VENTRICULAR SEPTAL DEFECT WITH A NOTE ON ACYANOTIC FALLOT'S TETRALOGY

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In reviewing all cases of congenital heart disease in which the diagnosis has been proved by means of cardiac catheterization at the National Heart Hospital and Brompton Hospital since 1948, we have been impressed with the infrequency with which cases of ventricular septal defect (V.S.D.) of the classical *maladie de Roger* type have been encountered. In the majority of cases sent to us with this label, the diagnosis proved wrong. On the other hand, most cases of V.S.D. were characterized by clinical features in no way covered by Roger's description, and these also had been frequently mislabelled. It is high time, therefore, that the clinical features of these two conditions (V.S.D., and its mild form that alone can be called the *maladie de Roger*) were reviewed.

HISTORICAL

Roger published his classical description of "a communication between the two ventricles without morbus ceruleus" in 1879. A few excerpts from Wozencraft's translation of this paper (Willius and Keys, 1941) are pertinent to our thesis: "This cardiac anomaly has no objective symptom which the eye can recognize; it is dependent almost entirely on auscultation, . . . a murmur of remarkable intensity . . . accompanied by no other physical signs (save only the purring thrill) . . . without alteration of general health." The murmur was maximum in "the superior third of the precordial region, and median." It was "greatly prolonged, beginning with systole and always covering the two normal sounds: . . . the murmur is coincident with a strong impulse of the total mass of the heart, without any very appreciable impact at the apex. . . . In spite of the existence of an uncomplicated defect of the interventricular septum, patients may attain or even surpass the average span of human life." Roger's interpretation of the bruit was based on a chance autopsy he had performed in about 1861 on a boy of 12 who had died as a result of comminuted fracture; the boy had not been cyanosed in life, yet there was a "failure of occlusion of the interventricular septum in its upper portion, without concomitant stenosis of the pulmonary artery." Roger was criticized for lack of autopsy proof of his thesis.

In 1877 Decaisne published an autopsy report on an acyanotic girl aged 26 months, who died of "*some pulmonary mishap*" six weeks after being admitted to hospital. The clinical findings included a typical systolic murmur and thrill of the type described by Roger; but there was also "*considerable bulging*," and as previously stated *the child died*. In reciting this case Roger stated that *pulmonary stenosis was excluded clinically because of the absence of cyanosis*. At autopsy the ventricular walls showed no alteration, but in the upper portion of the interventricular septum there was an orifice establishing a communication between the two ventricles. Roger regarded this information as giving him "proof on all points."

Reluctantly, we wish to dispute this: the italics in the above quotations are ours, and they signify that Roger was unaware that pulmonary stenosis with normal aortic root did not ordinarily give rise to cyanosis, and he could not therefore, have distinguished these conditions from V.S.D.; also that the case in which proof of the diagnosis was established died in infancy in a manner sharply reminiscent of the way cases of severe V.S.D. die today.

Roger's observations were confirmed by Dupré (1891) in a child, aged 4 years, who had the physical signs described by Roger and died of intercurrent disease. Here again the effect of the lesion could have been sinister. This was the first case of ventricular septal defect diagnosed in life and confirmed at necropsy; Dupré suggested that the name *maladie de Roger* should be applied to the condition.

Later authors such as Perry (1931), Muir and Brown (1934), and East (1937), reported fairly large numbers of cases with the physical signs described by Roger. All remarked on the absence of symptoms in the condition, although one of Perry's cases was cyanosed on exertion. During this period the diagnosis of *maladie de Roger* was based on the murmur and thrill described above, and was never seriously questioned.

The general attitude was expressed by Brown (1950): "It is possibly the commonest of all congenital abnormalities, but the condition is so benign and symptomless that many cases escape observation or are designated by some other diagnosis."

Weiss (1927) described a case of ventricular septal defect with a loud murmur and thrill in a man aged 79 years who died from renal failure. Pallasse (1935) described a similar case which had been recognized 20 years before by Gallavardin; the patient died at the age of 67 and the diagnosis was confirmed at necropsy. Cases of this kind bolstered up the slender thesis so vigorously put forward by Roger—that acyanotic cases of V.S.D. were free from symptoms, had a good prognosis, and could be recognized only by auscultation (apart from the thrill).

In 1912, however, Gallavardin referred to two acyanotic cases of V.S.D. that had died of the disease in early childhood, and Laubry and Pezzi (1921) made a similar observation from the literature. Nevertheless both these papers expressed the belief that V.S.D. was ordinarily well tolerated. Taussig (1948) was rather sceptical about the alleged cause of some of these harsh murmurs over the centre of the heart and remarked that the clinician seldom had the opportunity to check the accuracy of his diagnosis. She also drew attention to a more severe clinical picture when the defect was large. Marquis (1950) reported four serious cases of V.S.D. in children, two of whom died from heart failure. Finally, Wood (1950) drew a very different picture of V.S.D. to that usually accepted, and the views he then expressed will be elaborated in the present paper. Our findings are in fairly close accord with those of Joly, Carlotti, and Sicot (1951), and we agree with most of their conclusions.

Embryology. We are in no position to discuss the embryology of V.S.D.; it has been described in detail by Keith (1909) and Spitzer (1923), and summarized by Brown (1950).

FREQUENCY

A totally erroneous impression of the frequency of V.S.D. has been given by authors who have estimated its incidence on the basis of Roger's description. Thus Perry (1931) found it accounted for 35 per cent of all cases of congenital heart disease in a school cardiac clinic; Muir and Brown (1934), analysing similar material, put the figure at 37 per cent. East (1937) considered V.S.D. to be the most common of all acyanotic congenital heart anomalies. None of these clinical observations was supported by physiological or pathological proof. Abbott (1932) found defects of the ventricular septum in 290 of her series of 1000 cases of congenital heart disease, but only 62 of them were uncomplicated (6%). Still (1924) found 4 cases of uncomplicated V.S.D. among 44 cases of congenital heart disease which had come to autopsy at the Hospital for Sick Children, Great Ormond Street. Many series were reported from centres in the United States and Canada. These are tabulated below together with the numbers of cases of congenital heart disease encountered at the same centres. The average incidence of V.S.D. in this material works out at 15 per cent, but not all the cases were uncomplicated.

TABLE I
INCIDENCE OF VENTRICULAR SEPTAL DEFECT

Authors	Date	Centre	Total necropsies		Percentage with V.S.D.
			Congenital heart disease	V.S.D.	
Leech	1935	Baltimore	75	12	16.0
McGinn and White	1936	Boston	67	5	7.5
Terplan and Sanes	1936	Buffalo	21	4	19.2
Nicholson	1936	Washington	37	4	10.8
Philpott	1937	Montreal	80	11 *	13.5
Rannels and Propst	1937	Philadelphia	36	7	19.4
Szypulski	1937	Philadelphia			
Ingham	1938	Rochester	87	3	3.4
Roberts	1937	New Orleans	42	6	14.3
Jacobius and Moore	1938	New York	169	29	17.1
Gibson and Clifton	1938	Chicago	105	12	11.4
Ash, Wolman and Bromer	1939	Philadelphia	32	3	9.3
Clawson	1944	Minneapolis	141	37	25.2

* All complicated cases.

In a consecutive series of 750 cases of congenital heart disease personally studied by one of us (P.W.), isolated V.S.D. was found in 8 per cent. V.S.D. also occurred as part of the Eisenmenger Complex in another 2.5 per cent, and in conjunction with pulmonary stenosis with normal aortic root in another 2 per cent, making a total incidence of 12.5 per cent, discounting cases of Fallot's tetralogy (11%), pulmonary atresia (1.5%) and transposition (1%). These figures agree fairly well with those tabulated from the U.S.A.

Uncomplicated isolated V.S.D. ranked only fifth in order of frequency in our series, the six commonest forms of congenital heart disease being as follows:

	per cent
Uncomplicated isolated A.S.D.	17
Uncomplicated isolated pulmonary stenosis	13
Uncomplicated isolated patent ductus	12.5
Fallot's tetralogy	11
Uncomplicated isolated V.S.D.	8
Coarctation of the aorta	7.5

If these figures approximate at all closely to the true relative frequency of these malformations, and there is good reason to believe that they do, then at least half, if not two-thirds, of the cases of V.S.D. reported by Perry (1931) and by Muir and Brown (1934) must have been diagnosed in error. This conclusion is supported by the remarkable rarity of uncomplicated pulmonary stenosis in these and similar reports prior to about 1950 (Abrahams and Wood, 1950), and by the fact that until very recently a positive diagnosis of V.S.D. made elsewhere (usually by a consulting physician) was proved wrong by means of cardiac catheterization twice as often as it was proved right (Wood, 1950).

NOMENCLATURE

The generally accepted clinical picture of V.S.D. has not altered appreciably since Roger's original description. Dupré (1891), in confirming Roger's observations, referred to the systolic murmur of V.S.D. as the Roger murmur, after which the condition became generally known as *maladie de Roger*. Gallavardin (1912), however, considered that the term *maladie de Roger* should be reserved for cases which complied with the syndrome described by Roger and should not apply to those cases in which ventricular septal defect was badly tolerated. Laubry and Pezzi (1921), on the other hand, thought that all simple defects of the ventricular septum should be classified as *maladie de Roger*. Taussig (1947) divided V.S.D. into two groups, those with small defects and little or no disability which she called *maladie de Roger*, and those with large defects situated high up in the ventricular septum which she referred to as high ventricular septal defects. She considered that the latter group differed from the *maladie de Roger* in that blood was shunted from the left ventricle directly into the pulmonary artery causing it to dilate. Selzer (1949) has criticized this concept, showing that in the vast majority of cases the defect is "located in and anterior to the membranous septum, connecting the area of the left ventricle immediately underneath the aortic valves with that of the right ventricle in front of the median leaflet of the tricuspid valves." Our physiological findings (*vide infra*) offer no support to the view that large defects with greatly increased pulmonary blood flows are situated higher than the small defects of *maladie de Roger*, or that blood is ever shunted directly into the pulmonary artery.

We feel ourselves that *ventricular septal defect* is the best label for the condition that it describes, and that it may be properly qualified by an adjective of degree, such as mild, moderate, or severe; we agree with Gallavardin that the term *maladie de Roger*, if used at all, should be reserved for those mild and symptomless cases that are characterized by the Roger thrill and murmur only.

MATERIAL

The 60 cases that comprise the basis of this report were seen privately, at the National Heart Hospital, or at the Brompton Hospital for Diseases of the Chest. In the majority (40) and in all

doubtful cases, the diagnosis was proved by means of cardiac catheterization. Doubtful cases, not yet investigated physiologically, have been excluded in view of the frequency of wrong diagnosis in this group. It has been suggested that the shunt in the *maladie de Roger* could be too small to be detected by means of cardiac catheterization; while admitting that defects measuring 1 to 2 mm. in diameter could not be detected with our technique, as discussed later, the fact remains that a different explanation for the physical signs was usually demonstrated. Nor are we prepared to accept the evidence that small ventricular septal defects occasionally close spontaneously, as described by Parkes Weber (1918) and others; unless the existence of the defect was proved beyond question, its apparent closure is more easily explained by supposing that the original diagnosis was wrong (Taussig, 1947).

Age and Sex. Of the 60 cases in our series, 30 were male and 30 female. In Selzer's series of 92 post-mortem cases mostly collected from the literature there were 46 males and 42 females (Selzer, 1949). The sex ratio is therefore about equal.

The number of cases in each age group is given below:

Years	No. of cases	Years	No. of cases
0-5	14	21-30	5
6-10	17	31-40	3
11-15	15	41-60	2
16-20	4		

Classification. The cases under review were classified as mild (22), moderate (18), severe (12), or pulmonary hypertensive (8) according to the degree and manner in which the physiology of the circulation was disturbed. This was assessed on clinical, radiological, and electrocardiographic grounds and confirmed by cardiac catheterization. Clinically mild cases answering to the classical description of *Roger* had normal cardiograms and skiagrams, and a pulmonary blood flow about one and a half times the systemic flow. Cases of moderate severity suffered no disability, but had distinctive physical signs in addition to the *Roger* thrill and murmur, and showed characteristic cardiographic and radiological changes; in these the pulmonary blood flow was between two and three times the systemic flow. Severe cases usually had some physical disability, and the physical signs of V.S.D. were florid; electrocardiographic and X-ray changes were also gross, and the pulmonary blood flow was three to five times the systemic flow.

Cases of V.S.D. with bidirectional or reversed shunt (*Eisenmenger's Complex*), due to a high pulmonary vascular resistance (averaging 15 units) have been excluded from this study and will be reported separately. A borderline group of severe cases with vasoconstrictive pulmonary hypertension and unidirectional left to right shunt is included, however, and in these the pulmonary blood flow was only about twice the systemic flow.

CLINICAL DIAGNOSIS

As previously stated, the diagnosis of ventricular septal defect has undoubtedly been made too frequently in the past, partly because it was considered to be the commonest form of congenital heart disease, and partly because other lesions that may cause the thrill and murmur described by *Roger* have not been sufficiently recognized. To cause confusion the murmur, usually accompanied by a thrill, should be more or less over the centre of the heart and unaccompanied by other *obvious* physical signs. A short discussion on the other common causes of such a murmur is included in the section on differential diagnosis.

The differential diagnosis of the *maladie de Roger* will be considered later after the clinical features of V.S.D. have been properly described. For the moment it must suffice that *several* examples of *each* of the seven conditions that are included there have been sent up to us with the tentative diagnosis of *maladie de Roger*.

General Appearances. Growth may have been restricted in severe cases, but not when the lesion was mild or moderate. The facies was normal or lean, never bloated, and rarely high coloured. Central cyanosis was excluded by definition. Neither arachnodactyly nor any other extra-cardiac congenital anomaly was especially associated with V.S.D., although thoracic deformity was noted in several instances.

The Pulse. The peripheral pulse was normal in the *maladie de Roger*, rather small in cases of moderate severity, and obviously small in severe V.S.D. In several instances it was also a little collapsing, like the pulse of mitral incompetence.

The *jugular venous pressure and pulse* were invariably normal unless there was heart failure.

The Cardiac Impulse. The increased pulmonary blood flow in V.S.D. is pumped equally by both ventricles. A hyperdynamic left ventricular cardiac impulse was recorded in two-thirds, i.e. in all but mild cases, and was as a rule more obvious than the lift over the right ventricle. The only cases in which the right ventricular lift sometimes dominated the cardiac impulse were those in which the pressures in the two circulations were equal, and the resistance was raised. In purely hyperkinetic pulmonary hypertension due to a large shunt, the left ventricle was nearly always clinically dominant. Only in the *maladie de Roger* proper was the cardiac impulse normal.

Pulsation over the pulmonary artery was less common than in A.S.D., but by no means rare. It was always associated with pulmonary hypertension, whether hyperkinetic or due to a high resistance.

Thrills. A systolic thrill was associated with the *Roger* murmur in 90 per cent of the cases. It was missing in the three mild cases, in two with moderate sized defects, and in two with marked pulmonary hypertension; it was never absent in severe cases with gross pulmonary plethora. Thus the clinical diagnosis of V.S.D. (without pathological proof) is barely tenable in the absence of a thrill; yet in their series of 40 clinical cases previously referred to Muir and Brown (1934) found a systolic thrill in only one-third.

Murmurs. In his original description *Roger* (1897) described the characteristic murmur of V.S.D. as "surprisingly loud, extending right through systole covering both heart sounds, and with its maximal intensity in a site atypical of acquired heart disease, namely over the upper third of the precordial region and chiefly median." Dupré (1891), however, stated that the murmur was maximal in the third left interspace. Later writers have described the murmur as being rough and vibrous (Laubry, Routier, and Soulie, 1933); low and blowing (White, 1944), and harsh (Levine, 1951); but little can be added to *Roger's* original description (Brown, 1950).

The murmur was loud in all but six of our cases and was usually discovered during routine medical examination. It was maximal in the third intercostal space at the sternal edge, in about half, but was a little lower (third and fourth spaces) in a quarter, and lower still (fourth space) in a quarter; it was maximal high up in the second space in only two instances. There was no correlation between the site of maximum intensity of the murmur and any of the other clinical or physiological findings. Phonocardiograms, when recorded, confirmed *Roger's* observation that the murmur began early and spilled over the aortic second sound (Fig. 1); this at once distinguished the murmur from that of aortic stenosis (Leatham, 1951), but not from the murmur of mitral incompetence.

A functional mitral diastolic murmur (Fig. 2), noted by Laubry and Pezzi (1921) and more recently described by Wood (1950) who attributed it to a torrential mitral blood flow, was heard in 90 per cent of uncomplicated severe cases, in 60 per cent of those with a moderate shunt (either moderate sized defects, or severe cases modified by a raised pulmonary vascular resistance), and in 10 per cent of mild cases.

A pulmonary diastolic murmur was heard in 14 per cent of the whole series, but only in those with marked pulmonary hypertension, either hyperkinetic or due to high resistance.

The Heart Sounds. The second heart sound was normally split in uncomplicated V.S.D. when both elements could be identified, but the long rough murmur often hampered analysis. The split was close, however, when there was pulmonary hypertension, especially when the resistance was raised, and the second or pulmonary component was then accentuated.

FIG. 1.—Phonocardiogram illustrating the pansystolic murmur of ventricular septal defect. HF, high frequency; LSE, left sternal edge; LF, low frequency; MA, mitral area; PA, pulmonary area.

FIG. 2.—Phonocardiogram showing a functional mitral diastolic murmur due to torrential mitral blood flow (top tracing). Lettering as for Fig. 1.

A third heart sound was frequently heard over the left ventricle, owing to the rapid early filling of that chamber.

RADIOLOGY

The earliest description of the radiological signs of V.S.D. is that of Vaquez and Bordet (1913) who described the heart as globular and overacting; this was confirmed by Laubry and Pezzi (1921). Roesler (1943) stated that when the defect was small there was little or no change in the shape of the heart, but that minor degrees of hypertrophy and dilatation of one or both ventricles was common; also that the pulmonary artery was often slightly dilated. When the shunt was large, enlargement of the right ventricle and pulmonary artery was more conspicuous, but then he suspected an associated congenital anomaly. To quote his own words: "radiological examination may be entirely negative or may show globular enlargement sometimes with associated prominence of the pulmonary artery. Very marked prominence of the conus, pulmonic arch, and in some cases of the interpulmonic vessels, together with a considerable right sided enlargement, must make one consider the presence of an Eisenmenger complex or associated anomalies."

Brown (1950) considered the globular shape to be rare and stated that there was generally no alteration in the size and shape of the heart shadow. "There may be some slight enlargement of the heart as a whole, with a tendency towards the assumption of a globular form in cases where there is a large septal defect. The pulmonary artery may be slightly dilated, imparting a straight left border to the heart. Considerable enlargement of the pulmonary artery and its branches . . . is exceptional and may be ascribed to structural changes in the pulmonary artery or to an associated patent ductus arteriosus."

In our series the radiological appearances were characteristic, although not necessarily diagnostic, and comprised varying degrees of pulmonary plethora (with or without a hilar dance), dilatation of the pulmonary artery, a small aorta, and enlargement and hyperactivity of *both* ventricles, especially the *left*, and fullness or slight dilatation of the *left* atrium but not of the right (Fig. 3).

FIG. 3

FIG. 4

FIG. 3.—Skiagram showing small aorta, slight dilatation of the pulmonary artery, considerable enlargement of both sides of the heart, particularly the left ventricle, and conspicuous pulmonary plethora in a case of severe ventricular septal defect with normal pulmonary resistance.

FIG. 4.—Normal radiological appearances in a case of *maladie de Roger*.

FIG. 5

FIG. 6

FIG. 5.—Skiagram in a case of severe ventricular septal defect with slightly elevated pulmonary vascular resistance and considerable shunt, showing gross dilatation of the pulmonary artery and its proximal branches—there was a conspicuous hilar dance.

FIG. 6.—Skiagram in a case of ventricular septal defect with severe aortic incompetence showing considerable enlargement of the left ventricle and very little pulmonary plethora.

The larger the shunt the more obvious these changes, and it was only in the mildest cases of *maladie de Roger* that the X-ray appearances were within normal limits (Fig. 4). In cases of V.S.D. with a raised pulmonary resistance the pulmonary artery and its proximal branches were more dilated than in uncomplicated cases (Fig. 5), and the peripheral pulmonary vascular markings were lighter.

THE ELECTROCARDIOGRAM

This was usually in close keeping with the physiological situation. Thus in *maladie de Roger* it was always normal, as it also was in half the cases of moderate severity. In the more severe cases, however, the tracing was always abnormal: as a rule, there was evidence of both left and right ventricular enlargement, there being deep Q waves, tall R waves, and perhaps inverted U waves, in leads V5 or V6, and small secondary R waves and perhaps inverted T waves in leads V1 and V2 (Fig. 7). When the pulmonary resistance was low and the shunt large, the graph was

FIG. 7.—Electrocardiogram in a case of ventricular septal defect showing a conspicuous Q wave in lead V6 over the left ventricle, and appreciable secondary R waves with inverted T waves in leads V1 and V3R due to dilatation of the right ventricle.

occasionally purely left-sided, and in one instance the T waves were inverted in leads V5 and V6 (Fig. 8). When the pulmonary resistance was raised, the tracing was more likely to show right ventricular preponderance, but large Q waves in leads V6 and V1 still pointed to enlargement of the left ventricle as well (Fig. 9). In 20 per cent of the whole series there was partial right bundle branch block as in atrial septal defect (Fig. 10), but in half of these cases deep Q waves in leads V5 and V6 or relatively deep S waves in leads V1 and V2 (over 6 mm.) suggested enlargement of the left ventricle in addition (Fig. 11).

Complete heart block, once considered to be not infrequently associated with ventricular septal defect (Yater *et al.*, 1933), was encountered only once.

FIG. 8.—Electrocardiogram showing great enlargement of the left ventricle in a case of ventricular septal defect with low resistance. Note the large Q waves and inverted T waves in V₅, V₆, V_L, and standard lead I.

FIG. 9.—Electrocardiogram in a case of ventricular septal defect with raised pulmonary resistance showing considerable right ventricular preponderance: prominent Q waves in leads V₆, V_L, and standard lead I, however, still point to a powerful left ventricle as well.

FIG. 10.—Electrocardiogram in a case of ventricular septal defect showing a partial right bundle branch block pattern as in atrial septal defect.

FIG. 11.—Electrocardiogram in a case of severe ventricular septal defect showing partial right bundle branch block from dilatation of the right ventricle, and normal Q waves in leads V5 and V6 with deep S waves in V2 suggesting enlargement of the left ventricle as well.

PHYSIOLOGICAL STUDIES

Of the 60 cases under review, 40 were proved by means of cardiac catheterization (see Table II). In 15 cases of *maladie de Roger* the average difference in oxygen saturation between pulmonary artery and right atrial samples was 7.5 per cent, the range being 4 to 13, and only two out of the 15 showing a difference of more than 10 per cent. The average pulmonary blood flow was 1.4 times the systemic flow, the range being 1.2 to 1.9 times. In only one-third of the cases of *maladie de Roger* was there any difference between samples taken from the infundibulum and from the body of the right ventricle, but in these 5 the difference was significant, for the infundibular sample was approximately the same as that from the pulmonary artery, whereas samples from the body

TABLE II
PHYSIOLOGICAL DATA IN VENTRICULAR SEPTAL DEFECT

	Gain in O ₂ saturation of R.V. samples	Pulmonary blood flow expressed as multiples of systemic flow	Pulmonary hypertension	Estimated size of defect (transverse diameter)
Maladie de Roger	4 to 13% Av. 7.5%	1.2 to 1.9 Av. 1.44	Absent	3 to 5 mm.
Moderate V.S.D.	9 to 22% Av. 13.5%	2 to 3 Av. 2.3	Trivial	5 to 10 mm.
Severe V.S.D. (uncomplicated)	18 to 33% Av. 28%	3 to 5 Av. 4	Hyperkinetic	10 to 15 mm.
Severe V.S.D. with high pulmonary vas- cular resistance	7 to 18% Av. 12.5%	1.7 to 2.8 Av. 2	Considerable	10 to 15 mm.

of the right ventricle were approximately the same as those from the right atrium. This difference was never found in the more severe cases of ventricular septal defect. The pulmonary vascular resistance was normal in these 15, and the pulmonary blood flow was always insufficient to cause hyperkinetic pulmonary hypertension; in other words, the pulmonary blood pressure was invariably normal in *maladie de Roger*.

There were 10 cases judged to be of *moderate severity* on clinical and radiological grounds: in these the difference in oxygen saturation between pulmonary artery and right atrial samples was 13.5 per cent, the range being 9 to 22, or nearly double the figure in the *maladie de Roger*; as previously stated, there was no difference between samples obtained from the infundibulum and from the body of the right ventricle, and these were both much the same as the pulmonary artery samples. The pulmonary blood flow averaged 2.3 times the systemic flow, the range being 2 to 3 times: in these 10 cases it was insufficient to cause more than trivial hyperkinetic pulmonary hypertension.

There were 7 *severe cases with the pulmonary vascular resistance normal* or under 5 units (400 dynes sec./cm.⁵): in these the difference in oxygen saturation between pulmonary artery and right atrial samples averaged 28 per cent, the range being 18 to 33; there was again no difference between infundibular and right ventricular samples, both of which approximated closely to samples from the pulmonary artery. The average pulmonary blood flow was 4 times the systemic blood flow, the range being 3 to 5 times. Hyperkinetic pulmonary hypertension (Fig. 12) was moderate in 2 instances, considerable in 2, and gross in 3; in these last 3, the pressures in the two circulations were balanced despite the fact that the pulmonary vascular resistance was not high (Fig. 13).

The fourth group comprised 8 *severe cases with a high pulmonary vascular resistance*, averaging 9 units (720 dynes sec./cm.⁵): in these the pressures in the two circulations were also balanced, but the shunt was far less, the pulmonary blood flow averaging only twice the systemic flow, with a

FIG. 12.—Pressure tracings from a case of ventricular septal defect showing hyperkinetic pulmonary hypertension; note that the systemic arterial pressure is higher than the right ventricular systolic pressure.

FIG. 13.—Pressure tracings from a case of severe ventricular septal defect showing equalization of pressures in the systemic and pulmonary circulations despite the absence of a high resistance ($R = 4.5$ units or 360 dynes sec./cm^5).

range from 1.7 to 2.8; the shunt was necessarily unidirectional (from left to right) since Eisenmenger's complex was excluded by definition. Here again there was no difference between high and low right ventricular samples. The average difference in oxygen saturation between pulmonary artery and right atrial samples was 12.5 per cent, the range being 7 to 18. The shunt in these 8 cases was much the same as in the group of moderate severity without a raised resistance; since the pressure gradient across the defect was obviously different in these two groups, the defect

must have been relatively large in those with a high pulmonary vascular resistance, probably at least as large as in the severe cases with a relatively low resistance and large shunt. It is clear that this pulmonary hypertensive group is closely related to Eisenmenger's complex, and if the resistance had been a little higher the shunt would have been reversed or bidirectional. Just why the pulmonary resistance was high in half the cases with a large defect and not high in the other half is unknown, but may depend upon some inherent difference in the individual response to pulmonary blood flows potentially greater than 3 times the systemic flow (Wood, 1952). The pulmonary resistance does not rise unless the defect is over a critical size. It may be added here that Nature is quite prepared to allow patients with large ventricular septal defects to die from heart failure without attempting to limit the shunt by raising the pulmonary vascular resistance. Finally, there is reason to believe that a high pulmonary vascular resistance does not develop slowly over the years, but is determined at or shortly after birth; in other words, it may be a matter of the foetal pulmonary resistance failing to drop rather than the other way round, as suggested by Civin and Edwards (1950).

V.S.D. WITH AORTIC INCOMPETENCE

Laubry and Pezzi (1921) described the autopsy of a case in which a high V.S.D., lying just below the aortic valve, had caused one of the valve cusps to be drawn down by a fibrous band towards the defect rendering the valve incompetent. Later Laubry, Routier, and Soulié (1933), describing the murmurs of V.S.D., referred to two cases with loud aortic diastolic murmurs and high pulse pressures; at necropsy both had a ventricular septal defect to which a cusp of the aortic valve was tethered by means of a fibrous band. They assumed that the aortic insufficiency was developmental and not infective in origin. More recently, Routier *et al.* (1949) described two further cases aged 5 and 13 years with similar features, and in these cardiac catheterization showed increased oxygenation of the blood in the pulmonary arteries, so that a diagnosis of patent ductus was made; the error was discovered at operation, which resulted in the death of one of the patients. Necropsy revealed the same kind of distortion of the aortic cusps.

Two cases of V.S.D. associated with marked aortic incompetence were diagnosed during the period under review, in addition to the 60 with isolated V.S.D. comprising the main series. One of them died suddenly in bed before any investigations were carried out, but in the other the diagnosis was confirmed as far as possible by means of cardiac catheterization. The fatal case, a young woman aged 21, had been known to have heart disease since the age of one year and had always complained of palpitation, fatigue, and shortness of breath on exertion. Her disability was increasing and she was no longer able to work. She was of good physique, and there was no cyanosis or clubbing. The pulse was markedly collapsing, Corrigan's sign was conspicuous in the neck, and the blood pressure was 110/50. A hyperdynamic left ventricular thrust was felt in the fifth left interspace, 13.5 cm. from the midline, but no pulsation could be felt over the right ventricle. A systolic thrill, accompanied by a loud pansystolic murmur, was present in the third and fourth left interspaces, and was followed by a long blowing aortic diastolic murmur. There was no evidence of pulmonary hypertension and there was no functional mitral diastolic murmur. The cardiogram showed considerable left ventricular preponderance (Fig. 14). Radiography showed a greatly enlarged hyperdynamic left ventricle, some enlargement of the right ventricle, no dilatation of the pulmonary artery, and only slight pulmonary plethora (Fig. 6).

At necropsy there was an oval defect measuring about 2 cm. in length in the membranous part of the ventricular septum; the anterior aortic cusp was partly prolapsed into the defect and was much thickened and rolled at its edge (Fig. 15). There was extensive subendocardial fibrosis at the base of the valve.

The other case was proved to have a V.S.D. by means of cardiac catheterization. There were marked signs of aortic incompetence in addition to those of V.S.D.

The syndrome is described in some detail because it is apt to be mistaken for patent ductus and may lead to a profitless and dangerous operation.

FIG. 14.—Electrocardiogram in a case of ventricular septal defect complicated by severe aortic incompetence showing considerable enlargement of the left ventricle alone.

V.S.D. WITH PULMONARY STENOSIS

Like atrial septal defect, V.S.D. may be associated with pulmonary stenosis and normal aortic root (Abrahams and Wood, 1950); the stenosis may be mild, moderate or severe, and may be valvular, infundibular, or both. The shunt is ordinarily unidirectional from left to right.

In our series of 750 cases of congenital heart disease, there were 11 with this combination, excluding 10 cases diagnosed as acyanotic Fallot's tetralogy (vide infra) some of which may have had a normal aortic root. Accurate clinical diagnosis depended on recognizing characteristic features of both conditions; but as a rule only the more important lesion was diagnosed at the bed-side, the subsidiary anomaly being revealed later by means of cardiac catheterization. In fact the stenosis was mild in six cases, and these were all diagnosed clinically as mild or moderate V.S.D.; in the other five the stenosis was moderate or severe, and the V.S.D. was initially overlooked. Severe pulmonary stenosis with normal aortic root and reversed interventricular shunt cannot be distinguished from Fallot's tetralogy, except at necropsy.

(A) DIFFERENTIAL DIAGNOSIS OF SMALLER DEFECTS

From Maladie de Roger. When there is little abnormal other than a systolic thrill and murmur maximal around the third left interspace the diagnosis lies between *maladie de Roger* and other conditions. We are now in a better position to sort out the confusion. The list of possible causes for such a murmur and thrill is a long one and includes,

- (1) Mild pulmonary valve stenosis with normal aortic root.
- (2) Mild infundibular stenosis with normal aortic root.
- (3) Acyanotic examples of Fallot's tetralogy.
- (4) Mild aortic or subaortic stenosis.
- (5) Mitral incompetence with anticlockwise rotation.
- (6) Relatively mild atrial septal defect.
- (7) So-called "innocent left parasternal murmur," whatever that may be.

FIG. 15.—Pathological appearances in a case of ventricular septal defect complicated by aortic incompetence showing the anterior aortic cusp (A) prolapsed into the defect, and extensive fibrosis at the base of the valve.

Mild pulmonary valve stenosis with normal aortic root may be recognized by the higher position of the thrill and murmur (usually maximal in the second space), by the slight delay in pulmonary valve closure causing rather a widely split second heart sound, and by the post-stenotic dilatation of the pulmonary artery. The latter is especially valuable for it is not a feature of the *maladie de Roger*, occurring in V.S.D. only when the pulmonary blood flow is considerable or when there is associated pulmonary hypertension.

Mild infundibular stenosis with normal aortic root is very difficult to distinguish from *maladie de Roger*, because the thrill and murmur are relatively low in each, and the pulmonary artery is not dilated; delay in pulmonary valve closure points to infundibular stenosis, but may be difficult to recognize clinically in truly mild cases. Pure infundibular stenosis may be thought too rare to bother about, but in our series of 750 cases of congenital heart disease its incidence was 2 per cent, which was nearly as high as that of *maladie de Roger* (3 per cent). There can be no doubt at all that many cases diagnosed clinically as *maladie de Roger* really have mild infundibular stenosis. We have made this mistake ourselves several times and will make it again, for if we cannot tell the difference from the second heart sound we have no other clinical means of distinguishing them. Cases of moderate severity, whether V.S.D. or infundibular stenosis, present no difficulty, but here we are not concerned with these.

Mild aortic and subaortic stenosis should be distinguished by the delayed onset and relatively short duration of the systolic murmur, which begins after the first heart sound and ends just before the second (Leatham, 1951). Again, in aortic stenosis there is usually demonstrable retraction over the right ventricle, the lesion being purely left-sided. Finally, the second heart sound may be single in aortic stenosis, the aortic element being delayed. Despite these distinguishing features, confusion may certainly arise, and we plead guilty to having made the error more than once.

Mitral incompetence with anticlockwise rotation of the heart and *atrial septal defect* will be considered in the later section on the differential diagnosis of V.S.D. with larger shunt.

Innocent left parasternal murmur remains to be discussed. The label refers to cases that have a loud systolic murmur without a thrill in the third or fourth left intercostal spaces near the sternum in the absence of demonstrable heart disease (Evans, 1948). Physiological investigations reveal nothing abnormal. When the sternum is depressed a murmur of this kind might be explained by turbulence set up by slight compression of the outflow tract of the right ventricle, and when the murmur varies greatly with respiration it may be ascribed to sudden expansion of a small segment of lung which has been compressed by the heart in diastole; but in the majority of cases these explanations are untenable. If the murmur is pansystolic a pin head defect of the ventricular septum is difficult to exclude, but it would have to be no more than 1 to 2 mm. in diameter. A defect of this size would pass less than half a litre a minute, and this could not be detected by ordinary methods of investigation. It should be clearly understood, however, that the great majority of cases referred to us erroneously as *maladie de Roger* were proved to have some other anomaly; relatively few were finally diagnosed as innocent left parasternal murmur.

ACYANOTIC FALLOT'S TETRALOGY

In our consecutive series of 80 cases of Fallot's tetralogy, ten (12.5%) were acyanotic at rest, exhibited no clubbing of the fingers or toes, had hæmoglobin values not exceeding 100 per cent (with one exception), and arterial oxygen saturations ranging from 87 to 97 per cent. None of these was referred to us with the correct diagnosis, and several were believed to have *maladie de Roger*; we made this mistake once ourselves, although we should not have done so. There was no clear history of cyanosis on effort in any of them, but we were able to demonstrate it in four. The clinical features were similar to *maladie de Roger* in that the arterial and venous pressure and pulse were normal, the heart was quiet, neither left nor right ventricle being convincingly enlarged clinically, and the loud systolic murmur accompanied by a thrill was maximal around the third space; but the second heart sound was single in all but one of the ten cases with Fallot's tetralogy and was very widely split in the exception. Thus the second heart sound alone should prevent confusion.

The X-ray appearances were not very helpful, for the pulmonary vascular markings were usually normal or nearly so, the heart was more or less normal in shape, and the pulmonary artery was not dilated or conspicuously hypoplastic. A right-sided aortic arch was not seen.

The electrocardiogram usually showed some evidence of right ventricular hypertrophy in the acyanotic cases of Fallot's tetralogy, whereas it was commonly normal in *maladie de Roger*. This is the second important point in differential diagnosis; but a normal cardiogram does not absolutely exclude acyanotic Fallot's tetralogy, for it was seen in three of the ten cases.

The third important difference is historical, those with *maladie de Roger* invariably being symptom free, whereas all those with acyanotic Fallot's tetralogy had some degree of effort intolerance, the average grade being 2/4; moreover, four of them squatted when breathless.

Physiologically these cases differed from the classical type only in the absence or near absence of a right-to-left shunt at rest. The right ventricular systolic pressure was identical with that in the aorta or brachial artery in all, and the pulmonary artery pressure was low (normal in three cases). Shunting was negligible in three, bidirectional in one, slight from right to left only in five, and slight from left to right only in one. The resistance offered by the obstruction was obviously very similar to the systemic resistance. When there was no appreciable shunt either way the presence of the defect in the interventricular septum was proved by passing a catheter through it, either during physiological investigation or at operation (all ten cases were operated on).

(B) DIFFERENTIAL DIAGNOSIS OF LARGER DEFECTS

Mitral incompetence with anticlockwise rotation of the heart gives rise to a rather small, slightly water-hammer pulse, hyperdynamic left ventricle without medial retraction, pansystolic murmur and thrill maximal in the fourth interspace in the left parasternal line, accentuated third sound, and short faint mitral diastolic murmur—physical signs also characteristic of V.S.D. The cardiogram, however, may show a P mitrale

and pure left ventricular dominance in mitral incompetence, and X-rays reveal dilatation and systolic expansion of the left atrium, absence of pulmonary plethora, pulmonary venous congestion in severe cases, and perhaps calcification of the mitral valve.

Atrial septal defect is recognized by the cardiac impulse, which is purely right ventricular, by wider splitting of the second heart sound, partial right bundle branch block without anything to suggest left ventricular enlargement as well, and dilatation of the right *atrium* radiologically. Of course it is only those cases of A.S.D. with a systolic thrill and murmur over the right ventricular outflow tract that are likely to cause confusion at all.

A.S.D. and V.S.D. are more likely to be confused when there is associated pulmonary hypertension due to a raised pulmonary vascular resistance, for the right ventricle then tends to dominate the clinical picture in both conditions, and the cardiogram and X-ray appearances are more alike; moreover, the second heart sound in A.S.D. becomes more closely split, so that all the major points of difference may disappear. To add to the difficulty, patent ductus complicated by a high pulmonary vascular resistance may present a similar picture. In such cases accurate diagnosis may have to await cardiac catheterization.

PROGNOSIS

During the five-year period in which the 60 cases of isolated V.S.D. were seen, none have died. During the same period one case of V.S.D. associated with coarctation died during an attempt to repair the coarctation, and one patient with V.S.D. associated with gross aortic incompetence died spontaneously. In the group with Eisenmenger's complex there have been no deaths, and none of those with V.S.D. associated with pulmonary stenosis have died. In so short a period, however, it is not possible to provide any valuable information in respect of final prognosis from our own experience.

While considering the prognosis to be favourable most authors have stressed the danger of superimposed bacterial endocarditis. Thus 57 per cent of the cases of *maladie de Roger* reported by Gelfman and Levine (1942) developed bacterial endocarditis, and Welch and Kinney (1948) recorded 6 instances among 11 cases of V.S.D. On the other hand Perry (1937) witnessed only one instance out of 87 alleged cases of *maladie de Roger*, and Muir and Brown (1934) encountered none in their series. The truth must lie somewhere between these extremes, and of course any necropsy series will yield a higher incidence of bacterial endocarditis than a clinical series. Selzer (1949) collected 80 cases confirmed at necropsy in which subacute bacterial endocarditis was the cause of death in 18 (22%). We have seen only one infected case during the five years in which we have studied the disease, i.e. one out of a total of 92 cases, if Eisenmenger's complex and V.S.D. associated with simple pulmonary stenosis are included. The true incidence is obviously unknown, but is unlikely to exceed 10 per cent.

DISCUSSION

From the foregoing data it will be appreciated that isolated V.S.D. is neither so common nor so innocent as is generally believed.

It seems to be only slightly more common than coarctation of the aorta, these two ranking fifth and sixth in order of frequency in our series of 750 cases of congenital heart disease. If the 20 cases of Eisenmenger's complex in the series are added, and also the two cases with aortic incompetence, the relative incidence of V.S.D. becomes 11 per cent, which brings it up level with Fallot's tetralogy to equal fourth place. If the six cases of V.S.D. associated with mild pulmonary stenosis are also included (it is hardly fair to include the five with dominant stenosis), its incidence rises to 12 per cent, which allows it to take fourth place, putting it just ahead of Fallot's tetralogy.

In respect of severity the findings are equally at variance with traditional opinion. Of the uncomplicated cases only one-third were truly mild, about a third were moderate, and about a third were severe (half of these having a raised pulmonary vascular resistance). If Eisenmenger's complex is included in the analysis, severe V.S.D. was twice as common as the *maladie de Roger*, or as common as the mild and moderate groups together; in other words, the *maladie de Roger* accounted for only one-quarter of all cases with isolated V.S.D. This is hardly surprising when

one considers the high pressure gradient across the defect; the hole must be remarkably small to prevent a large shunt. Using the hydraulic formula described by the Gorlins (1951), a shunt of 1.5 to 3 litres a minute, which covers most cases of *maladie de Roger*, means a defect measuring 0.3 to 0.5 cm. in diameter. A round defect 1 cm. across would produce a shunt of the order of 12.5 litres a minute if the pulmonary resistance remained so low that hyperkinetic pulmonary hypertension did not occur. Pathological reports describing the size of ventricular septal defects harmonize with these theoretical considerations; thus in *maladie de Roger* the hole is usually described as small, admitting only a probe (2 to 3 mm. in diameter); whereas in severe cases it may admit the little finger (about 1.5 cm. in diameter).

It should also be observed that a round ventricular septal defect measuring 1 cm. in diameter (area = 0.79 cm.²), would produce a pulmonary blood flow of at least 15 litres a minute (shunt = 12.5 litres/minute) with normal pulmonary resistance and pressure, and that this is about the maximum pulmonary blood flow that adult pulmonary vessels can accommodate without a rise of pressure (hyperkinetic pulmonary hypertension). In this sense then, a defect 1 cm. across is critical. Anything larger must cause hyperkinetic pulmonary hypertension, and perhaps reactionary pulmonary vasoconstriction. It is unlikely that a raised pulmonary vascular resistance occurs with defects measuring 0.5 to 1 cm. in diameter, for these comprise our moderate group in which no instance of pulmonary hypertension was seen. In Eisenmenger's complex proper the defect is always relatively large (at least 1 cm. in diameter).

SUMMARY AND CONCLUSIONS

In a consecutive series of 750 more or less proved cases of congenital heart disease, isolated uncomplicated V.S.D. was found in 8 per cent, which was fifth in order of frequency. V.S.D. also occurred as Eisenmenger's complex in 2.5 per cent, in conjunction with simple pulmonary stenosis in 2 per cent, as part of Fallot's tetralogy in 11 per cent, and in combination with other anomalies in 2 per cent. Thus in one form or another V.S.D. occurred in one-quarter of all cases of congenital heart disease.

Roger's description is reviewed and it is recommended that the term *maladie de Roger*, if retained at all, should be applied only to cases of mild V.S.D.

Out of 80 cases of isolated V.S.D., 22 were mild, 18 moderate, 20 severe (some with raised pulmonary resistance), and 20 had pulmonary hypertension with reversed shunt (Eisenmenger's complex).

In mild cases the pulmonary blood flow averaged about one and a half times the systemic flow and the defect was calculated to measure less than 0.5 cm. in diameter. In cases of moderate severity the pulmonary flow was two to three times the systemic flow and the defect was estimated to measure between 0.5 and 1 cm. in diameter. In severe cases the pulmonary flow was between three and five times the systemic flow, unless the pulmonary vascular resistance was raised (when it averaged only twice the systemic flow), and the defect was believed to be between 1 and 1.5 cm. in diameter. Eisenmenger's complex will be discussed in another paper.

The most important clinical features of isolated uncomplicated V.S.D. included a small pulse, normal jugular venous pressure and pulse, hyperdynamic left ventricular thrust at the apex, variable movement over the right ventricle, a pansystolic murmur and thrill usually maximal in the third left space and embracing both heart sounds as described by Roger, a functional mitral diastolic murmur, and normal splitting of the second heart sound.

The electrocardiogram usually showed evidence of enlargement of both ventricles, but was always normal in *maladie de Roger*.

Radioscopy showed varying degrees of pulmonary plethora, dilatation of the pulmonary artery, and left ventricular enlargement; right ventricular enlargement was less easily demonstrated unless the pulmonary resistance was raised, and the right atrium was rarely dilated.

The differential diagnosis of *maladie de Roger* includes mild pulmonary valve stenosis, mild

infundibular stenosis, acyanotic Fallot's tetralogy, mild aortic stenosis, mitral incompetence with anticlockwise rotation, and innocent left parasternal murmur.

The differential diagnosis of the more severe forms of V.S.D. includes mitral incompetence, A.S.D., and when the pulmonary resistance is raised patent ductus arteriosus.

Physiological studies revealed a significant difference between high and low right ventricular samples (high samples being similar to those from the pulmonary artery and low samples being similar to those from the right atrium) in one-third of the cases of *maladie de Roger*, but never when the defect was moderate or large.

The syndrome of V.S.D. complicated by aortic incompetence is discussed and illustrated.

Ten cases of acyanotic Fallot's tetralogy are described in some detail.

V.S.D. complicated by pulmonary stenosis with normal aortic root is also briefly described.

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