Auscultatory and Phonocardiographic Signs of Ventricular Septal Defect with Left-to-Right Shunt

By Aubrey Leatham, F.R.C.P., and Bernard Segal, M.D.

The signs of ventricular septal defect depend on the size of the defect and the pulmonary vascular resistance, these factors determining the direction and degree of the shunt and producing the well-known variations in the characteristics of the systolic murmur. Abnormally wide splitting of the second heart sound is a feature of ventricular septal defect with left-to-right shunt which seems to have escaped general recognition, probably because the loud pansystolic murmur drowns aortic closure.

We have investigated 23 subjects with isolated ventricular septal defect with left-to-right shunt and normal or slightly elevated pulmonary vascular resistance (aged 4 to 18 years, average 11 years), and have divided them into two groups: Group 1—minimal defects as described by Roger (less than 0.5 cm. diameter; Wood et al., 19541) these patients had a loud systolic murmur without evidence of ventricular hypertrophy, clinically or on the electrocardiogram, normal right-sided pressures and a normal x-ray appearance. Group 2—larger ventricular septal defects with moderate or large left-to-right shunts. The auscultatory and phonocardiographic differential diagnosis will be discussed and also the separation of these patients from the inoperable Eisenmenger group with high pulmonary vascular resistance and bidirectional shunts.

Method

Following clinical, electrocardiographic, and x-ray examination, each subject was investigated with phonocardiography by means of simultaneous recordings from different sites, before and after amyl nitrite inhalation, and a study was made of the effect of respiration on splitting of the second heart sound by a specially accurate time marker. The paper speed was 100 mm. per second, the photographic recorder responded well to frequencies up to 800 cycles, and measurements were made, during the expiratory and inspiratory phases of continued respiration, from the onset of electrical activation (QRS) to the onset of the first sound and to the onset of aortic (A2) and pulmonary (P2) components of the second sound.

Carotid pulse tracings were taken in each subject by a method designed to correspond closely to a central aortic pulse, using an air-filled cuff and a linear manometer and amplifying system.5,6 Measurements were made from mitral closure (M1) to carotid rise (corrected for delay in the system by subtracting the A2—dicrotic notch interval) and were assumed to give an approximation to the isometric contraction time of the left ventricle. Measurements from the carotid rise to the dicrotic notch gave the ejection time of the left ventricle and each measurement was compared with the ejection time at the same heart rate on a table compiled from 80 young normal subjects.7

Right heart catheterization was performed in all subjects with a Cambridge manometer and a Brinkman hemoreflector allowing rapid serial sampling. Where possible, measurements were made from the onset of electrical activation (QRS) to the rise of the right ventricular pressure (RV) and to the rise of pulmonary artery pressure (PA) at paper speeds of 100 mm. per second. Measurements from the onset of RV rise to PA rise gave the isometric time, and from PA rise to dicrotic notch the ejection time of the right ventricle, and these were compared with 10 normal subjects (table 1). The delay in the system was only 0.005 second and no correction was made. The cardiac output was estimated by the Fick principle and intracardiac shunts by the method of Bing. Indicator dilution curves were taken in most patients and intracardiac phonocardiograms in five patients. Cineangiography in the left anterior oblique view at 32 frames per second was performed in 12 patients using selective injection of 76 per cent Urografin (1 to $1\frac{1}{2}$ ml. per Kg. in 1 to 1.5 seconds) into the right ventricle through a special catheter (N.I.H.) with blocked end hole and four spirally placed side holes.

Results

Group I

Of 13 subjects thought to have small ventricular septal defects, a certain diagnosis as
shown by increased oxygen saturation in the right ventricle was achieved in only five patients; these will be discussed first. By definition, the electrocardiogram, x-ray appearance, and right heart pressures were normal, and the left-to-right shunt as shown by the pulmonary to systemic flow ratio varied from 1.2-1.9 to 1. Cineangiography confirmed the diagnosis by showing recirculation of contrast medium through the defect in four subjects and contrast medium appeared to shunt from right to left in three during a period of ectopic beats. The systolic murmur was loud (grade 4 to 5 of Levine's 6 grades), invariably pansystolic, and usually maximal at the left sternal edge in the fourth intercostal space, and tended to drown aortic closure on auscultation in this area (fig. 1). Splitting of the second sound, however, could usually be detected in the pulmonary area or above and lateral to it, and phonocardiogram showed that the width of the splitting in the expiratory phase of continued respiration was abnormally wide in four of the five subjects, varying from 0.030 to 0.040 second. On inspiration the width of splitting increased in the normal manner (fig. 2). Measurements of the time interval between the onset of the first sound and aortic and pulmonary closure showed that the inspiratory increase in splitting was due to shortening of left ventricular systole and lengthening of right, mainly the latter, as in normal subjects. Amyl nitrite invariably diminished the intensity of the systolic murmur.

In the remaining eight subjects the diagnosis of a small ventricular septal defect could not be proved by the technics available in our laboratory, but there could be little doubt in the six patients with a loud pansystolic murmur at the lower left sternal edge which diminished in intensity with amyl nitrite inhalation. Splitting of the second sound was abnormally wide in expiration in five of the eight subjects, varying from 0.030 to 0.066 second. On inspiration the width of splitting increased normally. In two of the eight patients the murmur, though loud and maximal at the lower left sternal edge, was confined to early systole (fig. 3); splitting of the second sound was abnormally wide, the murmur diminished with amyl nitrite, and a cineangiogram in the left oblique view appeared to show a right-to-left shunt during a period

Table 1
Measurements in Normal Subjects Compared with Ventricular Septal Defect with Abnormally Wide Splitting of the Second Heart Sound

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Ventricular septal defect with abnormally wide splitting of second sound (17 subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electromechanical interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right side Q—RV</td>
<td>0.05 mean in 10 subjects (0.04—0.06)</td>
<td>0.08 mean in 12 subjects (0.07—0.12)</td>
</tr>
<tr>
<td>Left side Q—M1</td>
<td>0.05 mean in 80 subjects (0.04—0.06)</td>
<td>0.05 mean (0.04—0.07)</td>
</tr>
<tr>
<td>Isometric contraction time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right side (RV—PA)</td>
<td>0.02 mean in 6 subjects (0.02—0.03)</td>
<td>0.02 mean in 14 subjects (0.02—0.04)</td>
</tr>
<tr>
<td>Left side (M1—car. rise)</td>
<td>0.03 mean in 80 subjects (0.03—0.04)</td>
<td>0.02 mean (0.01—0.04)</td>
</tr>
<tr>
<td>Ejection time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right side (PA rise—</td>
<td>Varied with heart rate from</td>
<td>Normal</td>
</tr>
<tr>
<td>dicrotic notch)</td>
<td>0.24 to 0.30 second—in 10 subjects</td>
<td></td>
</tr>
<tr>
<td>Left side (Car. rise—</td>
<td>Varied with heart rate from</td>
<td></td>
</tr>
<tr>
<td>dicrotic notch)</td>
<td>0.22 to 0.30 in 80 subjects</td>
<td></td>
</tr>
</tbody>
</table>

Catheter delay (0.005 second) not subtracted. Carotid delay subtracted (A2—dicrotic notch).
Group II

The 10 patients with moderate or large defects and shunts differed from patients in group I in that symptoms were present. They experienced dyspnea on moderate exertion and frequently gave a history of recurrent bronchitis and bouts of pneumonia. The electrocardiogram showed biventricular hypertrophy in eight and right bundle-branch block in two patients. X-ray showed a large heart, increased pulmonary flow, and dilatation of the pulmonary artery in all cases. The systolic pressure in the pulmonary artery varied from 30 to 50 mm. Hg, and the pulmonary flow measured from 1.3 to 3.5 times the systemic flow. The pulmonary vascular resistance varied from 2 to 6 units.* Dye-dilution curves in eight patients all demonstrated a left-to-right shunt. Selective right ventricular cineangiography in four patients showed the passage of opaque medium from right to left ventricles through the defect during the time that the electrocardiogram showed ectopic beats of right bundle-branch block pattern: when the left ventricle was opacified there was recirculation or refilling of the pulmonary artery.

On palpation both ventricles felt hypertrophied and hyperdynamic. In all 10 subjects, a loud high-frequency pansystolic murmur (grade 3-5) was recorded over the left sternal border at the third and fourth intercostal spaces, diminishing in intensity toward the axilla and sternum. In seven patients amyl nitrite caused a drop in systemic pressure and a diminution in the intensity of the murmur. In six patients with greatly increased pulmonary flow there was an additional ejection murmur superimposed on the pansystolic murmur, resulting in a slight middiastolic accentuation of the murmur in the pulmonary area. In these patients a middiastolic murmur was recorded at the mitral area, beginning 0.14 second after A2 and lasting 0.04 to 0.09 second.

The second sound was abnormally widely split during expiration in eight of the 10 patients, varying from 0.034 to 0.075 second. On inspiration, the width of the splitting increased normally by 0.010 to 0.026 second (fig. 4). The pulmonary component of the second sound was not accentuated when compared with the aortic component.

Measurements of the Electromechanical Interval, Isometric, and Ejection Times of Right and Left Ventrices

In order to elucidate the mechanism of the wide splitting of the second sound in ventricular septal defect these measurements were made in the 17 patients in groups I and II with abnormal splitting of the second sound and were compared with the six subjects with normal splitting, and with normal subjects

*One unit is equivalent to 80 dynes sec./cm.**

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Small ventricular septal defect. The pansystolic murmur drowns aortic closure at the lower left sternal edge. Abnormally wide splitting of the second heart sound in expiratory phase of respiration measures 0.04 second, increasing to 0.06 second on inspiration.

(table 1). The electromechanical interval of the right ventricle (Q-RV time) was prolonged in 12 of the 17 patients with abnormal splitting to an average of 0.08 second (normal 0.04 to 0.06 second). In only two patients was it explained by complete right bundle-branch block, when the Q-RV time was prolonged to 0.12 second. The electromechanical interval of the left ventricle (as measured indirectly, Q-Mi) was normal. The isometric contraction time of the right ventricle, although difficult to measure, appeared to be normal (RV-PA rise averaged 0.02 second) but the isometric time of the left ventricle (indirect) was a trifle shortened (Mi—carotid rise averaged 0.02 second compared with normal of 0.03 second). The ejection time of the right ventricle was normal when compared with 10 healthy subjects, and the ejection time of the left ventricle measured from the indirect carotid tracing was also normal when compared with 80 healthy children. In five patients these measurements did not give a clue as to the cause of the abnormal splitting. In the six patients with ventricular septal defect and normal splitting, the right- and left-sided electromechanical intervals, the isometric times, and the ejection times were normal, despite a 2:1 left-to-right shunt in two of these patients.

Discussion

Murmurs

The classification of systolic murmurs into two main groups, pansystolic regurgitant murmurs and midsystolic ejection murmurs, has been applied to the systolic murmurs of ventricular septal defect. It is well known that when the resistance to right ventricular outflow is normal or low there is a large pressure gradient between the ventricles throughout systole so that both flow and murmur are pansystolic. The high velocity of the flow through small and moderate-sized defects accounts for the high intensity and frequency of the murmur, whereas in large defects with high pulmonary vascular resistance (Eisenmenger's syndrome), or pulmonary stenosis (tetralogy of Fallot), the small flow at low velocity is silent. In two subjects thought to have a small ventricular septal defect it was, therefore, a surprising finding that the loud high-frequency murmur at the lower left sternal edge was early and short (fig. 3). The evidence for ventricular septal defect obtainable in our laboratory was not certain, but the murmur was shown to be present in the right ventricular cavity in one subject and diminished with a fall in left
Ventricular septal defect with a moderately large left-to-right shunt and no pulmonary stenosis. A pansystolic murmur is well localized to the LSE drowning A2. Wide splitting of the second heart sound, on expiration 0.06 second, increasing to 0.08 second on inspiration.

The short ventricular filling murmur (mitral diastolic murmur) due to the large flow across the mitral valve was only present when the pulmonary flow was at least twice the systemic. It is important to stress again that these murmurs were short and confined to the rapid-filling phase and thus easily distinguished from the long murmur of mitral stenosis. There was no immediate inspiratory augmentation, thus distinguishing this murmur from a tricuspid flow murmur.

Heart Sounds

There was no obvious abnormality of the first heart sound and no ejection sound in the left-to-right shunting group, but observations on systolic sounds were difficult owing to the loud pansystolic murmur. The aortic component of the second sound preceded the pulmonary as in normal subjects, but abnormally wide splitting of the second heart sound was frequently present. This was a surprising finding especially in the Roger group with little hemodynamic disturbance, and also in the others, for the increased flow involved...
both ventricles equally. The splitting was often difficult to detect, since aortic closure tended to be drowned in the loud pansystolic murmur, and it was frequently best heard with a rigid diaphragm above or lateral to the pulmonary area where the systolic murmur was less loud. The abnormality was found to lie in the width of separation of the two components of the second sound and not in their respiratory movements. The wide splitting might have been due to premature aortic closure or retarded pulmonary closure, and it was found that both were responsible. Early aortic closure could have been due to shortening of the left-sided electromechanical interval and isometric or ejection times. Slight shortening of the isometric time of the left ventricle was suggested by the finding of a diminished time interval between the initial high-frequency components of the first heart sound (presumably mitral closure) and the upstroke of the carotid tracing. This could be attributed perhaps to diastolic overloading of the left ventricle from increased diastolic filling. There was no equal increase in diastolic overloading of the right ventricle to cancel this effect, for the left-to-right shunt into the right ventricle occurred during systole. There was no shortening of ejection time of the left ventricle as in mitral regurgitation, the volume of blood regurgitated is probably less through small or moderate-sized ventricular septal defects and with large defects the elevated pulmonary vascular resistance is usually elevated and diminishes the shunt.

Delay in pulmonary closure was probably associated with the slight prolongation of the right-sided electromechanical interval. This must have been caused by delay in electrical conduction, but examination of the electrocardiogram did not yield a satisfactory explanation. Right bundle-branch block was only present in two patients and an rsR' complex in three. It has been suggested that the deep and broad Q wave in left chest leads in some patients with ventricular septal defect is due to septal hypertrophy delaying the spread of conduction from the left to the right bundle of His, and this should delay activation of the right ventricle. In our patients, however, there was no correlation between a large Q and wide splitting of the second sound. In eight patients with abnormal splitting it was possible to superimpose the tracings from the right ventricular outflow tract and body and there was no asynchrony, unlike atrial septal defect. There was no relation between the width of splitting and the size of the shunt.

The respiratory movements of A2 and P2 were normal in all cases and in the 17 with a wide expiratory split, the gap widened from an average of 0.045 second in expiration to 0.065 second during inspiration. The mechanism of these changes could only be elucidated by abolishing the respiratory rhythm and thus the effect of succeeding cycles on each other, and has been shown to be due to

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**Figure 5**

Large ventricular septal defect with large left to right shunt (hyperkinetic pulmonary hypertension, pulmonary artery pressure at systemic level) and moderate elevation of pulmonary vascular resistance (not in this series). Ejection sound and ejection systolic murmur in the PA and accentuation of P2 which is transmitted to the mitral area (MA). The defect itself is silent. The separation of the two components of the second sound excludes an Eisenmenger type of ventricular septal defect.
the inspiratory increase in the volume of blood returning to the heart, first affecting the right ventricle and later the left. Following a short halt in expiration, inspiration had no effect on $A_2$ but caused an immediate delay in $P_2$, presumably from increased stroke volume of the right ventricle as blood was drawn from the extrathoracic venous reservoir. A few seconds later there was delay in $A_2$ as the inspiratory increase in stroke volume reached the left ventricle. At normal respiratory rates the inspiratory increase in stroke volume of the right ventricle with delay in $P_2$ coincided with diminishing stroke volume of the left ventricle and earlier $A_2$ (wide split), while in expiration increasing stroke volume of the left ventricle and later $A_2$ coincided with diminishing stroke volume of the right ventricle and earlier $P_2$ (close split). In any case there would seem to be no reason in ventricular septal defect without ventricular failure for any alteration from the normal respiratory variations in diastolic loading of the ventricles. With an interatrial communication, however, inspiration increases the loading of the right and left hearts equally so that $A_2$ and $P_2$ delay simultaneously, producing fixed splitting of the second sound.\textsuperscript{16}

Differential Diagnosis

The diagnosis of ventricular septal defect frequently depends on the interpretation of a systolic murmur. While a pansystolic murmur at the lower left sternal edge is very suggestive of a ventricular septal defect, other possibilities are tricuspid and mitral regurgitation. Tricuspid regurgitation is, fortunately, extremely rare as an isolated abnormality and can usually be recognized by its association with pulmonary hypertension, by the form of the venous pulse, and by the inspiratory augmentation of the systolic murmur in some cases. Differentiation from mitral regurgitation may be more difficult. In pure mitral regurgitation the left ventricle alone is hypertrophied (as opposed to the biventricular hypertrophy of ventricular septal defect), but systolic expansion of the left atrium may thrust the right ventricle forward in systole making it appear overactive, and, rarely, the right ventricle may be truly hypertrophied from high pulmonary vascular resistance complicating the mitral regurgitation. Furthermore, the second heart sound may be widely split in mitral regurgitation, due to diminished resistance to left ventricular outflow causing a shortened ejection time, and in both conditions inspiration increases the splitting, and rapid ventricular filling may produce a short mitral diastolic murmur. Respiration and raising or depressing the peripheral vascular resistance with drugs should equally affect both systolic murmurs. The diagnosis of ventricular septal defect can usually be made, however, by the localization of maximal intensity of the murmur to the lower left sternal edge (fig. 4), by the presence of a normal or short LV isometric time (long in mitral regurgitation) and long $Q$-$RV$ time, by the absence of shortening of ejection time on the carotid tracing, absence of specific enlargement of the left atrium, and by the presence of increased pulmonary blood flow. Of special investigations, intracardiac
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Figure 7

Intracardiac phonocardiogram in a patient with isolated pulmonary infundibular stenosis, gradient of 20 mm. Hg. An ejection systolic murmur is present in the right pulmonary artery increasing in the main pulmonary artery and infundibular chamber and disappearing abruptly in the body of the right ventricle where a murmur from a ventricular septal defect would be maximal.

phonocardiography may prove of value because murmurs are surprisingly localized. Regurgitant murmurs are confined to the chamber into which blood is regurgitating, and a systolic murmur is found in the right ventricle in ventricular septal defect, but is not expected there in mitral regurgitation. Confirmation of the diagnosis of a small ventricular septal defect by detecting increased oxygenation in the right ventricle is well known to be unreliable and the injection or inhalation of indicators (dyes, nitrous oxide, radioactive krypton) downstream to the defect with early detection in the right ventricle has proved more sensitive. Contrast medium selectively injected into the right ventricle of a patient with a small ventricular septal defect without raised right ventricular pressure may shunt right-to-left during periods of low pressure from runs of ectopic beats, but is difficult to differentiate from tricuspid regurgitation. Injection of contrast medium into the left ventricle is likely to show even a small ventricular septal defect, but is scarcely justifiable in these patients with minimal defects who do not require surgery.

An interesting finding in our patients with ventricular septal defect was the high frequency of ectopic beats of right bundle-branch block pattern during stimulation of the right ventricle by the contrast medium or the catheter; ectopies occurred in 16 cases, and in 13 were of right bundle-branch block pattern, suggesting that they originated from stimulation of the left ventricle or left bundle. Ectopic beats during stimulation of the right ventricle in 40 patients without ventricular septal defects were of left ventricular pattern in only five. It is possible that the left bundle is unusually accessible from the
right ventricle even in small defects, and it has been described as lying in the floor of the defect.\textsuperscript{21} Alternatively the left septal mass may reach the cavity of the right ventricle.\textsuperscript{22}

A basal ejection midsystolic murmur due to increased pulmonary flow in patients with ventricular septal defect and large left-to-right shunts may be superimposed on a pansystolic murmur from the defect, and occasionally the ejection murmur is the only systolic murmur (fig. 5) if the ventricular septal defect is so large as to generate a high velocity jet, though in most of these cases there is some elevation of pulmonary vascular resistance. Thus it is important to appreciate that a large ventricular septal defect with unidirectional left-to-right shunt (and therefore operable) may have only a pulmonary ejection systolic murmur, but the wider splitting of the second sound and a mitral diastolic murmur should distinguish them from the Eisenmenger group. In Eisenmenger’s syndrome (equal pulmonary and systemic vascular resistance and a small bidirectional shunt), the greatly dilated pulmonary artery is associated with an ejection systolic murmur preceded by an ejection sound, a loud single second sound (superimposed A\textsubscript{2} and P\textsubscript{2}), and often a pulmonary regurgitant diastolic murmur (fig. 6). In these patients the ventricular septal defect is large and the flow small, so that the shunt murmur is absent. The synchrony of the right and left ventricular events in this group may be simply due to the free communication between the two chambers allowing them to function as a single chamber.

The right-sided basal ejection systolic murmur of pulmonary stenosis, though finishing long before the delayed P\textsubscript{2}, may happen to terminate at A\textsubscript{2} and be mistaken for a left-sided pansystolic murmur from ventricular septal defect, for the sites of maximal intensity occasionally coincide. In pulmonary stenosis of any severity the splitting of the second sound is wider, P\textsubscript{2} softer, and, if valvular, there is usually an ejection sound. An intracardiac phonocardiogram should show that the ejection systolic murmur is only present downstream to the stenosis (fig. 7). Amyl nitrite should increase the pulmonary flow and, therefore, a pulmonary ejection systolic murmur, while diminishing left ventricular pressure and regurgitant flow through a ventricular septal defect.

In atrial septal defect, the short ejection systolic murmur is easily distinguished from the pansystolic murmur of ventricular septal defect, and the fixed splitting of the second sound is extremely useful, particularly when there is an additional pansystolic murmur associated with an atrioventricular canal. Inspiration causes an immediate increase in the intensity of the tricuspid diastolic murmur of atrial septal defect, but has no immediate effect on the mitral diastolic murmur of ventricular septal defect. In left ventricular-right atrial shunt the pansystolic murmur may suggest a ventricular septal defect, oxygenation of right atrial blood, an atrial septal defect,\textsuperscript{23,24} but the absence of fixed splitting of the second sound should strongly suggest that the interatrial septum is intact. We have seen two patients with left ventricular right atrial shunts (and mild elevation of pulmonary vascular resistance) and in both the pansystolic murmur was associated with very close expiratory splitting of the second sound (increasing normally on inspiration), which would be unusual for ventricular septal defect.

Finally, it must be stressed that for the sake of clarity, the emphasis of this discussion has been confined to the auscultatory signs, but in practice it is much easier to draw conclusions from auscultation after eliciting the other physical signs.

**Summary**

Ventricular septal defect with low pulmonary vascular resistance and left-to-right shunt is well known to be closely associated with a pansystolic murmur caused by the regurgitant shunt of blood at high velocity across the defect. With very high flows a pulmonary ejection murmur is superimposed on the pansystolic murmur and is occasionally the only systolic murmur if the ventricular septal defect is so large that the velocity of
the shunt is small. In two patients thought
to have small ventricular septal defects the
shunt murmur was confined to early systole,
probably because the defect was in the muscu-
lar septum and was closed by systolic con-
traction of the ventricle.

The second heart sound is abnormally
widely split in the majority of patients, even
with small defects. The mechanism is diffi-
cult to elucidate but there appears to be
slight shortening of the left ventricular iso-
metric time (early A₂) and delay in contra-
tion of the right ventricle (late P₂). The
splitting of the second sound is a useful way
of differentiating the large defects with left-
to-right shunt from the Eisenmenger group
of large defects with equal pulmonary and
systemic vascular resistances and a loud sin-
el second sound.

The auscultatory differential diagnosis of
ventricular septal defect is discussed.

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