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THE PROGNOSIS OF ATRIAL SEPTAL DEFECT

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[WITH SPECIAL PLATE]

Atrial septal defect as an entity that could be recognized clinically was first described in this country by Bedford *et al.* (1941). Since then the diagnosis has been made with confidence and increasing frequency. The patients of earlier series were mostly between 20 and 40 years old, an age incidence very different from that of most congenital lesions; many in early life had noticed few symptoms, and often the physical signs had not even drawn attention to their hearts. We were therefore surprised when we began to see so many young patients with the classic picture, and thought that children with such large hearts, even when they had few symptoms, must have a more severe type of defect and a worse prognosis than patients seen in adult life. But this has not proved so, and hardly a child in this group has lost ground over the subsequent ten years. We have, of course, seen patients becoming worse during this time, but they were older, generally over 30 or even 40 years of age.

In view of the progress of surgical treatment, we wish to consider the natural prognosis of atrial septal defect. We have included some cases where the diagnosis was made on clinical grounds alone, as this gives a more balanced picture. If we include only those where it has been proved by catheterization there is a bias of selection, as most physicians do not advise this without some special reason, or did not until recently when surgical treatment became more practicable. We have included all patients where catheterization proved a left-to-right shunt into the right atrium, even if the shunt was partly due to anomalous pulmonary veins or if there was some degree of pulmonary stenosis (see Table II).

Diagnosis

The contrast between the paucity of symptoms and the large heart is characteristic of atrial septal defect. Nearly all the children are thin and slightly built, with a long, narrow chest and long limbs (the gracile habitus), but true arachnodactyly is rare. They often have a pigeon-chest with more prominence of the left side, and the more severe this deformity the greater the likelihood of a large heart and a large shunt.

Physical Signs

A good account of the auscultatory signs has been given by Leatham and Gray (1956). The most characteristic sign is the discrepancy between the small pulse and the widespread overactive precordial pulsation, seen all the more easily because of the thin chest. The excessive pulsation has three components: (1) an apex beat that is tapping in character and displaced outwards; (2) a right ventricular thrust or lift that is usually visible and almost always palpable in the third left intercostal space; and (3) a large pulmonary artery that may give rise to visible systolic pulsation in the second space and may be felt to thrust against the hand. A precordial thrill is frequently felt, but a striking "cat's purr" thrill is uncommon in atrial septal defect.

The radial pulse is small. The pulse pressure is rarely more than 40 mm. Hg and the systolic pressure usually 120 mm. or less, with lower levels in children. The jugular venous pressure is increased only if cardiac failure supervenes, but Reinhold (1955) has noted that in the jugular venous pulse there are often large *v* waves, frequently exceeding the *a* waves in amplitude.

The first sound may be abrupt and loud. The second sound is widely split and is slightly, but not much, louder than normal; it is not easily palpable unless the pressure is high. Wood (1950) and Barber *et al.* (1950) described *wide* splitting of the second sound as an important physical sign, and we have found it most valuable, but it is not common in children under 3 years of age or in patients with much pulmonary hypertension.

The systolic murmur of atrial septal defect is often heard first some months after birth rather than from birth; it is generally heard best in the second or third left spaces, but may be difficult to localize sharply. It is blowing rather than rasping, soft rather than loud. Considering how soft it is, it is well heard in the interscapular region at the back (Taussig, personal communication), perhaps owing to backward conduction through the large left pulmonary artery, as well as to the large heart and thin chest.

A blowing murmur in early diastole was heard at and below the pulmonary area in about one-eighth of our

patients, more often in older ones but once in a woman aged 20; it was thought to indicate pulmonary regurgitation. A short diastolic murmur at the apex was heard in half our patients, and more frequently in those who were seen several times and in those with a large shunt and a large heart. When this murmur becomes prolonged and continues to the first heart sound it is hard to exclude associated mitral stenosis, but this is less common than was thought, and cannot be diagnosed with certainty in life unless the catheter confirms a gradient across the mitral valve.

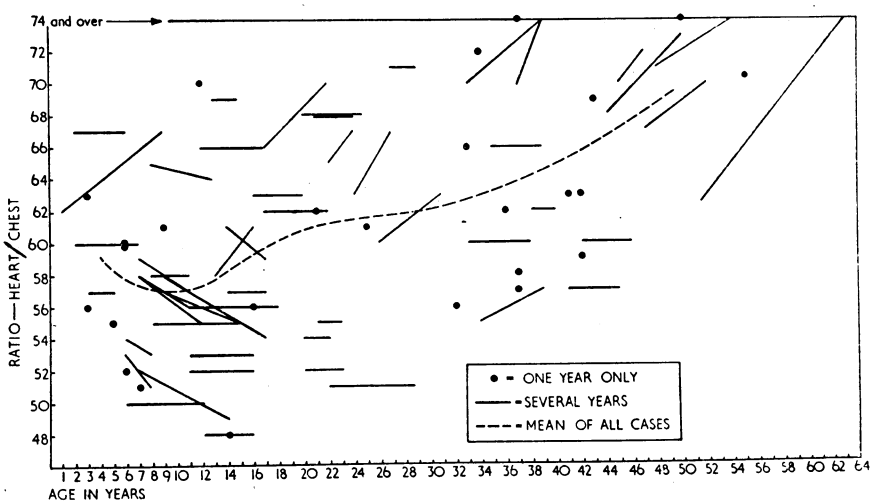
The physical signs are altered if severe pulmonary hypertension develops. The systolic murmur is softer and the second sound louder and easily palpable; the patient may be cyanotic and is more likely to have a pulmonary diastolic murmur. It may then be difficult to decide the site of the shunt, sometimes even after catheterization.

Radiology

This shows the triad of a large right side of the heart, large pulmonary arteries, and a hilar dance with expansile pulsation spreading to the smaller branches—features that were emphasized by Bedford *et al.* (1941). The negative findings on radioscopy—namely, absence of enlargement of the aorta, of the left ventricle, and of the left atrium—are equally important for diagnosis. The pulmonary arteries may become aneurysmal; later if they become thrombosed the pulsation may diminish.

As in most conditions, no heart shape is pathognomonic, though a film with the above features should suggest the possibility of an atrial septal defect, but can be due to mitral stenosis or other left-to-right shunts with secondary pulmonary hypertension. Typical examples are shown in the Special Plate: in Fig. 1 for children, in Fig. 4 for adults. and in Fig. 2 for those where the large right atrium is more prominent than in Fig. 1. The pulmonary trunk is often large before there is any rise of pulmonary arterial pressure (P.A.P.). The heart is sometimes smaller with the same prominent pulmonary arc, presumably when the left-to-right shunt is smaller.

Some less usual shapes are shown in Special Plate, Figs. 3 and 5. The heart is very large with a straight left border in Fig. 3 A, the pulmonary artery is so large that the heart looks rectangular in Fig. 3 B, and the right-sided enlargement is enough to make the heart appear tilted in Fig. 3 C. The pulmonary artery is often very large—in Fig. 5 A with a large heart and in Fig. 5 B with a heart that is smaller than usual, from a woman, now aged 43, who has been under observation with a large pulmonary artery for 30 years. Aneurysmal dilatation of the *right* atrium is seen in Fig. 5 C; the positions of the catheter on two separate films are both included to show that all this enlargement was the right atrium.



GRAPH 1.—Diagram showing changes with age in the cardio-thoracic ratio of hearts in atrial septal defect, and the average curve for all our patients. Some decrease is more common than an increase in the school period, and the average figure, after dipping from 59%, returns to this at 17 and is no more than 62% at 30 years. After this it increases more rapidly, but patients seen then are not likely to be doing well and others may not show this rise.

The Size of the Heart

At first we were surprised to see children with such large hearts, often with cardio-thoracic ratios (C.T.R.) of 60%, and thought that they must have unusually large defects and a poor prognosis, but this is not so. Large hearts are common at all ages, and the only striking difference is that hearts that are not very large (C.T.R. below 55%) are seen in about one-quarter of the patients under 30 but rarely after this age; and that enormous hearts (C.T.R. 70%) become common after 30 but not before. This might suggest that the heart increases slowly but progressively throughout life, but this does not happen for a long time. Generally it is large in infancy and childhood (C.T.R. 55–64%), and, having reached a position of equilibrium, remains about this size for 20 or 30 years, and only then starts getting larger as the patient gets more severe symptoms. The size of the heart as measured by the cardio-thoracic ratio at various ages is shown in Graph 1; the average is about 58% in the first decade, and does not pass above 62% till the start of the fourth decade. It was under 60% in two-thirds of those under 20 years, but over 60% in more than two-thirds of those over 30 years (Table I).

TABLE I.—*Heart Size with Age in Atrial Septal Defect*

Age (Years)	Cardio-thoracic Ratio				
	Up to 54%	55–59%	60–64%	65–69%	70% and Over
0–19	25	42	20	11	2
20–29	22	10	30	30	8
30–39	0	31	23	16	30
40–59	0	14	20	20	46

Many of the children have been followed up for five to ten years, and generally the heart size has remained the same during this time. In fact it has more often become smaller than larger. The only exception in the first decade in Graph 1 is wrongly included, as a clinical diagnosis of ventricular septal defect was wrongly changed to one of atrial septal defect after the first catheterization (see Case 2 below). There were, however, two exceptions in the second decade—two girls aged 13 and 18—where it increased during five years (C.T.R. 57–61% and 65–70% respectively). Otherwise an increase was never seen before the age of 18 and rarely before 25 years. Against this there were several cases, all in schoolchildren under 17, where the heart became smaller. This is too late for the change that takes place normally with growth when the heart assumes a lower and more vertical position; perhaps it becomes accustomed to the large flow when the children are not allowed to play energetic games, though leading a normal life otherwise.

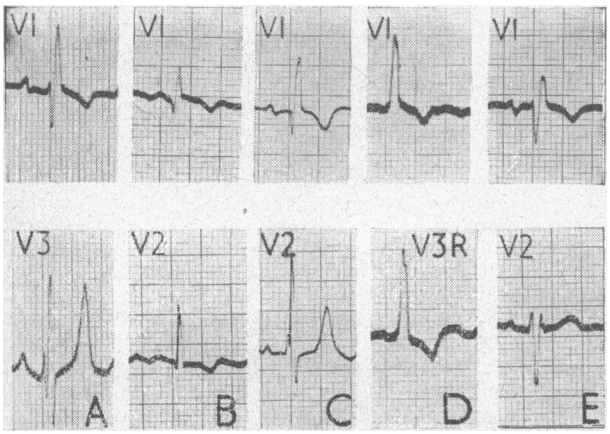
To sum up, the heart is very large in infancy and childhood and remains the same until about 25 or 35, when, with the onset of increasing symptoms, it may become still larger.

The Electrocardiogram

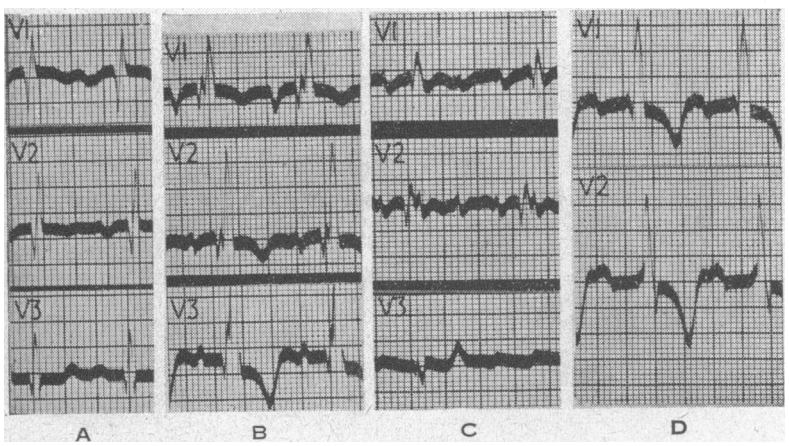
Bedford *et al.* (1941) found the P wave large or bifid in a quarter of their cases and the P–R interval prolonged in a third, but in our series of, in the main, younger subjects these changes have been less

common; they found the QRS width over 0.10 sec. in more than half. Barber *et al.* (1950) thought that "partial or complete bundle-branch block" was present in 95% of cases, and that the diagnosis should not be made without this unless proved by catheterization. The validity of this has been widely accepted, but it depends on the meaning to be attached to the term, and this has rarely been defined. We think the term should be avoided and a direct statement made about the presence of primary and secondary R waves and the width of QRS, for the pattern is one that is easy to accept at sight but more difficult to define. We define a primary R wave as one visible to the naked eye where the downstroke returns to or below the isoelectric line. Even the width of the QRS complex can be difficult owing to uncertainty about the exact end-point, especially with direct-writing machines; there may be an error of at least 0.10 sec. where R or S is slurred as it reaches the isoelectric line. When there has been any doubt we have taken the shorter estimate.

In 47 of our cases where the diagnosis was proved by catheterization or by necropsy the QRS width was no more than 0.09 sec. in 13, 0.10 sec. in 11, 0.11 in 8, and 0.12 sec. or over in 15. Where the QRS width was 0.10 sec. or less, there was neither a primary r wave nor notching of the R wave in four cases (Graph 2 B; Graph 3 A); there were only notched R waves in six (Graph 2 C and D), and in the remaining 14 there was a primary r wave with or without notching of R in addition, most often in V1 but sometimes in other chest leads. The primary r wave was generally small, often only 1 or 2 mm., and sometimes so minute that it was difficult to be sure about its presence (Graph 2 A, C, and E). Where the QRS was 0.11 sec. or more there was almost invariably a primary r wave, and when the QRS was 0.12 sec. or more it was generally fairly large. Of the 40 examples of V1 illustrated by Barber *et al.* (1950), 17 had moderate or large primary and secondary R waves often with some widening of the QRS complex, and 14 had a small primary r wave, but in our opinion three had only qr waves and six had only notched R waves, figures very similar to those in our series.



GRAPH 2.—Five electrocardiograms from proved cases of atrial septal defect showing less usual patterns. In each case the upper figure is Lead V1. (A) The primary r wave is very small in V1 but larger in V3. (B) Both leads V1 and V2 show only a qR complex. (C) qR complex only in V1, but enough notching of R in V2 to signify primary and secondary R waves. (D) Right ventricular hypertrophy due to pulmonary hypertension where the notching of R is shown in V3R but hardly in V1. (E) qR only or perhaps rsR′, with a very minute primary r in V1 and a less usual type of rSr′ in V2.



GRAPH 3.—Four electrocardiograms from proved cases of atrial septal defect with less usual patterns. In A there are QR waves only in V1 and V2. In B there is an unusual notched R wave preceded by a small q, and in C only qr waves, but in B and C the QRS width is 0.12 sec. In D there are only a very minute r and a small s before a large R, but again the QRS is nearly or quite 0.12 sec. in width.

We agree that the emphasis on this rSR′ pattern often with a wide QRS is valuable, and that in its absence the diagnosis should be made only after careful consideration; but some cases even with a large defect do not show features (Graph 2, B and C; Graph 3, A and C). Although a distinction has been made between true primary r waves and notching of R, the presence of either, however small, can help when there is doubt about the site of the defect; both may occur without any increase in the QRS width in normal hearts (Sokolow and Friedlander, 1949) and in other forms of congenital heart disease—perhaps in one-tenth of the cases—but are not so common in ventricular septal defect. Notching of the S wave alone is uncommon in atrial septal defect, and if this is the only change the diagnosis should be reconsidered in favour of a ventricular septal defect.

Neither the height of the primary r wave nor the degree of notching of R is closely related to the size of the heart or to the size of the shunt. Nor do they seem to have increased during the time many of these cases have been under observation. We do not know at what age these changes first appear, but it is early in childhood, and thereafter they remain static until progressive myocardial disease changes the pattern.

S–T depression and T-wave inversion occur in the older patients, especially where auricular fibrillation or cardiac failure supervenes. In younger patients such changes are uncommon in uncomplicated atrial septal defect, but occurred in one boy aged 18 without, and in one girl aged 16 with, pulmonary hypertension. They were, however, found in 3 of 6 patients with anomalous pulmonary venous drainage, all under 20 years of age. The greater frequency of S–T depression and T inversion was the only difference in the cardiograms of the two groups.

Differential Diagnosis

Failures to diagnose mild pulmonary stenosis or to recognize that a large septal defect might be ventricular were the most frequent errors. Now that surgical closure is possible, recognition of a left-to-right shunt at atrial level is not enough, for this may be partly or entirely from anomalous pulmonary veins or through a more primitive defect such as an ostium primum or a common A-V canal.

Ostium primum is important since severe symptoms may develop early, but it is fortunately uncommon after infancy. The defect extends downwards to the A-V valve and complete surgical closure may be impossible. A jet of blood from the left ventricle into the right atrium may be felt at operation, and this suggests the clues to a correct clinical diagnosis. The patient has all the signs and catheter findings of an atrial defect, but in addition there may be a pansystolic murmur due to mitral regurgitation, an enlarged left ventricle on screening, and a bizarre electrocardiogram showing left ventricular hypertrophy as well as the rSR′ pattern.

Anomalous pulmonary venous drainage is discussed later with the cases included in our series.

Ventricular septal defect is differentiated by the harsher and longer systolic murmur and the more purring thrill, maximal lower down the left sternal border. The second sound in the pulmonary area is not widely split, and this was the only sign militating against the defect being atrial in two cases where catheterization proved it to be ventricular. Where there was difficulty in deciding the site before catheterization, any suggestion of left ventricular hypertrophy on screening or electrocardiography was found to be a correct guide. A little apparent fullness of the left ventricle may be due to the heart's being pushed over by a large right ventricle, but if both seem about the same size the defect is almost certainly ventricular.

Simple pulmonary stenosis with a closed ventricular septum gives rise to a more rasping systolic murmur and thrill in the pulmonary area. We have confused these on occasion, before we realized how much pulsation there might be in the left pulmonary artery beyond the stenosis; this, however, rarely applies to the right pulmonary artery. In any case, there is no difficulty unless the pulmonary stenosis is slight or the atrial septal defect small, when the differentiation is not of so much practical importance.

General Difficulties

Even after investigations the diagnosis may still be difficult. In three cases the increase in oxygen saturation suggested a ventricular as well as an atrial septal defect; in one of these the clinical diagnosis of atrial septal defect alone was confirmed by necropsy, so well-mixed blood that included the flow through the defect was not obtained in the atrial sample, but only in the ventricular one; in the other two cases samples were obtained from the superior but not from the inferior vena cava, and this led to a wrong deduction that there was an atrial as well as a ventricular septal defect.

Generally, when there is pulmonary hypertension the left-to-right shunt persists, but may not do so always. In two patients who we feel sure have an atrial septal defect and pulmonary hypertension, catheterization confirmed the latter but showed no shunt. We think we have seen patients with a small atrial septal defect and with less distinctive signs, comparable with the *maladie de Roger*, but a shunt cannot be proved by catheterization unless it is 2 or 3 litres a minute. Cases of these two groups have been excluded.

No patients with cyanosis from infancy have been included, for we do not think that any of these had a reversed shunt secondary to pulmonary hypertension from an uncomplicated atrial septal defect. Of two cases where the final answer is known, one had a common A-V canal (Campbell and Missen, 1957), and a second had a left-to-right shunt into the atrium from anomalous pulmonary veins and a right-to-left shunt through the atrial septal defect owing to the presence of pulmonary stenosis (Case 1, Deucher and Zak, 1952).

TABLE II.—*Age and Sex Incidence of Atrial Septal Defect*

	Sex	Age (Years) 0–4	5–9	10–19	20–29	30–39	40 and Over	Total
A.S.D. proved by catheter or necropsy*	M	3	6	4	1	4	0	18
	F	1	8	2	4	14	11	40
A.S.D. clinical diagnosis	M	1	2	3	1	0	0	7
	F	3	5	7	8	2	2	27
A.S.D. and P.V.S. (proved by catheter)	M	0	2†	1	0	0	0	3
	F	0	2	2	1†	0	0	5
Total ..	M	4	10	8	2	4	0	28
	F	4	15	11	13	16	13	72
Total both sexes		8	25	19	15	20	13	100

* Includes 7 cases with anomalous pulmonary venous drainage.
† One case in each of these groups has been omitted because the shunt was small and the stenosis dominant.

Sex and Age Incidence

We have 66 cases where the diagnosis was proved by catheterization or necropsy, including seven with added anomalous pulmonary venous drainage and eight others with pulmonary valvular stenosis in addition. To these we have added the first 34 where the diagnosis seemed certain on clinical grounds, to make 100 in all (Table II).

Sex Incidence

There were 72 girls and women and 28 boys and men, a proportion of 2.5 : 1. The female preponderance was less among those with additional pulmonary stenosis or with anomalous pulmonary venous drainage, but these numbers are small. Taking all ages together, however, hides an interesting difference, for in those under 20 the sex incidence was more equal (30 girls and 22 boys), while in those over 20 it was very unequal (42 women and only 6 men). The mortality seems, therefore, to be more serious in men, though we have no direct evidence of this and the following figures are against it.

Brigden (1956), among patients referred to him after mass radiography, saw 52 where the diagnosis seemed certain after full clinical examination; their ages ranged from 17 to 65 years. The female preponderance (1.5 : 1) was not so high as in our series; it was the same in those under 30 and those over 30, and if they were divided into those under and over 35 it increased from 1.35 : 1 to 1.75 : 1 only. This is against any heavier mortality among men and makes our figures difficult to explain.

Age Incidence

Patients who have and those who have not had catheterization have been combined, since most of the former were children under 10 or women over 30, while more of the latter were 20 to 29—an age when most patients are too well to need investigation. Those who had pulmonary stenosis as well were, however, all under 14, except one woman, aged 22. Combining the figures, 33 were 9 years of age or less, 19 were between 10 and 19, 15 between 20 and 29, and 33 over 30, 13 of these being over 40—a much older age incidence than for most congenital diseases, although many more children were seen than in most previous series of atrial septal defect.

Course and Prognosis

Infancy

Many small children with a large shunt and a large defect suffer from recurrent respiratory infections and a slow gain in weight; often they show less dyspnoea, less susceptibility to infection, and less difficulty in gaining weight, after 2 years of age. Occasionally a large defect seems to be the cause of death in an infant; the reason is not obvious, as most patients survive without difficulty. Brinton and Campbell (1953) included two such infants, aged 2 and 7 months, among 55 necropsies of patients with congenital heart disease, and Bonham-Carter informs us that he has seen several examples. Apart from these we have seen no deaths from uncomplicated atrial septal defect before the age of 27 years, though two children with anomalous pulmonary venous drainage in addition have died.

First Decade

We have seen 33 children between 2 and 9 years of age and many have been followed up for six to ten years; 22 have had catheterization. With two exceptions all these have done well, without any loss of ground, without a raised pulmonary arterial pressure, and without any further increase in the size of the heart. The first exception, a girl aged 5, was admitted for attacks of cyanosis in three of which she had been semiconscious, and had a pulmonary arterial pressure of 74/10 mm., so that her outlook is uncertain. The second, a girl aged 8, with anomalous pulmonary venous drainage and probably an atrial septal defect in addition, seemed well, but had a large heart (C.T.R.

70%) and a P.A.P. of 100/65 mm.; she was not cyanosed and not much disabled, but died a year later at home with "bronchitis" which may really have been pulmonary arterial thrombosis (*Case 1**).

A third patient whose septal defect had been thought to be ventricular was included because catheterization seemed to show that it was atrial; during eight years he was often in hospital and his heart became larger (C.T.R. 62 to 68%), but recatheterization when his parents agreed to operation confirmed the original clinical diagnosis (*Case 2*).

Nearly all these patients have large hearts (C.T.R. generally 54–65%; one-third over 60%), but two have hearts of normal size and one of these had a large shunt.

Second Decade

Most of these patients were children under 15, and had been referred to hospital because of a murmur heard at school rather than because of symptoms; 9 of the 19 had catheterization. All but one are leading normal, quiet lives without increasing symptoms, and their pulmonary arterial pressures are normal although they have large shunts. All but three have large hearts (C.T.R. 56–68%).

The exception, a girl aged 12, had a very large heart, signs of mitral incompetence, and right-sided failure. Investigations showed a large atrial septal defect, at least one pulmonary vein entering the right atrium, and a pulmonary arterial pressure of 85/25 mm. that was due to the large flow and not to a raised resistance. She died after operation, and veins from the upper and middle right lobes drained into the right superior vena cava near its junction with the right atrium; opposite this there was a large atrial septal defect, and there was also slight mitral stenosis (Ross, 1956) (*Case 3*).

Third Decade

Even at this age, 10 of the 15 patients were sent to hospital because of a murmur and had few symptoms. Most of them had a large heart (C.T.R. 60–70%), though in three it was still no more than 54%. Five of the six who had catheterization, however, were increasingly dyspnoeic, three so much so that they had to give up work. Two had pulmonary hypertension severe enough to produce some reversal of the shunt and central cyanosis, one had a raised pressure of 87/27 mm., and the other two had right-sided failure soon after the onset of fibrillation, at 22 and 24 years. One of these died when she was only 27; true, this was after operation, but she had been in congestive failure for two years and would not have lived long (see Table III). One girl with a large heart (C.T.R. 68%) already had pulmonary regurgitation when she was 20, and central cyanosis (arterial oxygen saturation 84%) from a partially reversed shunt before she was 25; she said she felt well, but her pulmonary arterial pressure was 115/35 mm., and it is remarkable that she was able to do so much (*Case 4*).

These are the earliest ages at which we have seen auricular fibrillation, pulmonary regurgitation, or a reversal of the shunt in uncomplicated atrial septal defect, but cyanosis became apparent in three others near the end of this decade, and one of these died when 29 with extensive pulmonary thrombosis.

One-third of our patients lost ground seriously during the third decade, but the true proportion is certainly less, for there are others who had few symptoms till the next decade and those who were too well to seek medical advice at any time.

Fourth Decade

Of the 20 patients, 15 have had catheterization. Their hearts were very large, with cardio-thoracic ratios of 62–79%, and only two, both still well, had figures as low as 56%. Nine had little increase in their symptoms when they were seen, and the pulmonary arterial pressure seemed normal in two and was proved to be so in seven. The other 11 became severely disabled during this decade. Six of the 11 died: one with pulmonary embolism after pregnancy, one with acute pulmonary oedema, one with right-sided heart failure, and three with central cyanosis and pulmonary hypertension. The first two will be discussed later (see p. 1380); the third died with heart failure three years after the onset of fibrillation; and the other three, who died within four years of the onset of severe symptoms, had pulmonary hypertension and a reversed shunt. One of them, a man aged 34 with anomalous pulmonary venous drainage, had the usual picture of atrial septal defect and carried on his work till he was 32; he then became increasingly cyanosed and disabled and died with extensive pulmonary arterial thrombosis (Trounce, 1953) (*Case 5*). Of the remaining five, two had pulmonary hypertension with a reversed shunt and also right-sided heart failure, but in one of these the cyanosis was slight. The other three were handicapped by severe dyspnoea and right-sided failure; the pulmonary pressure was still normal in two, and was 72/18 mm. in the third, who has had a successful operation.

Fifth and Sixth Decades

Among the 13 patients, only two, aged 42 and 46, are still without severe symptoms, but both have large hearts and one has paroxysms of fibrillation.

Of the eight who had catheterization, two have pulmonary pressures at about the systemic level, and both have reversed shunts and are severely disabled, though one, now 45, had remained well without any mention of her heart till she was 40. Four had pulmonary systolic pressures between 56 and 80 mm.; in one of these the disability followed "pneumonia" which may have been pulmonary arterial thrombosis, but in the others it seemed due to the onset of auricular fibrillation rather than the rise of pulmonary pressure. Of the remaining two, one was still well and one was disabled by right-sided failure.

Of the five who did not have catheterization, one was well and one was still working with failure that had started soon after the onset of fibrillation. This was followed closely by severe symptoms in two others, but not for 10 years in the fifth. In the last of these we have no doubt that the pulmonary pressure was high and the shunt reversed (she has since died), but in the others cyanosis was no more than terminal.

Of the four patients who died, two died within a few years of the onset of severe symptoms, but the third lived for 10 years, and the fourth was well till she was 46, developed fibrillation at 56, and lived till she was 63. She was the oldest patient in our series, but since then we have seen a typical case in a woman, aged 66, who came to hospital only because of a urinary infection and was still leading an active life as manageress and was on her feet most of the day. She looked younger and was doing more work than most people of her age.

Coulshed and Littler (1957) have reported five typical cases of atrial septal defect in elderly patients: a woman aged 79, who was unaware of any cardiac defect till she was 54; two men aged 68 and 67, one of whom was still working as a fitter; and two younger patients, aged 58. Some of these were getting congestive failure, but all had been well and active during the greater part of their lives. Similarly, four of the patients of Brigden (1956) seen at mass radiography were over 55 and two were over 60 years of age.

Mode of Heart Failure and Death

In what ways do these patients become worse? We have taken all age groups together, and, including those with anomalous pulmonary venous drainage, 31 patients have reached a stage of incapacity that suggests how the heart is likely to fail or have already died. The most common cause is right-sided heart failure, and the next pulmonary hypertension with central cyanosis and some reversal of the shunt. Where a necropsy was available, some results are given in Table III.

*Five patients are numbered as Cases 1–5 to save repetition when they are referred to again.

With Right-sided Heart Failure (13 Patients)

In most of these the pulmonary arterial pressure was still normal or nearly so. In four of the 13 it was not measured; in six it was hardly raised, being normal in four and under 35 mm. in two; but in three it was rising (60, 85, and 105 mm.) although they were still acyanotic. Three reached the ages of 63, 44, and 39 respectively before they died. Four others died aged 47, 47, 27, and 12; though this was after operations, they had been in right-sided failure for some time and seemed unlikely to live long. One has been greatly improved by operation, and the others are able to carry on better than might be expected from their congestive failure.

TABLE III.—*Details of Necropsies of Patients with Atrial Septal Defect*

Sex	Age at Death	Age at Onset of Severe Symptoms	Age at Onset of Cyanosis	Age at Onset of Moderate Symptoms	Pulmonary Arterial Pressure (mm. Hg)	Heart Size (C.T.R.)	Heart Weight (g.)	Size of A.S.D. (mm.)	Cause of Death and Remarks
F	63	56*	T	46	—	62–80%	750	50×35	C.H.F. Very active till 41
F	56	45*	54	45	—	70%	600	38×28	Pulm. thromb. and C.H.F. Very well till 44
F	47	45*	—	41	60/25	69%	—	35×25‡	C.H.F.†
F	47	44*	—	(30)	—	68%	—	20 (diam.)	C.H.F.† Pulm. vein from right upper lobe to right S.V.C.
F	44	43*	T	43	—	69%	600	15×9	C.H.F. Very active till 43. Mitral stenosis
F	39	37*	T	35	—	69–73%	550	37×14	C.H.F. Mitral stenosis
F	38	35	31	31	140/62	64%	410	49×32	Pulm. thromb. Ostium primum. Active nurse till marriage at 29
M	34	31	32	?	80/10	75%	700	20 (diam.)	Pulm. thromb. and C.H.F. Pulm. veins to R.A. (Trounce, 1953)
F	32.	—	31	31	—	—	400	20×20	Pulm. emb. No symptoms till pregnancy
F	31	29	—	26	88/27	61%	—	25 (diam.)‡	†
M	29	27	27	24	64 m.	71%	680	24×17	Pulm. thromb. and C.H.F. Army service in Palestine
F	27	24*	—	24	30/9	62–68%	—	35 (diam.)	C.H.F.†
F	12	11	—	11	85/25	70%	550	30 (diam.)	C.H.F.† Pulm. vein from right upper lobe to right S.V.C. Mitral stenosis

* This was the age of onset of atrial fibrillation also. † Died after operation. ‡ Estimated at operation. T=terminal only.

With Pulmonary Hypertension and Central Cyanosis (11 Patients)

All but one of these have had catheterization and the pulmonary arterial pressure was generally about the systemic level. All had central cyanosis, though it was not always severe, and most had right-sided failure as well. Five have died and two seem unlikely to live long. In each of the four who had a necropsy the main pulmonary arteries were partly or almost completely occluded by layers of thrombosis (see Table III).

A rise of pulmonary pressure to near the systemic level nearly always causes severe disability, but Case 4 and one other patient were striking exceptions. A woman aged 35 led an active life, including hunting, although she had free pulmonary regurgitation, a pulmonary arterial pressure of 119/51 mm., a pulmonary resistance of 10 units, and a left-to-right shunt that had been reduced to a litre a minute.

Severe Symptoms with Some Rise of Pulmonary Pressure (5 Patients)

This is the third largest group. All five patients were becoming disabled with pulmonary systolic pressures between 56 and 90 mm., but had not developed right-sided heart failure. It is uncertain if they will die from right-sided failure before the pressure has risen high enough to reverse the shunt and make them cyanotic, so they cannot yet be put into either of the preceding groups. One had a successful operation and one has died after operation; only one other has died (Case 1).

Left-sided Heart Failure (1 Patient)

Left-sided failure in atrial septal defect is difficult to understand because the large volume output, and sometimes the high pressure against which it has to be expelled, throw much extra work on the right and none on the left ventricle. Dexter (1956), however, thinks that it occurs especially when there is also mitral disease. One of our patients who had right-sided failure and some central cyanosis certainly has severe orthopnoea as well. Since completing this series we have seen a case in a man aged 49, who presented with left ventricular failure and a blood pressure of 220/130 mm., where, to our surprise, the characteristic signs on radioscopy showed that a widely split second sound had been a correct clue to the diagnosis of atrial septal defect. He responded well to treatment with hypotensive drugs, and catheterization then showed a pulmonary flow of 9 litres a minute with a pulmonary pressure of 45/25 mm. and a resistance of only 3 units; since leaving hospital, however, he has developed right-sided failure. Another patient who clinically seemed an ordinary uncomplicated case died suddenly and unexpectedly with acute pulmonary oedema.

A woman aged 33 had led a normal quiet life. Her main complaint was palpitation since she was 15, probably paroxysmal tachycardia. When seen she had classic signs of an atrial septal defect with a large heart (C.T.R. 66%), and as her symptoms were not severe she was advised to continue her work as a clerk but to take more rest. Three weeks later she suddenly developed pulmonary oedema, and, after coughing up much frothy blood-stained fluid, died on the way to hospital. Necropsy was not performed. There was nothing to suggest that she had mitral stenosis as well, but this cannot be excluded, and she may have had a paroxysmal arrhythmia.

Pulmonary Embolism (1 Patient)

This woman, aged 31, was well before her pregnancy, but died from pulmonary embolism a week after her delivery by caesarean section; the shape of the thrombus suggested that it had originated in the right atrium, and no clot was found in the veins of the leg.

Comment

Bedford *et al.* (1941) emphasized how slight the dyspnoea may be considering the size of the heart, even for 20 years; then the dyspnoea becomes worse and within a few years there may be cyanosis on exertion and congestive failure. This and pulmonary infarction are the commonest causes of death, which rarely occurs before 30 and may not be till 60 years of age. The average age at death was 39 years in our series, 36 in that of Roesler (1934), and 37 in that of Burrett and White (1945). Wood (1950) says that there may be no symptoms till the third or fourth decade, after which congestive failure and central cyanosis may develop. Métianu and Durand (1954) agree that the first signs of heart failure are after the fourth decade, but add that after the onset of fibrillation death generally follows in a year. Bedford *et al.* (1941) found that fibrillation did not occur before the age of 50 unless there was also mitral stenosis. We agree with this general picture of the prognosis, but think that there are many exceptions to these last two statements.

Fifteen of our patients had auricular fibrillation. We do not know always if they had mitral stenosis, but of those where we do know from necropsy or operation, four had and five had not. Mitral stenosis was suspected and found at operation in one of the two youngest patients, aged 23

and 24, but was shown to be absent at necropsy in the other. The age at the onset of fibrillation averaged 39 years (by chance the same as the average age at death of those who have died), but we have not found it of such grave significance as some authors. Four of our patients are working two, four, five, and six years respectively after its onset, but two have recently been in hospital with second attacks of failure; three others are able to do something, but not to work, three, five, and six years after its onset. One other was severely disabled, but had a successful operation five years after the change of rhythm.

Four of the remaining seven with fibrillation have died, one, two, seven, and ten years respectively after its onset. The other three died after operation, but in at least two of them congestive failure was difficult to control and we think it unlikely that they could have lived more than five years after its onset. It is clear, therefore, that the onset of auricular fibrillation is generally serious: some patients will die within a year or two, though others will live for five or even ten years at a reduced level of activity.

Anomalous Pulmonary Venous Drainage

When all the pulmonary veins drain into a persistent left superior vena cava the condition may sometimes be recognized by the "cottage-loaf" shape of the heart. When only some of them drain into the right superior vena cava or directly into the right atrium the clinical diagnosis is extremely difficult. The cardiogram may help by showing unequivocal right ventricular hypertrophy with T-wave inversion across most of the chest leads at an early age, though Hickie *et al.* (1956) found no differences. We think the prognosis is rather worse, perhaps because the left-to-right shunt is a fixed one that cannot become smaller with exercise. The general picture and the haemodynamic effects are the same as with atrial septal defect, but on catheterization the oxygen saturation in the right atrium is often very high—over 85%—and remains so throughout the right side of the heart. These two points may lead to the correct diagnosis, but selective angiocardiography and dye studies may be needed before operation when there is a left-to-right shunt at atrial level without the classic findings of an ostium secundum defect.

Surprisingly, none of our patients had the characteristic cottage-loaf-shaped heart, though many such have been described (Snellen and Albers, 1952; Gardner and Oram, 1953; and Whitaker, 1954). Gott *et al.* (1956), however, analysing 30 cases of total anomalous pulmonary venous return, 23 of which were verified at necropsy, thought that the heart was more often box-shaped, most patients having slight cyanosis and a systolic murmur that was not diagnostic; and they found that the most common pathways were into a persistent left superior vena cava, the coronary sinus, or the right atrium.

It is difficult to generalize about our mixed series of patients, for they range from those with few symptoms to those with serious symptoms, sometimes with severe pulmonary hypertension that in two cases led to death. In the minor cases we think only one or two pulmonary veins, most often from the right upper lobe, drain into the right atrium, while in the more severe cases half or more of the pulmonary veins drain into the right side of the heart; in addition there is often a left-to-right shunt through an atrial septal defect.

Of our seven patients, four were relatively well, though the size of the shunt suggested that all the venous return from one lung (the right) entered the right atrium (unless part of the shunt was through an atrial septal defect as well). In these four, including one man aged 38, there was no cyanosis and the heart was of normal size. The pulmonary arterial pressure was normal in three and 50/17 mm. Hg in the fourth, a youth of 18, who had also situs inversus and bronchiectasis. The other three patients all had large hearts (C.T.R. over 70%); two were cyanotic; in two there was severe pulmonary hypertension, and in the third the right ventricle was not entered at catheterization. Two have died (Cases 1 and 5), and we are not certain of the complete diagnosis in the third, a boy aged 2, but think the left-to-right shunt was from pulmonary venous drainage into the superior vena cava and the right-to-left shunt through an atrial septal defect, perhaps an ostium primum.

We have not included two patients, both of whom had an operation, where the septal defect seemed to be of major importance, though one or more pulmonary veins drained into the right atrium. In one the atrial septal defect was closed and the right pulmonary vein that entered the right superior vena cava successfully transplanted, but she died suddenly six weeks later and necropsy did not reveal the cause. In the other (Case 3) a vein from the right lower lobe also was thought at catheterization to drain into the right atrium, but only the veins from the middle and upper lobes actually did so, and we know of other examples of this mistake, so that it is clearly difficult to be sure whether the catheter has entered this vein from the right or from the left atrium.

Nor have we included a few cases where the main abnormality was elsewhere and it was only at catheterization that a pulmonary vein was found to enter the right atrium. For example, a woman with pulmonary stenosis and a right-to-left shunt through an unsealed foramen ovale has done well for seven years after a successful valvotomy, and the pulmonary vein that entered the right atrium had no obvious effect on the clinical picture. This was also the case in a girl, aged 9, who was thought to have pulmonary atresia with a patent ductus, where a subclavian–pulmonary anastomosis on the other side led to great improvement.

Atrial Septal Defect with Pulmonary Stenosis

In general, there is no gradient across the pulmonary valve as the result of the large pulmonary flow. There are, however, some patients with a gradient of doubtful significance and others with undoubted pulmonary stenosis. The systolic gradient was 5, 6, and 9 mm. respectively in three and 13 mm. in two others; possibly the last two had trivial stenosis, but even in retrospect the physical signs hardly justified this diagnosis, though the systolic murmur had been noted as loud in the pulmonary area. One of them was recatheterized after five years and again found to have a gradient across the pulmonary valve—this time of 8 mm. We think that no significance should be attached to gradients of less than 10 mm., and probably of less than 20 mm.

We have seen 12 patients with some degree of pulmonary stenosis—that is, with a systolic gradient of 20 mm. or more; generally it was not difficult to make the double diagnosis on clinical grounds. The patients usually have few symptoms, and to some extent the separate malformations compensate for each other, though both throw extra work on the right ventricle. We have included eight of them in Table II because, in spite of the stenosis, there was a large left-to-right shunt (and two others of this type have been seen since), but in the other two the pulmonary stenosis was the main lesion and the left-to-right shunt had always been or had become small.

In seven of the 12 the atrial septal defect was the main lesion, the left-to-right shunt being large—4–14 litres a minute—and the pressure gradient across the pulmonary valve small—between 20 and 40 mm. In three interesting cases, however, both lesions were important, since the left-to-right shunt was very large—7–14 litres a minute—and the pressure gradient between 70 and 90 mm. In the other two the dominant lesion, both clinically and on catheterization, was pulmonary stenosis and the left-to-right shunt was less than one litre a minute; it is surprising that the shunt had not been reversed, and likely that it will be. These two patients showed a striking *a* wave in the jugular pulse, so in atrial septal defect it may sometimes indicate associated pulmonary stenosis, though more commonly pulmonary hypertension (Reinhold, 1955). The stenosis was at the pulmonary valve in all of them, but in one it was thought to be infundibular as well.

Underdevelopment and recurrent respiratory infections had been present in five of the ten patients with large shunts, but not in the two with dominant pulmonary stenosis. In all ten the cardiac murmur was typical of pulmonary stenosis, even when the stenosis was mild with a pressure gradient of only 20–40 mm.; the harsh grating murmur and thrill maximal in the second left space, produced by the narrowed valve, might indeed be expected to obscure the more diffuse and fainter murmur typical of atrial defect. The pulmonary component of the second sound was diminished in the five with more severe stenosis, and was widely split in four of the seven with a large shunt and mild stenosis.

The physical signs were thus predominantly those of pulmonary stenosis, even where this was the minor lesion. Screening, however, revealed increased pulmonary arterial pulsation seen farther out in the lung fields than in pulmonary stenosis, though only in three a hilar dance. The discrepancy between physical signs and radioscopy was the usual reason for catheterization. The cardio-thoracic ratio ranged from 52 to 65% in those with a large shunt, but was normal in the two with dominant stenosis.

The electrocardiogram showed the usual rsR′ pattern in V1 in eight patients, but in three of these the tall secondary R wave and slight S-T depression or T inversion indicated more right ventricular preponderance than in most children with uncomplicated atrial septal defect. The case of the child with infundibular stenosis was unusual and had dominant S waves all across the chest leads. The usual picture of right ventricular preponderance was found in the two patients with dominant stenosis and in one of the three with a large shunt and moderate stenosis.

Only three of the group were over 20 years of age, but during the three to nine years they have been followed up they have shown no progressive symptoms and, with one exception, no increase in heart size.

Haemodynamic Findings

We have adequate data of cardiac catheterization in 46 patients, excluding those with added pulmonary stenosis. A large left-to-right shunt and a large pulmonary flow without any rise in pulmonary arterial pressure or resistance were found in nearly all the children and in nearly half the adults (Group A). In the remainder the haemodynamic findings were different: instead of being normal, the pulmonary arterial pressure was increased, the systolic pressure being at least 50 mm. and generally much more, and often the resistance also was increased. These can be divided into two groups: eight who still had a large left-to-right shunt and were clinically acyanotic (Group B), and nine who had a pulmonary pressure high enough to make the left-to-right shunt smaller, though sometimes still large, and to cause a right-to-left shunt and varying degrees of central cyanosis (Group C).

Group A: With a Large Left-to-right Shunt but no Increase of Pulmonary Arterial Pressure or Resistance (29 *Patients*).—This group included 17 of the 19 children and 12 of the 27 adults. The children were all between 6 and 13 except one boy aged 17, since we have had little occasion to investigate, or even to see, patients between their leaving school and reaching 25 years of age. Only two of the adults were under 30, and the average age was 36 years.

Most of the physiological data were normal, including the systemic flow and the pulmonary arterial pressure and resistance. Clinically, the patients were without central cyanosis, and the arterial oxygen saturation was always 94% or more. The systemic flow was normal, averaging 4.7 litres a minute in the adults and 4.0 litres a minute in the children, and the cardiac index (cardiac output per unit of surface area) was normal in the children but lower, and sometimes a little below normal, in the adults. Naturally the pulmonary flow was greatly increased. In the children it was generally between 8 and 12 litres and averaged 10 litres a minute, and in the adults it was generally between 10 and 16 litres and averaged 13.3 litres a minute. This means the shunt was large, and on the average 62% (generally between 50 and 75%) of the blood that reached the left atrium from the lungs passed to the right atrium and back to the lungs, and only 38% passed to the left ventricle. The pulmonary resistance was always normal or reduced; it averaged 1.1 units and was never above 2.0 units. Thus in spite of the very large flow the pulmonary arterial pressure was normal or only slightly raised, the highest figures being 44/10, 42/7, and 40/12 mm. Hg; it averaged 30/11 mm. in the children and 30/10 mm. in the adults.

All the children and several of the adults were still leading a fairly active life, but four of the latter had suffered from congestive failure. Clearly, congestive failure can occur, and it seems likely that it can prove fatal, before there is any great rise of pulmonary arterial pressure or any great reduction in the large left-to-right shunt.

Group B: With a High Pulmonary Arterial Pressure, but Still with a Large Left-to-right Shunt and no Right-to-left Shunt (8 *Patients*).—Five of these were adults with an average age of 39 years, but a boy aged 19, and two girls aged 5 and 12, reached this group earlier in life. We do not know why they behaved in this way—unusual for their age—but patients with a large pulmonary flow vary greatly in the length of time needed to develop any progressive rise of pulmonary arteriolar resistance, depending perhaps on the degree of intra-arterial thrombosis. Some have not done this after 50 years; about half our patients did so after 25–40 years, and a few did so sooner. These differences are the same as those we have found in cases with a large left-to-right shunt through a persistent ductus arteriosus where the tendency to develop increasing pulmonary resistance seems even less. In one girl who also had anomalous pulmonary venous drainage (Case 3) the flow was so large that the pulmonary pressure was 85/25 mm. though the resistance was only 2.0 units; in the other girl it was 3.5 units and the pressure (in the right ventricle) 74/4 mm.

In these eight patients the systemic flow was only a little lower than in the first group—3.9 instead of 4.7 litres. There was as yet no change in the size of the left-to-right shunt or of the pulmonary flow, which averaged 12.3 litres a minute. This means that 68% of the inflow to the left atrium shunted through the atrial septal defect—at least as high a proportion as in the first group. The pulmonary arterial pressure had increased to an average figure of 82/30 mm., but in spite of this the pulmonary resistance was normal or only slightly increased. Clinically, most of these patients were acyanotic, but two showed the degree of cyanosis that may be seen with mitral stenosis when the heart is failing. The arterial oxygen saturation was always between 90 and 95%, so a small right-to-left shunt may have been developing although the shunt was still predominantly left-to-right.

Group C: With a High Pulmonary Vascular Resistance, a Diminishing Left-to-right Shunt, and Increasing Right-to-left Shunt (9 *Patients*).—All these were between 33 and 52 except two, aged 24 and 27 years. Most of them were developing a tinge of cyanosis, and many showed deep central cyanosis. The arterial oxygen saturation averaged 86%; it was between 72 and 88% in all but three, where it was between 91 and 93%.

The systemic flow was further reduced; it averaged 3.4 litres a minute, and was above 4.0 litres in one patient only. The pulmonary flow was larger than the systemic, but small compared with the previous groups; it averaged 5.2 litres a minute and was never above 7.0 litres. The shunt was more difficult to calculate because of the additional right-to-left shunt, but, except perhaps in two patients, it was always present, and on the average 34% of the blood reaching the left atrium from the lungs shunted to the right atrium.

The pulmonary arterial pressure was always high, generally about the same as the systemic pressure; it averaged 104/39 mm., but once it was lower and once a good deal higher (140/62 mm. against 120/85 mm.). The pulmonary resistance was greatly increased, generally to 5–10 units and once much more than this.

The Pressures in the Atria

Generally the pressure in the left atrium is a little, if at all, above that in the right to account for the large left-to-right shunt. We agree with the view of Barger *et al.* (1948) and Dexter (1956) that the atria act as a single chamber, the flow depending on the resistance in the two ventricles and their circuits.

We did not find any significant difference between the pressures in the right and left atria. In no case was the difference in the systolic pressure more than 3 mm., and sometimes it seemed slightly higher in the right. On the average the pressure was 10.1/3.2 mm. in the left atrium and 9.6/2.4 mm. in the right, and, where only mean pressures were measured, 5.7 mm. in the left and 5.5 mm. in the right—figures that are substantially the same. The left atrium was entered in 25 of our 46 cases, but the pressure was measured in only 18 of these. There was no difference as between the children and adults except that the left atrium was entered more often in adults.

Changes Found on Recatheterization

The occasion to repeat catheterization in the same patient does not often arise, but there are five cases where, for various reasons, this was done. In the first, a boy aged 5, the right ventricular pressure five years later had fallen from 34/1 to 22/1 mm.; the only conclusion to be drawn is that a small rise does not always mean that it will be progressive. The second patient had a very large shunt when she was 47 and was verging on congestive failure, but was not much worse seven years later; her right ventricular pressure had risen from 33/5 to 56/5 mm. without any change in the large left-to-right shunt. Both these patients were acyanotic and in both the arterial oxygen saturation was over 95%. The third patient, aged 44, with congestive failure and slight cyanosis (arterial oxygen saturation 91%), had a P.A.P. of 59/25 mm., and two years later it had risen to 68/26 mm. without any great change in her general condition. The fourth, aged 34, had congestive failure and gross tricuspid incompetence, and during the next year her pressure rose from 95/30 to 110/45 mm., but she was still acyanotic and still had a large left-to-right shunt. The fifth patient had reached a later stage with a right-to-left shunt and an arterial oxygen saturation of 86% when she was first catheterized at the age of 33; four years later she was more disabled, more persistently cyanotic, and the left-to-right shunt had fallen from 3.5 litres to under 1 litre per minute, but the pulmonary pressure was unchanged (100/36 mm.).

Summary and Conclusions

We have discussed the physical signs and radiology of 100 patients with atrial septal defect, in two-thirds of whom the diagnosis was proved by catheterization or necropsy. We have tried to assess the course and prognosis from their history and from the progress of those who have been observed for several years.

After infancy has been passed, the first two decades are a good period when the patients lead a life that is nearly normal but generally without active games. We think that 95% are still doing well when they are 20, and 85% when they are 30 years of age. The prognosis in the fourth and fifth decades is much less good, and only about half of those seen at hospital are still well at 40 and less than a quarter at 50 years. The children are, we think, a representative sample, but adults are less likely to be seen unless they have symptoms, so the real prognosis is better; this is supported by the chance finding of older patients with atrial septal defect at mass radiography and elsewhere.

Usually in early childhood the electrocardiogram already shows the rSR′ pattern; the QRS is widened to more than 0.10 sec. in only about half, and a quarter do not show real primary and secondary R waves, though often these show some notching of the R wave. Usually the heart is large, often with a cardiothoracic ratio between 55 and 65%—a size that would generally indicate a poor prognosis—but nearly all patients who survive the first year or so do well without the heart becoming any larger till 25, and more often 35, years of age. Then in an increasing number, but not in all, the strain of the large right ventricular output produces increasing dyspnoea, sometimes made worse by the onset of auricular fibrillation, and ultimately right-sided heart failure. This may happen while the pulmonary arterial pressure is still normal in spite of the large pulmonary flow. In others, however, though rarely before 30, the pressure gradually rises, sometimes high enough to reverse the shunt and produce central cyanosis. Such patients have a higher incidence of pulmonary arterial thrombosis, which may be extensive; it may be the cause of the rising pressure rather than the consequence.

Nearly always for 25 years, and sometimes for 50 years, the shunt through the atrial septal defect remains large, so that the pulmonary flow is between 10 and 16 litres with a normal systemic flow of 4 or 5 litres a minute. In the smaller number where the pulmonary arterial pressure rises to about systemic level, the left-to-right shunt may gradually be mixed with a smaller right-to-left shunt and may in the end become quite small.

About one-tenth of patients with an atrial septal defect have some pulmonary veins from the right lung draining into the right atrium or large veins. Nearly the same proportion have some degree of pulmonary valvular stenosis as well as the atrial septal defect, still with a large left-to-right shunt and its characteristic features. In some of these reversal of the shunt seems likely, though we have not seen this happening.

We have not discussed the surgical treatment of atrial septal defect; at present several methods are in use and a standard perfected method is still being developed. In general, although there is no risk of bacterial endocarditis, the disability and the course and prognosis are not very different from, but rather worse than, those of persistent ductus arteriosus. Surgical treatment is, therefore, likely to become a routine procedure.

References

Barber, J. M., Magidson, O., and Wood, P. (1950). *Brit. Heart J.*, **12**, 277.
Barger, J. D., Edwards, J. E., Parker, R. L., and Dry, T. J. (1948). *Proc. Mayo Clin.*, **23**, 182.
Bedford, D. E., Papp C., and Parkinson, J. (1941). *Brit. Heart J.*, **3**, 37.
Brigden, W. W. (1956). Personal communication.
Brinton, W. D., and Campbell, M. (1953). *Brit. Heart J.*, **15**, 335.
Burrett, J. B., and White, P. D. (1945). *Amer. J. med. Sci.*, **209**, 355.
Campbell, M., and Missen, G. A. K. (1957). *Brit. Heart J.*, **19**, 403.
Coulshed, N., and Littler, T. R. (1957). *British Medical Journal*, **1**, 76.
Deuchar, D. C., and Zak, G. A. (1952). *Guy's Hosp. Rep.*, **101**, 1.
Dexter, L. (1956). *Brit. Heart J.*, **18**, 209.
Gardner, F., and Oram, S. (1953). Ibid., **15**, 305.
Gott, V. L., Lester, R. G., Lillehei, C. W., and Varco, R. L. (1956). *Circulation*, **13**, 543.
Hickie, J. B., Gimlette, T. M. D., and Bacon, A. P. C. (1956). *Brit. Heart J.*, **18**, 365.
Leatham, A., and Gray, I. (1956). Ibid., **18**, 193.
Métianu, C., and Durand, M. (1954). In Donzelot, E., and d'Allaines, F.: *Traité des Cardiopathies Congénitales*. Masson, Paris.
Reinhold, J. (1955). *British Medical Journal*, **1**, 695.
Roesler, H (1934). *Arch. intern. Med.*, **54**, 339.
Ross, D. N. (1956). *Guy's Hosp. Rep.*, **105**, 376.
Snellen, H. A., and Albers, F. H. (1952). *Circulation*, **6**, 801.
Soklow, M., and Friedlander, R. D. (1949). *Amer. Heart J.*, **38**, 665.
Trounce, J. R. (1953). *Guy's Hosp. Rep.*, **102**, 140.
Whitaker, W. (1954). *Brit. Heart J.*, **16**, 177.
Wood, P. (1950). *Diseases of the Heart and Circulation*. Eyre and Spottiswoode, London.

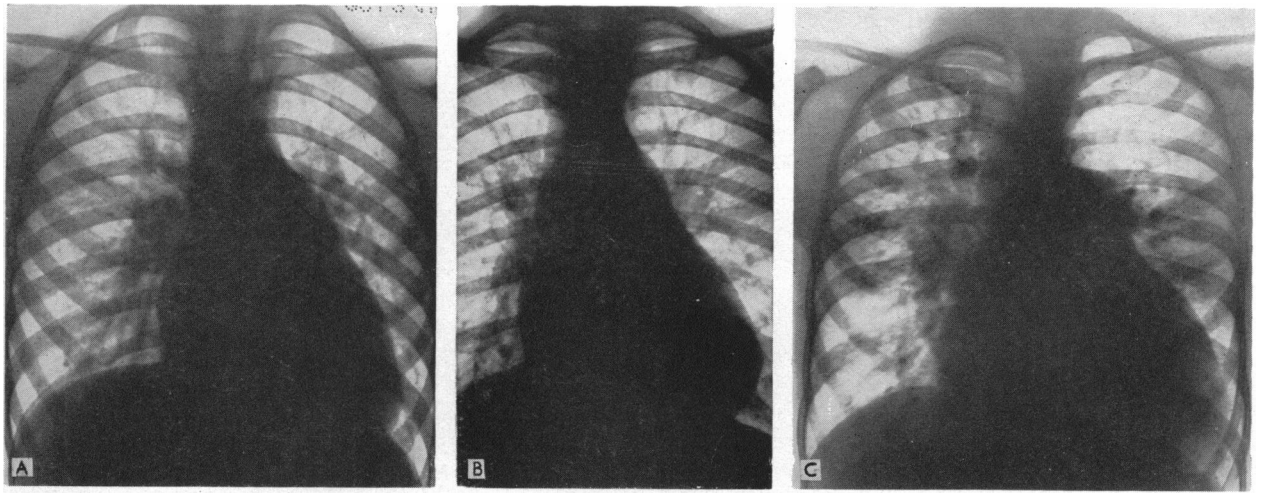


FIG. 1.—Characteristic teleradiographs from children with atrial septal defect. (A) From a girl aged 10 (C.T.R. 55%; P.A.P. 39/0 mm. Hg). (B) From a girl aged 10 (C.T.R. 55%; P.A.P. 42/5 mm.). (C) From a girl aged 14 (C.T.R. 67%). All three patients in good health six years later.

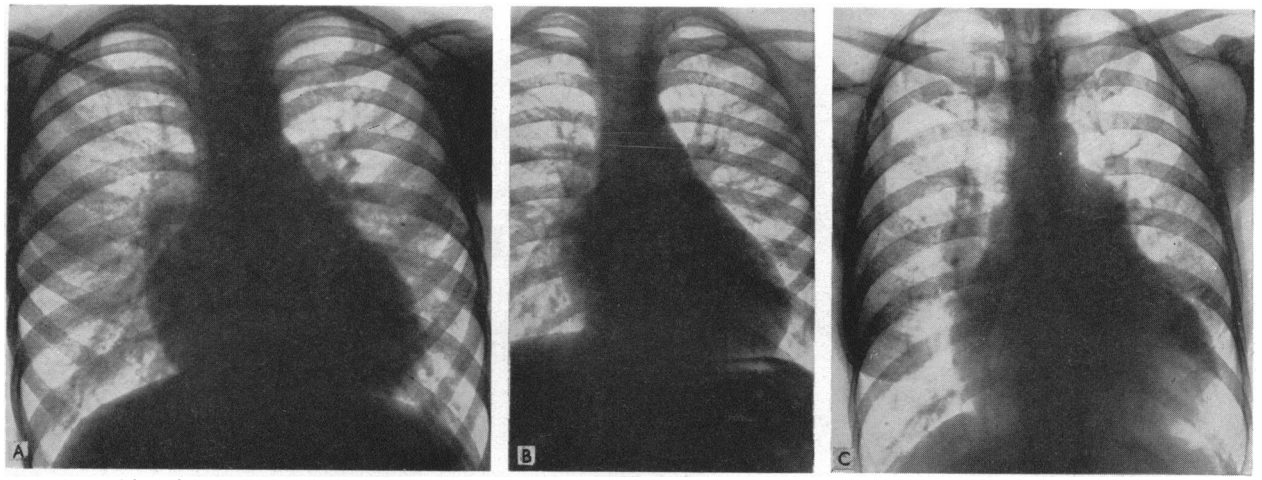


FIG. 2.—Teleradiographs characteristic of atrial septal defect with greater prominence of right atrium. (A) From a girl aged 9 (C.T.R. 60%; P.A.P. 40/? mm.). (B) From a boy aged 11, whose heart has since become smaller (C.T.R. 60%; P.A.P. 35/? mm.). (C) From a woman aged 48 (C.T.R. 70%; P.A.P. 33/12 mm.).

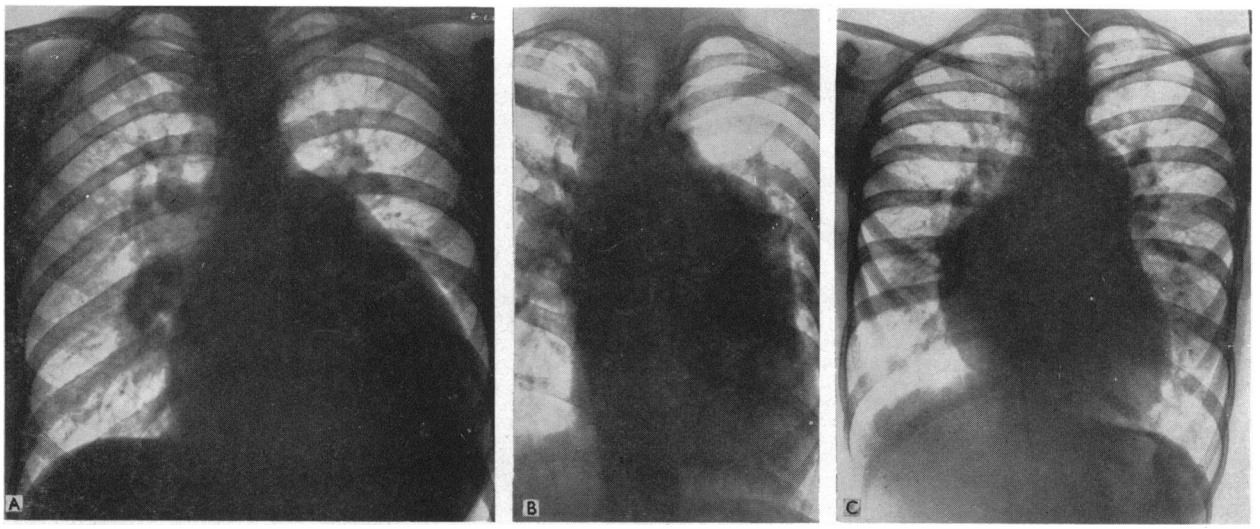


FIG. 3.—Three large hearts with shapes that are less usual in atrial septal defect. (A) A very large heart from a man aged 27 (C.T.R. 66%; P.A.P. 64 mm. mean). (B) A very rectangular heart owing to the large pulmonary trunk, from a boy aged 16 (C.T.R. 63%; P.A.P. 74/56 mm.). (C) A heart that appears lop-sided from the very large right atrium, from a woman aged 26 (C.T.R. 63%; P.A.P. 87/27 mm.).

M. CAMPBELL, C. NEILL, AND S. SUZMAN: ATRIAL SEPTAL DEFECT

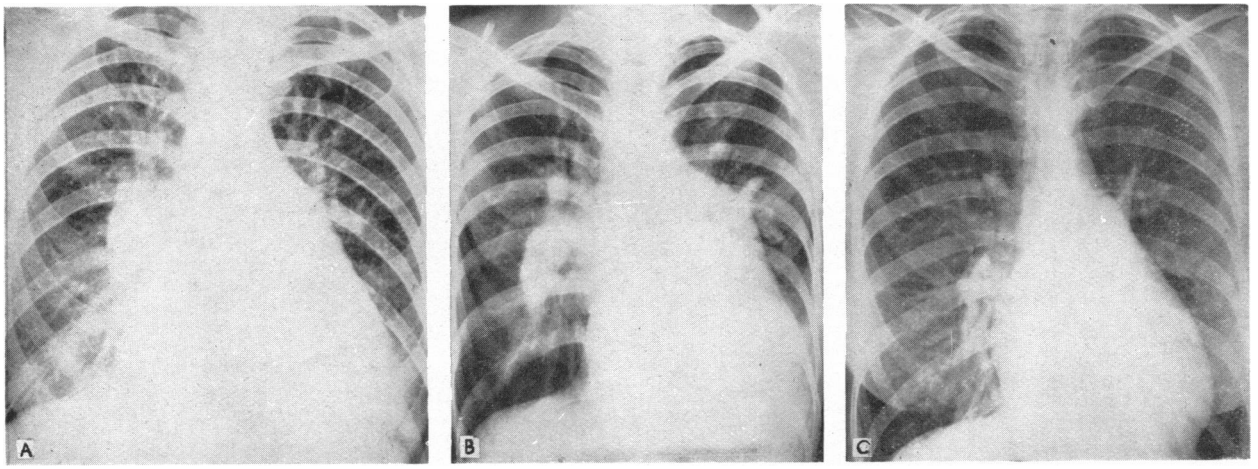


FIG. 4.—Characteristic teleradiographs from adults with atrial septal defect. (A) From a woman aged 37 (C.T.R. 63%; P.A.P. 30/13 mm.). (B) From a woman of 33 (C.T.R. 60%; P.A.P. 100/40 mm.). (C) From a woman aged 37 (C.T.R. 57%; P.A.P. 27/7 mm.).

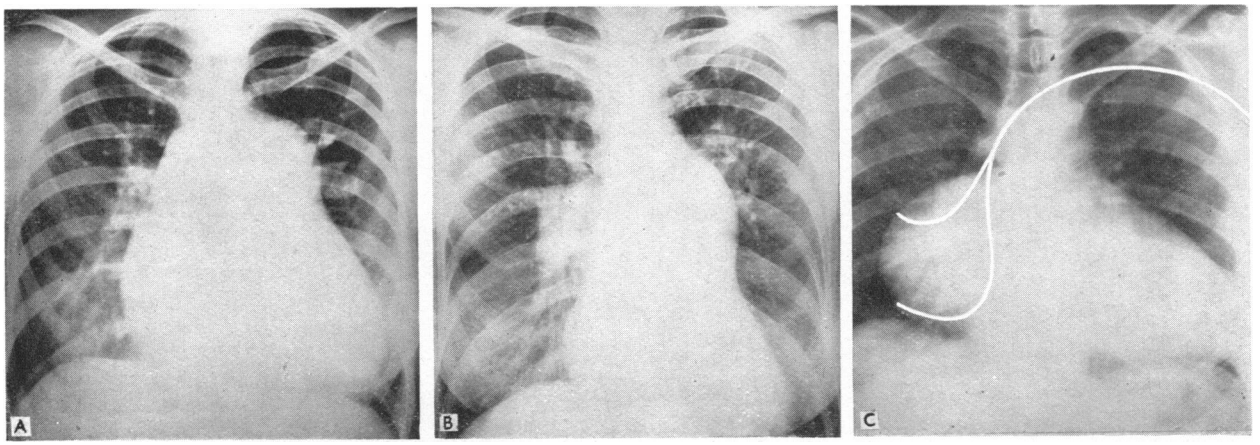


FIG. 5.—Three more hearts of unusual shape, all from adults with atrial septal defect. (A) From a woman aged 20, the youngest example of pulmonary regurgitation from hypertension (C.T.R. 68%; P.A.P. 115/35 mm.). (B) Unusual prominence of pulmonary artery which has been noted for 30 years without gross enlargement of heart, from a woman now aged 43 (C.T.R. 56%). (C) Aneurysmal dilatation of *right* atrium as demonstrated by two positions taken up by the catheter, from a nurse aged 37, who is still doing some work four years later (C.T.R. 79%; P.A.P. 11 mm. mean).

A. M. STEWART AND J. McKENZIE: FOETAL SEX DETERMINATION

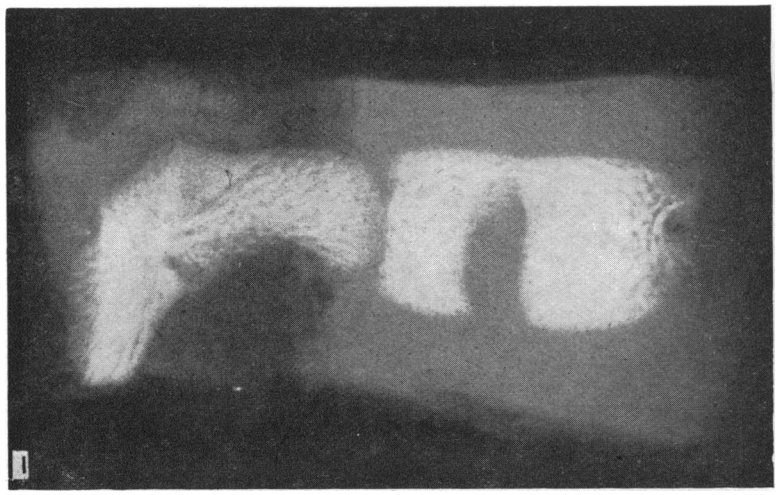


FIG. 1.—Radiograph of dissected specimen of coronal cleft vertebra showing typical defect. (×6.)

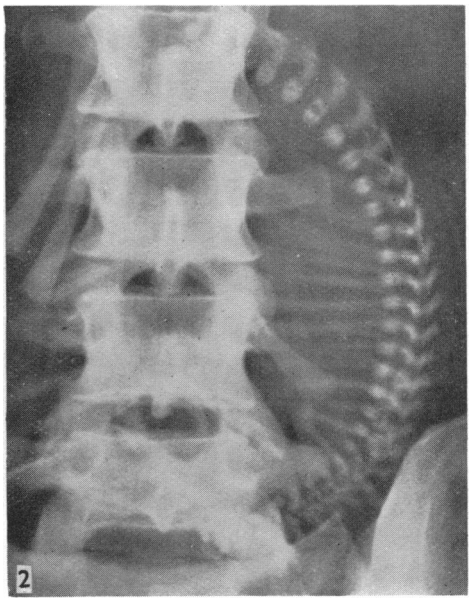


FIG. 2.—Postero-anterior radiograph of intrauterine foetal spine demonstrating almost complete coronal cleft of LV 2 and partially closed cleft of LV 3 and 4.