium and the grossly distorted and thickened aortic valves render surgical repair an extreme risk. On the other hand, it is hard to justify submitting children who are asymptomatic and who have only mild aortic regurgitation to major cardiac surgery. Our attitude at the present time is to watch closely the progress of the patients with ventricular septal defect. If aortic regurgitation appears, at least half-yearly follow-up examinations with chest x-rays and electrocardiograms are indicated. If no progression of the lesion is noted by any of the discussed factors, the patient is managed conservatively. The patients are warned specifically to observe prophylactic measures against bacterial endocarditis and to avoid competitive exercise. If the pulse pressure widens or the heart increases in size or the electrocardiogram shows progressive evidence of left ventricular hypertrophy, corrective surgery is suggested to the patient. A surgical approach should encompass correction of both defects, since closure of the ventricular septal defect alone usually does not decrease the extent of the regurgitation.

Information reported in the literature pertains predominantly to the age group of 15 to 30 years, the period during which many patients with ventricular septal defect and aortic regurgitation experience serious difficulties from progressive aortic regurgitation. Sex distribution, clinical and catheterization findings, and surgical and autopsy data are, in general, in good accord with our findings. With the exception of three reports, there is a notable absence of the observation that a relatively high percentage of these patients also have infundibular pulmonic stenosis. The actual development of aortic regurgitation was observed only by Starr, Menashe, and Dotter and by Spencer, Bahnson, and Neill, who reported a total of five such patients in whom aortic regurgitation developed between the ages of 4½ and 8 years, which corresponds very well with our own observations. The differential diagnosis of ventricular septal defect with aortic regurgitation has been discussed thoroughly by other authors.

**Summary**

Thirty-four patients with ventricular septal defect and aortic regurgitation, representing less than 5 per cent of our patients with ventricular septal defect, are discussed.

A loud, systolic murmur, characteristic of ventricular septal defect, is noted during infancy, whereas evidences of aortic regurgitation (protodiastolic murmur and wide pulse pressure) does not usually appear until sometime between 2 and 10 years of age.

Clinical and catheterization data indicate that the principal hemodynamic load is aortic...
regurgitation, whereas the ventricular septal defect does not usually result in a large pulmonary blood flow or high pulmonary arterial pressure. In about 50 per cent of the patients, a significant pressure gradient across the right ventricular outflow tract exists.

Detailed pathologic studies indicate that the ventricular septal defects are high and anterior and encroach to a greater or lesser degree on the membranous bulbar septum. The right coronary cusp is the one most severely involved, and, by its prolapse, causes aortic regurgitation; the noncoronary cusp is always less severely affected. The anatomic basis of the pressure gradient observed across the right ventricular outflow tract is not always clear.

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References

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