ATRIAL SEPTAL DEFECT

PART II: ENDOCARDIAL-CUSHION DEFECTS*

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Endocardial-cushion defects are far less common than secundum defects, produce more disturbance of function, and are a greater threat to life. Furthermore, the clinical symptoms and signs vary far more than secundum defects, because of the wide variety of haemodynamic disturbances the defects produce. Fundamentally, however, the condition can be subdivided into two major syndromes,[1] namely that of an atrial septal defect and that of a ventricular septal defect. Since deformity of one or of both of the atrio-ventricular valves (mitral and tricuspid) is an integral part of the malformation, the haemodynamic disturbances produced by incompetence of these structures may be added to the disturbances produced by the perforate septa. Bearing this in mind the diagnosis of endocardial-cushion defect can usually be made at the bedside with the additional crucial information supplied by the electrocardiogram. A precise anatomical diagnosis, however, is often more difficult to achieve even with the aid of cardiac catheterization and angiocardiography.

In recent years surgical repair of these defects has been performed in many centres where open-heart surgery with cardiac bypass is practised.[2-6] The operative mortality, however, is much higher than in secundum defects and depends upon the extent of the malformation. The immediate risk for endocardial-cushion defect without ventricular septal defect varies from 4%[2] to 16%,[6] whereas in the complete defect the risk is generally as high as 66 - 75%.[2,3,6] In our Unit 20 patients with a partial defect have been operated on with 2 deaths, and 5 patients with the complete defect (ventricular septal defect) with 2 deaths. In contrast to secundum defects, patients with endocardial-cushion defects have far severer symptoms and seldom survive beyond the third decade. One is therefore justified in recommending surgical correction even though the risks are considerable.

It is the purpose of this paper to present the clinical and laboratory features in 39 consecutive patients with endocardial-cushion defects, to indicate the diagnosis of the condition, its anatomical variants, severity, and complications, and to differentiate this condition from the secundum defect and point out the features that indicate the presence of an additional ventricular septal defect.

Anatomical Considerations

The embryological details of the development of the atrial septa were discussed in Part I,[7] but the part played by the endocardial cushions requires some amplification. The dorsal and ventral endocardial cushions divide the common atrio-ventricular canal into a right (or tricuspid) orifice and a left (or mitral) orifice, thereby separating the atria from the ventricles. Growth to the left helps to form the antero-medial leaflet of the mitral valve and growth to the right helps to form the septal leaflet of the tricuspid valve. Growth upward fuses with the atrial septum and growth downward fuses with the ventricular septum.[8] The endocardial cushions thus serve a threefold purpose: (1) They separate the atrial septum from the ventricular septum, (2) they take part in the formation of the atrio-ventricular valve leaflets, and (3) they contribute towards the formation of the cardiac septa.

Classification of Defects

Failure of the endocardial cushions to develop and to fuse properly leads to a variety of anomalies, and several anatomical classifications have been proposed.[8-10] For practical purposes we recognize two groups,[1] as follows:

A. *Endocardial-cushion defects without ventricular septal defects.* Sufficient ventricular septal tissue has developed to prevent communication between the two ventricles. Deficiency of the atrial septum always persists, resulting in incomplete division of the atria, and varying degrees of maldevelopment of the antero-medial leaflet of the mitral valve and septal leaflet of the tricuspid valve are associated. The defects in atrial septation may vary from complete absence of the atrial wall (single atrium[11]) to degrees of partial absence of the septum (ostium primum defect, partial endocardial-cushion defect). As a result a low atrial septal defect is always present, a cleft in the mitral valve is generally associated, and involvement of the tricuspid valve occasionally occurs. Clefts in the mitral and tricuspid valves do not necessarily interfere with their competence. On the other hand gross mitral incompetence may be present with a trivial atrial septal defect.[12]

B. *Endocardial-cushion defects with ventricular septal defects.* All three functions of the endocardial cushions are interfered with. Thus (1) the atria are incompletely separated from the ventricles, (2) the mitral and tricuspid valve leaflets are incompletely formed, and (3) the atrial and ventricular septa are both defective. Varying degrees of ventricular septal defect are present, from complete absence of the ventricular septum to deficiency only of the upper portion resulting in lack of fixation of the atrio-ventricular valves. As a result, the haemodynamic disturbances of the ventricular septal defect are added to all the disturbances produced by the defective atrial septum and deficient atrio-ventricular valves. On rare occasions ventricular septal defects with cleft atrio-ventri-

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cular valves and no atrial septal defect[12] have been encountered.

Haemodynamic Changes produced by Endocardial-cushion Defects

The haemodynamic changes produced by endocardial-cushion defects depend upon the three cardinal anomalies present in this complex, namely the atrial septal defect, the malformed atrio-ventricular valves and the ventricular septal defect. The haemodynamic changes produced by the atrial septal defect are the same as those found in secundum defects (see Part I)[7] and are dependent upon the size of the defect and the pulmonary vascular resistance. However, dye-dilution studies show very similar curves from right and left lungs,[14] indicating more complete mixing of oxygenated and venous blood and less streaming. This is attributed to the low situation of the defect in contrast to what is found in secundum defects. For the same reason a small right-to-left shunt from the inferior vena cava and not the superior vena cava is generally present.

Malformation of the mitral valves is always present in endocardial-cushion defect, usually consisting of a cleft, often with accessory mitral chordae.[15] If these valves are incompetent the effects of mitral incompetence are superimposed on the changes produced by the patent septa. Because the left and right atria are in free communication, the haemodynamic effects of this incompetence are dissipated through both atria, perhaps accounting for the slight elevation of pressure in the atria and the absence of back pressure on the pulmonary capillaries. Detection of mitral incompetence from the pressure curves in the atria is thus uncommon. However, with the use of dye-dilution or angiocardiographic studies from the left ventricle the regurgitation of blood from the left ventricle into the right atrium can sometimes be demonstrated. Because of the cleft valve and the low position of the atrial septal defect a catheter can be withdrawn from the left ventricle into the right ventricle without transgressing the atrium. Such a finding does not necessarily imply the presence of a ventricular septal defect. The tricuspid valve is less frequently involved and, when it is, mitral deformity is nearly always associated. The effects of tricuspid incompetence can then be added to those of mitral incompetence. In spite of the fairly gross anatomical malformation of the atrio-ventricular valves they often function very adequately and incompetence is by no means invariable.

The haemodynamic changes due to the ventricular septal defect do not differ in any way from those produced by an uncomplicated ventricular septal defect except that blood can be shunted directly from the left ventricle into the right or left atrium[13] or from left ventricle into right ventricle and right atrium, because of the associated valve deformities. The effects of the ventricular septal defect depend on its size and the pulmonary vascular resistance. When the septal defect is small the shunt will be small, although a loud murmur may be produced. When the septal defect is large the volume of the shunt will depend upon the pulmonary vascular resistance. Where the resistance is normal or only slightly elevated marked pulmonary plethora will result. Where the pulmonary resistance is high the shunt is reduced, and where the pulmonary resistance is greater than the systemic, reversal of shunt with cyanosis and pulmonary hypertension results (the Eisenmenger syndrome[16]).

The complexity of the haemodynamic disturbances that are encountered in endocardial defect can now be appreciated. Roughly speaking, however, the following patterns emerge:

(*a*) An atrial shunt without a-v valve malfunction—a situation identical to that in secundum defect.

(*b*) An atrial shunt with mitral, and in rare cases tricuspid, valve incompetence.

(*c*) An atrial and ventricular shunt without a-v valve malfunction—a situation identical to that seen in ventricular septal defect with tricuspid incompetence or independent atrial and ventricular septal defects.

(*d*) An atrial and ventricular shunt with a-v valve malfunction.

The pulmonary vascular resistance and the presence or absence of associated defects such as pulmonary stenosis will modify the haemodynamic situation accordingly.

Case Material

Of the 39 patients with endocardial-cushion defects the diagnosis was confirmed at necropsy alone in 3 and at surgery in 25 (including 4 necropsies). In the remaining 11 it was based on good clinical grounds supported by the electrocardiogram (ECG) and catheterization.* The series included 29 patients without a ventricular septal defect (ostium primum defect, partial defect) and 10 with a ventricular septal defect (atrio-ventricular communis, common a-v canal, complete defect). A systolic pressure difference of 15 mm.Hg or more across the pulmonary valve was found in 4 patients.

There was no special selection of patients for investigation; consecutive cases were studied, the indication for study being the clinical suspicion of congenital heart disease. Patients with complex additional deformities, such as transposition of the great vessels, were excluded from this analysis. Endocardial-cushion defects were approximately a third as common as secundum defects.

Routine clinical examination included ECG, phonocardiography and radiology. Antero-posterior X-rays were taken in all patients. Right heart catheterization was performed in 37 patients by the usual techniques described elsewhere,[17] and in half of these dye-dilution studies were included. Patients with clinical and ECG features of ostium secundum type of defect were excluded from this report; they are described in Part I.[7]

Age, Sex and Race

The age incidence varied from 3 months to 47 years and the sex ratio was females to males 2·5:1 (i.e. 5 females to 2 males). The age, sex and race incidence is shown in Table I. The incidence differed from that of secundum defects in that familial incidence was not noted, and the condition was quite common in the Bantu.

* The diagnosis was based on a left-to-right shunt at the atrial level, or at both atrial and ventricular levels, associated with evidence of atrio-ventricular valve disease, mitral or tricuspid, and left axis deviation with a counter-clockwise loop in the frontal plane in the ECG.

TABLE I. AGE, SEX AND RACE OF 39 PATIENTS WITH ENDOCARDIAL-CUSHION DEFECTS

Age	*Male*	*Female*	*White*	*Coloured*	*Bantu*
Without VSD					
0 - 9	1	11	7	3	2
10 - 19	1	7	4	1	3
20 - 29	3	1	3		1
30 - 39	1	1	2		
40 - 49	1	1	2		
With VSD					
0 - 9	2	4	5		1
10 - 19	2	3	2	3	
Total	11	28	25	7	7

Symptoms

Attention was drawn to the heart far earlier in endocardial-cushion defect than in secundum defect, either because of symptoms associated with the heart defect (14 patients) or because of murmurs (25 patients). In 10 of the 39 patients murmurs were heard before the age of 1 year, and in 20 before the age of 3 years. The defect was discovered before the age of 15 in all but 3 patients.

Of the 39 patients only 9 were asymptomatic. In 20 there was moderate disability and in 10 the disability was severe. The commonest symptoms were exertional dyspnoea, usually moderate (25 patients), fatigue (15), troublesome palpitations (4), and frequent respiratory infections (7). There were 4 patients with congestive cardiac failure at some or other time during their illness. A clear-cut history of rheumatic fever was present in 2. Subacute bacterial endocarditis developed in 3 patients, fatal in one. A fourth patient developed this complication a year after surgical repair; recovery followed treatment. Cerebral embolism with residual hemiplegia (presumably bland) developed in one child at the age of 2. One subject, a man of 46, had extensive calcification of the pericardium, presumably unrelated and tuberculous in origin. One of the 2 mongolian idiots in this series was cyanotic from birth. Many of the children were small and underdeveloped for their age; growth and development tending to be much more affected than in secundum defects.

When a ventricular septal defect was present the disability was far greater than in partial defects. Thus only one of the 10 patients was asymptomatic. There were 4 deaths in this group (2 surgical, one from subacute bacterial endocarditis and one from congestive cardiac failure). The condition with VSD was encountered particularly in young patients, the oldest in this series being 15.

Physical Signs

The clinical findings were either those of an atrial septal defect[7] or of a ventricular septal defect,[18] with or without the additional signs of mitral or tricuspid disease. However, common to all cases were poor body development and retardation of growth, particularly marked in the presence of a ventricular septal defect. Arachnoidactyly and a high arched palate were not noted. An accessory auricle was found in one patient and syndactyly in another. One patient was cyanosed and clubbed from birth owing to severe pulmonary hypertension with reversal of shunt, and one was clubbed from subacute bacterial endocarditis.

The *jugular venous pressure* tended to be a little higher than in secundum defects, but it was normal in 32 patients and in 6 it was 6 cm. or more above the sternal angle.

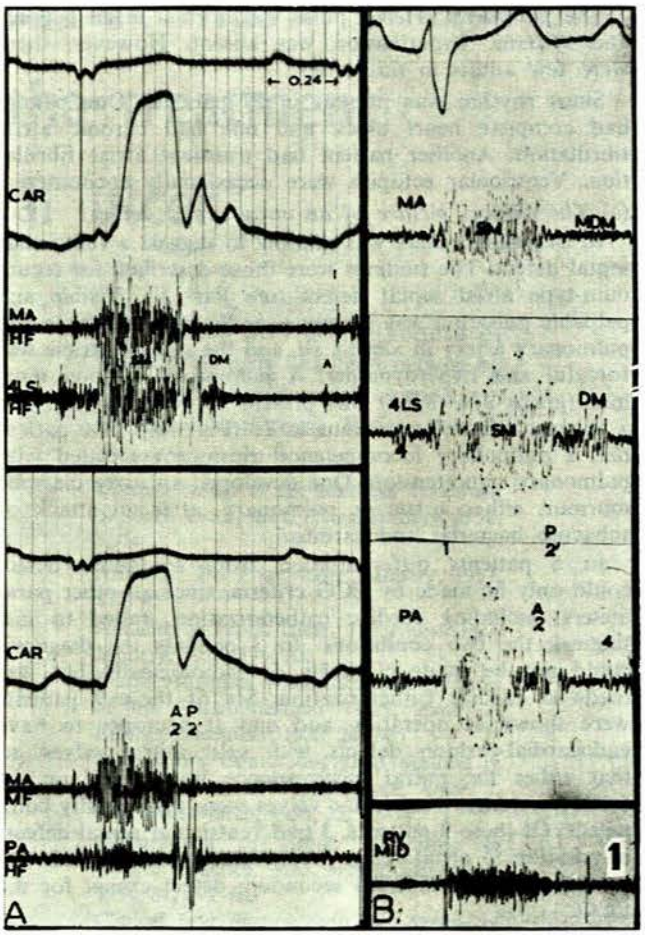

Fig. 1. Phonocardiographic tracings from (A) a patient with endocardial-cushion defect and mitral incompetence but no ventricular septal defect and (B) from a patient with endocardial-cushion defect, mitral incompetence and ventricular septal defect. In (A) a pansystolic murmur of mitral incompetence is shown at the apex (MA). Because of the peculiar situation of the incompetent jet, the murmur radiates well medially and is recorded at the tricuspid area (4LS). At the pulmonary area (PA) the murmur is much shorter, being 'ejection' in type, associated with rapid flow across normal pulmonary valves. The tricuspid diastolic murmur (DM) is well shown at the tricuspid area. Wide splitting of the second sound (A2, P2) is associated with the atrial septal defect and an atrial sound (A) is well shown. In (B) the pansystolic murmur of mitral incompetence with a low-pitched mid-diastolic murmur is shown at the apex (MA). At the tricuspid area (4LS) the pansystolic 'regurgitant' murmur of the ventricular septal defect is followed by the high-pitched tricuspid diastolic murmur; an atrial sound (4) can also be seen. At the pulmonary area the pulmonary systolic murmur is short and 'ejection' in type, differing completely from the two other regurgitant murmurs; wide splitting of the second heart sound is present, associated with the atrial septal defect. The phonocatheter tracing from the right ventricle records the pansystolic regurgitant murmur, proving the presence of the ventricular septal defect.

The 'a' and 'v' waves of the jugular venous pulse were of equal amplitude except in the one patient with atrial fibrillation and calcific pericarditis, in whom a large 'v' wave was present.

The *peripheral arterial* pulse was normal in all patients and systemic hypertension was absent. However, there were few adults in this series.

Sinus rhythm was present in 27 patients. One patient had complete heart block and one had chronic atrial fibrillation. Another patient had transient atrial fibrillation. Ventricular ectopics were occasionally encountered.

(a) *The clinical picture of an atrial septal defect*

In 24 patients there was nothing to suggest a ventricular septal defect. The findings were those described for secundum-type atrial septal defect (see Part I). Visible and palpable pulsation was present over the right ventricle and pulmonary artery in almost all, and the right ventricle was forceful and hyperdynamic. A pulmonary ejection murmur (grade 2/6 - 3/6[19]) was present in every patient, and a tricuspid diastolic murmur in 21 (Fig. 1A). One patient had a pulmonary incompetence murmur associated with pulmonary hypertension. One developed an early diastolic murmur, either aortic or pulmonary, after an attack of subacute bacterial endocarditis.

In 6 patients differentiation from secundum defect could only be made by ECG criteria, since all other parameters, including cardiac catheterization, failed to distinguish the two conditions. In 3 patients the diagnosis could not be made clinically or radiologically but was made at cardiac catheterization. Six of these 9 patients were shown at operation and one at necropsy to have endocardial-cushion defects with split mitral valves, so that either the mitral incompetence was silent[20] or the malformed atrio-ventricular valves were functionally competent. Of these 9 patients, 3 had ventricular septal defects in addition to atrial. Thus partial or complete defects can be indistinguishable from secundum defect except for the ECG.

In 15 patients there was clear-cut evidence of mitral valve disease because of a pansystolic murmur maximal at the apex, radiating medially and laterally (Fig. 1A). In 6 an accompanying apical mid-diastolic murmur distinguishable from the tricuspid diastolic murmur was present and the apex beat was left-ventricular in type. One of these 15 patients was shown at operation to have a ventricular septal defect, not suspected clinically. The clinical picture was that of atrial septal defect with mitral incompetence.

(b) *The clinical picture of ventricular septal defect*

There were 13 patients in whom a ventricular septal defect was suspected because of a loud murmur, with or without a thrill, at the fourth left intercostal space. In 4 of these there was no evidence that the mitral valve was involved, although operation showed the presence of cleft mitral and tricuspid valves and a complete defect in 2, and catheterization proved the diagnosis in 2. In 9 patients mitral murmurs were also present (Fig. 1B). Only two of these have been shown to have ventricular septal defects. This can be explained by the peculiar situation of the mitral valve deformity, which results in an anteromedially directed jet. Consequently the pansystolic mitral regurgitant murmur is frequently best heard at the tricuspid area, where it cannot be distinguished from the murmur of a ventricular septal defect. A tricuspid systolic murmur sometimes produces the same confusion. However, accentuation of the murmur on inhalation of amyl nitrite helps in differentiating the latter.[21]

One patient presented the clinical picture of pulmonary hypertension with reversed shunt (Eisenmenger's syndrome[16]) with cyanosis, a pulmonary ejection click, and no murmurs.

(c) *Another clinical picture*

There was one patient with signs of atrial septal defect and isolated tricuspid valve disease, i.e. a tricuspid systolic and diastolic murmur with wide splitting of the second heart sound and no evidence of mitral valve disease.

Phonocardiography

Phonocardiographic tracings were available in all patients but the findings will not be discussed in detail. Wide, relatively fixed splitting of the second heart sound was found in all patients without pulmonary hypertension. The presence of pulmonary systolic and mitral systolic murmurs and those of ventricular septal defect were confirmed (Fig. 1). Mitral and tricuspid diastolic murmurs were recorded and occasionally an opening snap could be shown.

Electrocardiogram

Sinus rhythm was present in 37 of the 39 patients. One of the remaining two had complete heart block, and atrial fibrillation was present in the other, a man of 46, with

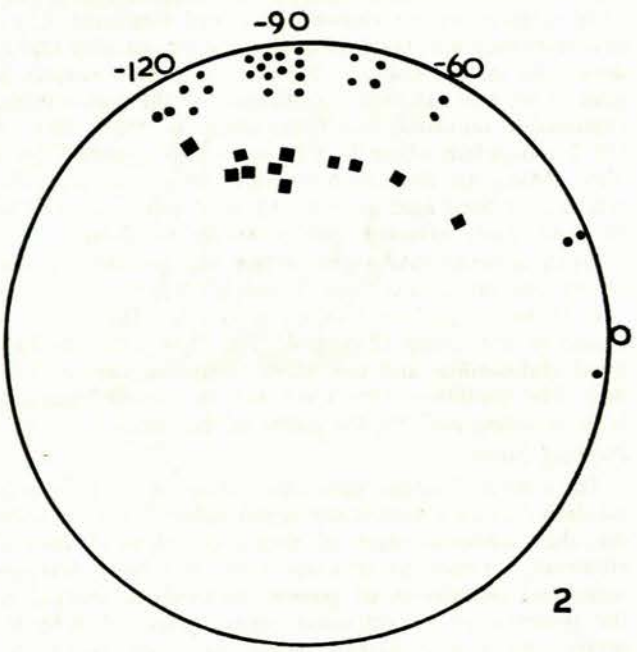

Fig. 2. The mean QRS vector in the frontal plane has been plotted in 38 patients. In 33 it lies between −60° and −120°. Only one is on the positive side of the zero axis. The circles represent partial defects and the solid squares endocardial-cushion defects with ventricular septal defects.

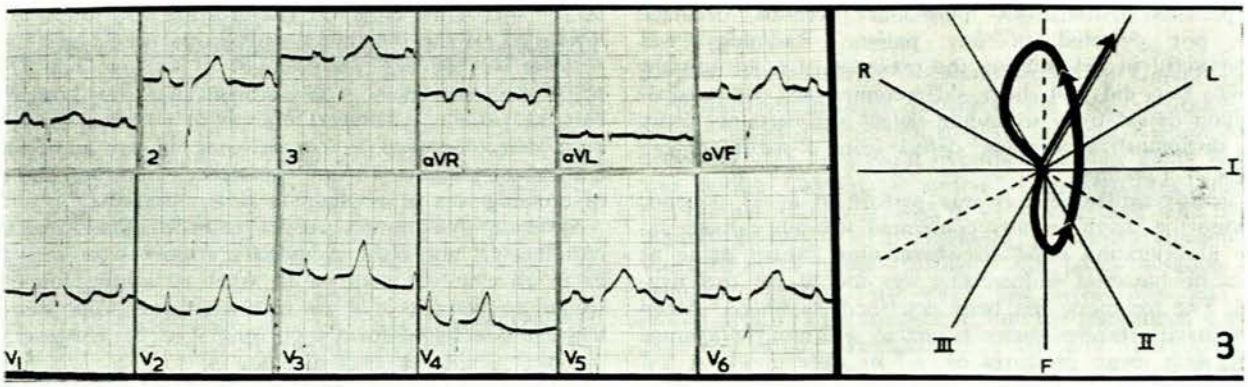

Fig. 3. Typical ECG found in endocardial-cushion defect. Left axis deviation is present with a mean axis of −65° and a counter-clockwise loop. A qR pattern of right ventricular hypertrophy is present in V1. Biatrial hypertrophy is present.

coexistent calcific pericarditis. Occasionally ventricular ectopics were encountered.

The P waves were normal in 26 patients. Right atrial hypertrophy was present in 7, left atrial hypertrophy in 3, and bi-atrial hypertrophy in 3. The P - R interval was less than 0·21 sec. in 33 patients and prolonged above this value in 6.

The mean QRS vector in the frontal plane lay between +10 and −125° in 38 patients. In the 39th the mean vector could not be determined. In 33 patients the range lay between −60 and −120° (Fig. 2). The loop was counter-clockwise in all subjects (Fig. 3).

A typical rsR′ or rsR′S′ pattern in V1 (incomplete bundle-branch block) was present in 14 patients, and an rR, Rs or RS pattern in 12. In 10 patients a qR or qRS pattern was found. One patient had complete right bundle-branch block unassociated with pulmonary hypertension. A small q wave in V5, V6 or V7 was found in 15 patients. The QRS complex varied from 0·04 to 0·12 sec. (mean 0·8). In patients over the age of 13 T inversion in leads V1 to V4 or more was found in 6, right ventricular hypertension being present in each case.

Radiological Findings

X-ray plates were available in 37 patients and at least half the patients were screened by one of us (V.S.). The average cardio-thoracic index was 60 (range 45 - 73), only 2 being below 50; cardiac enlargement was entirely due to enlargement of the right heart chambers and the main pulmonary artery. Enlargement of the right atrium (Fig. 4) was a feature in a third of the patients. Left atrial enlargement was demonstrated on barium swallow in the right oblique view in 7 of the 13 patients on whom this examination was performed. Left ventricular enlargement is always difficult to assess in the presence of right ventricular enlargement (see Part I[1]) but was thought to be present in 3 of these 13 patients. The aorta appeared to be small or normal in all patients. In all but 4 the lung fields showed the classical features of pulmonary plethora, as previously described;[22] 3 of the 4 exceptions had severe pulmonary hypertension, the fourth having a small shunt. Hilar dance with pulsation of the distal pulmonary arteries was observed fluoroscopically in all patients screened, except the one subject with severe pulmonary hypertension (Fig. 4B). Peripheral pruning was present in 2 patients with severe pulmonary hypertension.

Vascular markings closely simulating Kerley B lines[23] were observed in

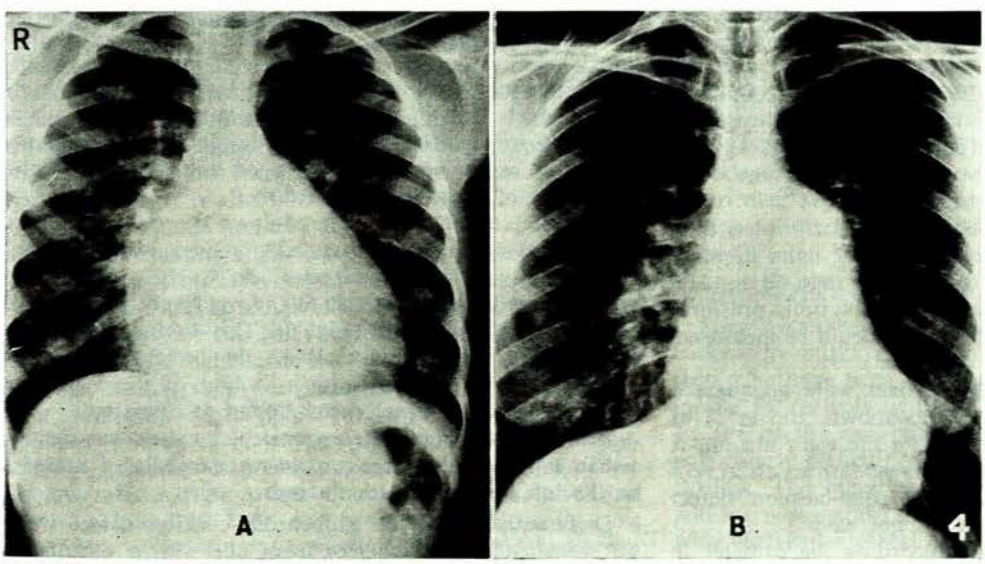

Fig. 4. (A) A-P X-ray from a patient with an endocardial-cushion defect and a large left-to-right shunt with normal pulmonary arterial resistance. Note the considerable cardiomegaly involving the right atrium, right ventricle and pulmonary arteries and the pulmonary plethora. (B) Severe pulmonary hypertension in a patient with endocardial-cushion defect in whom a moderate left-to-right shunt persists.

3 patients. Anomalous pulmonary venous drainage was not detected in any patient. Radiology was very useful in determining the presence of a left-to-right shunt, but did not help differentiate an endocardial-cushion defect from secundum defect and certainly could not distinguish a complete defect from a partial defect.

Catheter Findings

Cardiac catheterization was performed in 37 patients. In one the diagnosis was confirmed without catheterization at operation done elsewhere. One patient dying of subacute bacterial endocarditis was too ill for investigation. The technique has been described elsewhere.[17] Mean right atrial pressures varied from 0 to +12 mm.Hg (average +5), with mean pressures of +7 or over in 14. A 'cv' wave of tricuspid incompetence was present in 4. The right ventricular systolic pressure was 30 mm.Hg or less in 8 patients, between 31 and 60 in 17 patients, and above 60 in 11. In 4 of the last-mentioned 11 patients a gradient of 15 mm.Hg or more across the pulmonary valve was present, but in every case the pulmonary pressure was elevated. In only one could the gradient be attributed to organic pulmonary stenosis—a patient with a right ventricular pressure of 120/5 and a pulmonary arterial pressure of 35/10.[7]

Pulmonary arterial wedge pressures tended to be a few millimetres higher than the right atrial or left atrial pressures when measured. In most of the 21 patients in whom the left atrium was entered, right and left pressures appeared to be of the same order. In 5 patients left atrial pressures were significantly higher than the right. In only one patient was mitral incompetence clearly shown on the pressure tracings. The left ventricle was entered in 21 patients, no significant gradient across the mitral valve being shown in any. Systemic and left ventricular pressures were within normal limits in all patients. Systemic output varied from 1·3 to 7 litres/min., excluding one highly nervous patient who had an output of 13·6 litres during catheterization. A mean of 3·9 litres was obtained, which was normal in our laboratory for this age group. Except for one patient, pulmonary flow varied from 4 to 28 litres/min. with a mean of 10·3 litres/min. In the one exception, severe pulmonary hypertension was present, with systemic flow exceeding pulmonary flow (2·9 : 2·0 litres/min.) because of reversal of shunt. Only one other patient had a significant right-to-left shunt.

The pulmonary vascular resistance varied from less than one to 34 units, with an average under 2 units in those patients with a pulmonary pressure of less than 60 mm.Hg. In the 7 patients with pulmonary arterial systolic pressures over 60 mm.Hg in whom the resistance could be measured, the mean was 10 units (range 2·2 to 34).

In all 35 patients in whom the data were adequate a left-to-right shunt at atrial level was shown, and in 27 of these the left heart was entered from the right atrium. It is generally easy to establish the presence of an atrial septal defect; differentiation of endocardial-cushion defect from secundum defect, however, is not easy.

In 20 patients X-ray pictures recording the catheter in the left side of the heart were available. In 4 the saphenous route was used so that the lower end of the defect was not outlined by the path of the catheter, and in 4 entrance was so oblique that no opinion could be given on the site of the crossing. The crossing was found to be low in 11 of the remainder and normal in 3. In 2 other patients the crossing was thought to be low, but X-ray plates were not taken. A low crossing was thus present in half the patients. However, analysis of our data in secundum defect showed a low crossing in an appreciable number of patients. In our experience, therefore, the site of crossing was of no help in differentiation.

Systemic dye-dilution curves recorded after injection into the left and right pulmonary arteries were recorded in 13 patients. In contrast to what is usually found in secundum defects, in 9 patients a similar proportion of blood was shunted from each lung (Fig. 5). However, in

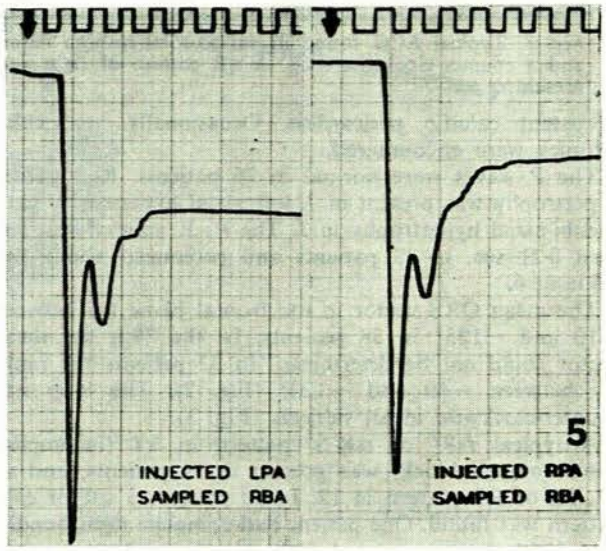

Fig. 5. Dye-dilution curves recorded at the brachial artery after injection into the left and right pulmonary arteries. The distortion of the disappearance slope indicates a large left-to-right shunt, of equal magnitude from both lungs, suggestive of an endocardial-cushion defect.

4 this was not so. Furthermore, in several of our secundum defects there was equal shunting from the two lungs, as in endocardial-cushion defects. This technique, therefore, could not be relied upon to differentiate the two types of atrial septal defects.

The left ventricle was entered from the right atrium in 21 patients and in 16 left atrial pressures were recorded on withdrawal of the catheter. In 5 the catheter tip passed directly from the left to the right ventricle without transgressing the atrium (Fig. 6). This excluded a secundum defect, but did not establish the presence of a ventricular septal defect, because in only 1 of the 5 patients was a ventricular septal defect found at operation.

Incompetence of the atrio-ventricular valves was suggested in 4 patients by large 'cv' waves, exceeding 5 mm.Hg, in the left atrial pressure tracings.

Differentiation of an endocardial-cushion defect without ventricular septal defect from one with a ventricular septal defect proved even more difficult. However, when a ventricular septal defect was present the arterial saturation tended to be lower and the pulmonary arterial pressure higher. Thus, the average arterial saturation in partial

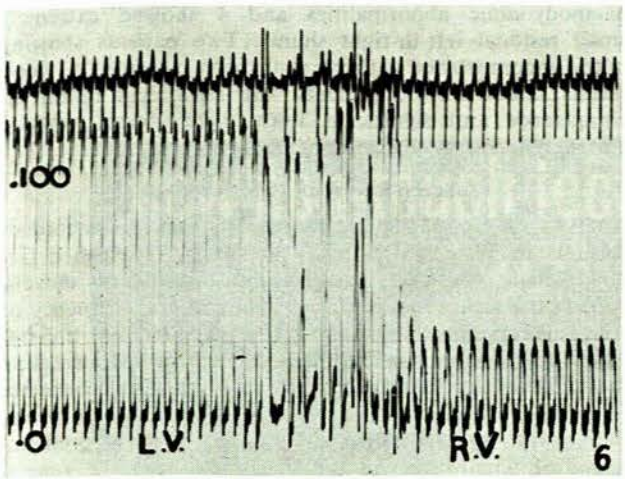

Fig. 6. A continuous withdrawal tracing from the left ventricle to the right ventricle without traversing an atrium. Note the numerous ventricular ectopics produced during the movement of the catheter.

defects was 95% (range 89-99), whereas in ventricular septal defect it was 85% (range 76 - 90). A right ventricular pressure of over 65 mm.Hg was present in 7 of the 9 patients with complete defects and in only 2 of those with partial defects. A significant right-to-left shunt was found only in complete defects (2 patients). The aorta was entered from the right ventricle in only one patient.

Rapid serial sampling from the right ventricle to the superior vena cava by oximetry was performed in 26 patients. In only 3 patients did the ventricular saturation exceed the right atrial by more than 2% and one of these patients had no ventricular septal defect. Conversely, in 23 patients, who included 5 with ventricular septal defects, the right atrial saturations were consistently higher than the right ventricular. Even, therefore, the most carefully performed multiple sampling technique fails to differentiate the two conditions.

In 8 patients systemic dye curves were recorded after injection into the left ventricle. In 5 the curve was normal, excluding both a significant shunt at ventricular level and significant mitral incompetence. The other 3 showed a distortion of the curve due to a ventricular septal defect in one and to mitral incompetence in the other. This technique, therefore, is also of little assistance.

Only 2 methods were of any value. A phonocatheter was passed into the right ventricle in 3 patients. In 2 of them, with a ventricular septal defect, a pansystolic murmur of ventricular septal defect was detected; in the other, without a ventricular septal defect, there were no murmurs in the right ventricle. In 3 patients left ventricular angiocardiography was performed showing the presence of a ventricular septal defect in 2 and its absence in one.

When severe pulmonary hypertension with high pulmonary resistance is present, systemic dye-dilution curves demonstrated a right-to-left shunt at ventricular level and this was found in 3 of our patients. Theoretically, this could also occur without a ventricular septal defect when tricuspid insufficiency is present.

In summary, cardiac catheterization was of assistance in differentiating endocardial-cushion defects from uncomplicated secundum defects in only 12 patients. It was able to differentiate the partial from the complete variety in only 5.

Surgical Treatment of Endocardial-cushion Defects

As discussed in detail elsewhere,[1] the only safe technique for the surgical correction of these defects is whole-body perfusion with or without hypothermia. The Helix Reservoir Bubble Oxygenator system[24] with high-flow normothermic perfusion was used in 13 patients and with hypothermic perfusion in 10 patients. A median sternotomy was used in all except 2 patients. Arterial cannulation was performed in the usual way.[1] The defect was next explored with a finger introduced into the right atrial appendage and careful evaluation of mitral and tricuspid valve function made. Venous cannulation was then performed. Cardiac asystole was not induced, because valve function could be better assessed in the beating heart; furthermore, heart block could be detected immediately and the stitch responsible for this condition detected and removed at once.

(a) *Endocardial-cushion defect without ventricular septal defect.* If abnormal restraints interfering with free mobility of the trigone of the antero-medial leaflet of the mitral valve were present they were divided.[1] Abnormal chordae that were not interfering with valve function were left undisturbed. The cleft was then repaired with interrupted No. 4 - 0 silk mattress sutures. If the cleft also involved the septal leaflet of the tricuspid valve this was repaired in a similar manner. If, however, mitral valve function appeared normal despite the cleft valve, the cleft was left or only partially closed at its base. The atrial septal defect was then closed, a prosthesis being used in every case, care being taken to avoid heart block.[1]

(b) *Endocardial-cushion defects with ventricular septal defect.* The technical problems and dangers in repair are far greater than in the absence of the ventricular defect. After mobilizing the atrio-ventricular valves, the ventricular septal defect was closed in such a way as not to narrow the left ventricular outflow or damage the conducting system of the heart. In 2 patients this meant insertion of a prosthesis ('ivalon' graft in one and pericardium in the other). In 3 patients the ventricular septal defects were closed by direct suture. The valve defect was then repaired and afterwards the leaflets were attached to the ventricular septum. The atrial septal defect was closed with a prosthesis as described, which was attached to the valves.

Surgical Results

There were two operative deaths in the 20 patients with endocardial-cushion defects without ventricular septal defects who have been operated upon in our Unit, but none in the 14 patients operated upon by one of us (C.N.B.) In one of the two patients who died, surgery was made particularly difficult by the presence of dense calcific pericarditis. The other had congenital complete heart block, and the postoperative course was stormy. Of the 5 patients with ventricular septal defect, 2 died and in both of these the defects were substantial, with severe pulmonary hypertension.

The postoperative course was essentially the same as

that in patients with secundum defects. Asymptomatic persistent heart block was present in one patient, with a

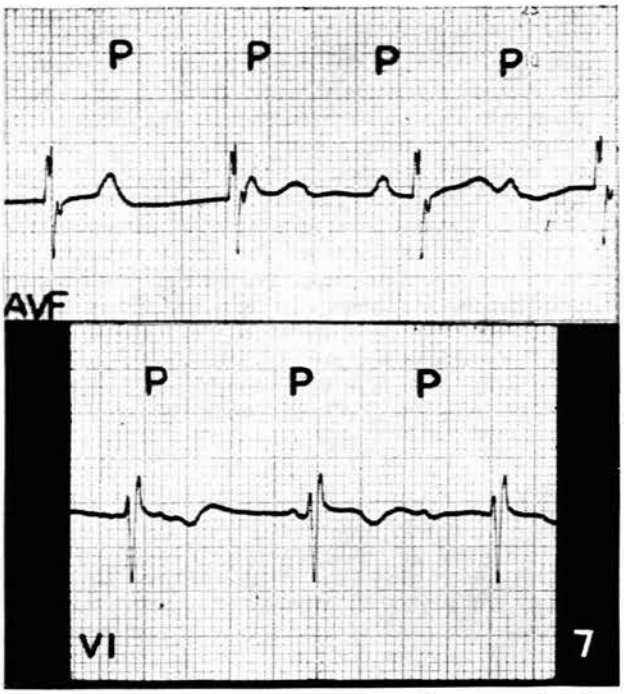

Fig. 7. Complete heart block produced at operation, in which the sinus node discharges at 100/minute and the atrio-ventricular node at 70. Incomplete bundle-branch block is shown in V1 (rSR′ pattern).

nodal rate often over 100 per minute (Fig. 7) and in another patient transient complete heart block occurred during surgery.

The follow-up system used was the same as in secundum defects. Recovery was rapid and improvement noted in all but one, who required re-operation. In 17 patients all the physical signs of a left-to-right shunt were abolished, but murmurs, usually minimal, indicative of mitral valve deformity persisted. Of the 18 survivors, 14 have been re-investigated about 1 year after the operation. In 3 the operation has been too recent for re-investigation, and 1 has not returned for study. Of the 14 patients re-investigated: 6 show no haemodynamic abnormality; 2 show complete closure of the defect but significant mitral incompetence (one of these patients developed subacute bacterial endocarditis 2 years after the operation, but responded to treatment; 4, 2 of whom had had ventricular septal defects, showed a minute residual shunt (less than 15%), but no mitral incompetence; 2 had significant residual shunts and mitral incompetence, one of whom required re-operation, at which a new defect in the atrial septum resulting from tension on the septum after the first repair was found and repaired, and the mitral valve was re-sutured after mitral valvotomy.

To summarize, all but one patient showed marked symptomatic improvement and disappearance of all clinical signs of left-to-right shunt. Of the 14 patients who were re-studied by cardiac catheterization, there were 10 with excellent results, 6 of whom showed no residual haemodynamic abnormalities and 4 showed extremely small residual left-to-right shunts. Two patients showing mitral incompetence with no shunt were regarded as good results. There were 2 patients with significant mitral incompetence and significant left-to-right shunts, one of whom required re-operation.

DISCUSSION AND CONCLUSIONS

Analysis of the data in 39 patients with endocardial-cushion defects confirms many previously established factors which contrast strongly with secundum defects, namely the severe nature of the anomaly, the frequency of congestive failure and respiratory-tract infection, the frequent diagnosis in infancy, the high incidence of increasing disability in the first few decades of life, the occurrence in mongolian idiots, and the common finding of severe pulmonary hypertension.[2,3,6,9,25-29] The marked predominance of females in this series has not been the general experience, an equal sex incidence[25] or a slight female dominance[4,6] being the general finding.

The 3 cardinal anomalies present in this malformation are the atrial septal defect, the ventricular septal defect, and the deformity of the atrio-ventricular valves. There were 29 patients without a ventricular septal defect and 10 with a ventricular septal defect, all having malformed valves.

Two major problems immediately present themselves for discussion. First the differentiation of endocardial-cushion defects from secundum defects, and secondly the differentiation of endocardial-cushion defects with ventricular septal defect from endocardial-cushion defect without ventricular septal defect.

There were only 9 patients in whom the clinical findings were identical with those found in uncomplicated secundum defect.[7] In 15 patients there was clear-cut evidence of mitral incompetence, the clinical findings being similar to secundum defect complicated by mitral incompetence.[7] Thirteen patients presented with a murmur, often with thrill, at the fourth left space, suggesting a ventricular septal defect and clearly separating this condition from secundum defect. One patient presented the features of tricuspid incompetence associated with an atrial septal defect clearly different from a secundum defect. One patient presented the features of severe pulmonary hypertension with cyanosis, and no murmurs.

Radiologically the condition could not be differentiated from secundum defect, though the heart was generally larger, particularly the right atrium. Cardiac catheterization could not be relied upon in differentiating the two conditions in more than a third of the patients.

The paramount importance of the electrocardiogram in separating endocardial-cushion defects[12,28-34] has again been established. The mean QRS in the frontal plane lay between 0 and —120° (Fig. 2) in 37 patients. A counter-clockwise loop was present in all. Burchell *et al.*[33] have analysed a large series of patients and reviewed the literature. They believe that this type of ECG is practically pathognomonic of defects in the region of the atrio-ventricular valves. This has been so in our experience, with few exceptions.[7] In very exceptional cases endocardial-cushion defects have been described without this typical pattern. Other findings of lesser significance were the in-

creased frequency of atrial hypertrophy and a long PR interval. The ECG differentiated endocardial-cushion defects in all our patients and made the problem relatively easy.

Differentiation of endocardial-cushion defects with a ventricular septal defect from endocardial-cushion defects without a ventricular septal defect is a more difficult problem. Both conditions can simulate a secundum defect, a secundum defect with mitral incompetence, or a ventricular septal defect. Radiology and ECG are unhelpful. Cardiac catheterization on the other hand is sometimes helpful, especially if a phonocatheter is used or if left ventricular angiocardiography is performed.

The subject would not be complete without a discussion of maladies that are often confused with malformation of the endocardial cushions. The most important is rheumatic heart disease. The physical signs produced by mitral, aortic and tricuspid valve disease closely resemble those of endocardial-cushion defect, and several of our cases masqueraded as rheumatic heart disease in the medical outpatient department for years. The major clues are the ECG features described above and the radiological evidence of pulmonary plethora. Brockenbrough *et al.*[32] have even described patients with all the features of rheumatic mitral incompetence in whom the ECG and X-ray were of no assistance and yet at operation split mitral valves with small atrial septal defects were found. Two not uncommon congenital heart conditions, namely secundum atrial septal defect combined with a ventricular septal defect, and ventricular septal defect with tricuspid incompetence, should also be mentioned. It may be extremely difficult or even impossible to distinguish these conditions, but here again the ECG is of crucial importance.

Lastly, certain associations and complications of endocardial-cushion defects should be mentioned. Pulmonary stenosis has been noted in most series. In the presence of so many murmurs it is often difficult to distinguish the contribution made by the pulmonary stenosis. A loud and long murmur with a thrill at the pulmonary area, associated with wide splitting of the second sound, suggested the diagnosis in one of our patients. The difficulty of differentiating a flow gradient from true organic stenosis has already been discussed.[7] Secundum defects occur commonly with primum defects and were found in 12 of Wakai and Edwards' 28 specimens.[25] This is important for the surgeon to appreciate. Additional secundum defects were closed in 3 of our patients. A double mitral valve is another occasional finding[25] (5 of 28 specimens[25]) and was found in 2 of our patients at operation. In 1 patient 3 orifices were present. Other defects of the heart and great vessels are occasionally found, but have not been included in this analysis.

Mongolism has been found to be frequently associated with congenital heart disease,[26] endocardial-cushion defect being particularly common.[25] It was present in 2 of our patients. Bacterial endocarditis is said to be rare in endocardial-cushion defects. Only 6 cases were found in the literature up to 1958 by Wakai and Edwards.[25] It was encountered in 3 of our patients, and in a fourth 2 years after operation.

SUMMARY

1. The embryological development of the endocardial cushions and the malformations resulting in endocardial-cushion defects is discussed.

2. The haemodynamic changes associated with these defects are described.

3. Thirty-nine patients with these defects are analysed, 29 without ventricular septal defects and 10 with ventricular septal defects.

4. The signs and symptoms of endocardial-cushion defects are analysed and their dependence on the presence of an atrial septal defect, a ventricular septal defect, and malformed atrio-ventricular valves, discussed. The great difficulty of differentiating patients without ventricular septal defect from those with ventricular septal defect is emphasized.

5. The extraordinary value of the electrocardiogram in differentiating endocardial-cushion defects from secundum defects, from rheumatic heart disease, and from ventricular septal defect, is confirmed.

6. The radiological appearances do not help in differentiating secundum from cushion defects, but cardiac enlargement is generally greater with the latter.

7. Cardiac catheterization is most helpful in establishing the presence of an atrial septal defect, the size of the left-to-right shunt and the pulmonary vascular resistance. It often fails, however, to distinguish an endocardial-cushion defect from a secundum defect. Differentiation of an endocardial-cushion defect without a ventricular septal defect from one with a ventricular septal defect is even more difficult; intracardiac phonocardiography and left ventricular angiocardiography are the best techniques available. When a ventricular septal defect is present pulmonary hypertension and a reduced arterial oxygen saturation are usually found.

8. The treatment of endocardial-cushion defects is surgical operation with the pump oxygenator and cardiac bypass. A mortality rate of 2 in 20 patients without a ventricular septal defect and 2 in 5 patients with a ventricular septal defect compares very favourably with figures reported from other centres. Postoperative catheterization has been performed in 14 patients and has indicated considerable improvement in the majority but complete cure in only 6. Since the disease carries with it considerable disability and mortality, operation is recommended in all patients with the partial defect. The nature of the malformation in the complete defect is such that a high operative mortality is only to be expected. At present, operation is probably not worth while in the advanced cases, particularly if severe pulmonary hypertension coexists.

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