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THE TREATMENT OF VENTRICULAR SEPTAL DEFECT

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The natural history of ventricular septal defect (V.S.D.) is such that few patients survive past the third decade (Brotmacher and Campbell, 1958). It is therefore fortunate that the introduction of the cardio-pulmonary bypass has permitted effective surgical treatment. This is now current practice in the U.S.A. (Kirklin *et al.*, 1957; Warden *et al.*, 1957; Gerbode *et al.*, 1958). The object of this paper is to present a series of 21 patients with V.S.D.s, operated on under total cardio-pulmonary bypass with the Melrose-N.E.P. pump-oxygenator at Hammersmith Hospital. These patients form the major group of a total of 40 operated on in this way for the correction of congenital cardiac defects during the last 18 months.

The Patients.—The ages of the 21 patients ranged from 2½ to 25 years, the average being 8½ years. Of these patients with V.S.D. four had in addition a patent ductus arteriosus. Of the cases without a duct three were unusual. One had a single ventricle, one had two V.S.D.s, and in one the V.S.D. was in an unusual site in relation to the tricuspid valve (Case 13).

Clinical Picture

Symptoms

Infancy is known to be a hazardous period in patients with large V.S.D.s, and over half of the 320 patients of Keith *et al.* (1958) died before the age of 1 year. Similarly, in our cases there was often a history of feeding difficulties, with breathlessness and cyanosis, and very slow weight gain in infancy. After the age of 1 year they did better, though frequent chest infections were still common, and when seen by us they were often remarkably asymptomatic and active. Dyspnoea on exertion was no more than slight in two-thirds and was severe in only one case (Case 2).

Signs

These children were commonly undersized for their age, being on average 18% below the expected weight. Chest deformity with uniform or asymmetrical bulging of the sternum and Harrison's sulcus was frequently noted (Fig. 7). Clubbing was never seen, but slight cyanosis was occasional and was usually peripheral,

the arterial oxygen saturation being always above 88%. No patient had congestive heart failure at the time of operation.

Jugular Venous Pulse.—This was abnormal in eight, consisting usually of a moderately dominant *a* wave; a really conspicuous *a* wave was seen only once (Case 13).

Arterial Pulse.—The volume was usually normal or slightly small and the rhythm regular. A slight-to-moderate waterhammer quality was found in 11. A striking suprasternal arterial pulsation was found in Cases 14 and 15, which had in addition a patent ductus.

Cardiac Pulsation.—The type of pulsation varied according to the size of the left-to-right shunt and the pulmonary resistance. When the shunt was considerable there was a localized hyperdynamic thrust at the apex, indicating left ventricular enlargement, and a diffuse parasternal heave due to enlargement of the right ventricle. When the shunt was smaller and the pulmonary resistance appreciably raised (around 9 units) the left ventricular thrust was less impressive and the dominant pulsation was that of the right ventricle.

Auscultation

V.S.D. Thrill and Murmur.—These were usually maximal at the left sternal edge, and in most cases the murmur was loud and long, indicating a substantial flow through the defect (Fig. 1A). In the patients with a pulmonary resistance of 9 units or more the murmur and thrill were softer and shorter, owing to reduction in flow through the defect (Fig. 1C).

Apical Diastolic Murmur.—A low-pitched delayed murmur at the apex attributed to a torrential mitral blood flow (Wood, 1956) was heard in all cases. When loud and long the left-to-right shunt was always large (Fig. 1A). We expected, when the murmur was soft and short, that the shunt would be small and the resistance high, but this was not always so. Of the six cases with this type of murmur, four had a large shunt and in two the shunt was small.

Basal Diastolic Murmur.—An early blowing diastolic murmur was heard in the left second to third spaces in eight patients. At operation three were shown to have a ductus, one was proved to have aortic incompetence, and one to have pulmonary incompetence. The cause

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of the murmur was not determined in the remaining three and disappeared after operation in one. In these three it was presumed to be due to aortic or pulmonary incompetence.

Second Heart Sound.—This was loud and narrowly split in all patients except three. One of these was found to have definite organic pulmonary valve stenosis at operation, one had aortic incompetence and infundibular obstruction and the other (Case 13) had an unusual defect, referred to later.

Other Sounds.—Two cases had a pulmonary ejection click and high pulmonary pressures, but with a substantial shunt. An ejection click at the apex, thought to be aortic, was heard in one patient who had also a patent ductus. No other abnormal sounds were heard in any patient.

Associated Non-cardiac Anomalies

These were usually absent, but one patient had stigmata of the "rubella syndrome" and also a patent ductus. Another patient had right basal bronchiectasis.

Methods of Study

Radiology

The heart was enlarged in every case, being usually moderate in degree with a cardio-thoracic ratio of 55–65%. Enlargement was considerable in two and slight in three. Both ventricles were enlarged in every case. The left ventricle tended to be less prominent in the cases with a high pulmonary resistance. Left atrial enlargement, of slight-to-moderate degree, was present in all save two, of whom one had substantial infundibular stenosis and the other a high pulmonary resistance (14 units). Impressive right atrial enlargement was seen only twice. One of these patients (Case 13) appeared at operation to have tricuspid incompetence; in the other patient (Case 21) clockwise cardiac rotation was found at operation.

• Enlargement of the main pulmonary artery was invariable, as was plethora of the lung fields. Intrinsic pulsation of the small branches was well marked in all. The size of the aorta was unremarkable.

Fig. 2 shows the radiological features in a typical case.

Aortography was performed on two patients and one was shown to have a patent ductus (Case 20).

Electrocardiography

Right atrial P waves were found in six cases and were gross in only one (Case 13). Left atrial P waves occurred in 11. Direct evidence of right ventricular hypertrophy (Hollman, 1958) was found in 11, and 7 of these had an RSR pattern in VI and one had complete right bundle-branch block. Direct evidence of left hypertrophy (Cabrera and Monroy, 1952) consisting variously of deep Q waves, tall R waves, or tall peaked T waves was found in 19 (Fig. 3).

Lone right hypertrophy was found in only one (Fig. 4), while solitary left hypertrophy occurred in six. Thus 14 patients had combined hypertrophy. In six of these the right ventricle appeared dominant and in three the left. We had expected that when the left ventricle dominated the

FIG. 1.—Phonocardiograms taken at the left sternal edge (L.S.E.) and at the mitral area (M.A.). (A) Loud long systolic murmur (S.M.) and long mitral diastolic murmur (M.D.M.) in a patient with a large left-to-right shunt and low pulmonary resistance. (B) Same patient as (A) showing disappearance of significant murmurs after closure of defect. A soft ejection systolic murmur is shown. Note appearance of right bundle-branch block. (C) Short soft systolic murmur in a patient with only a small left-to-right shunt and high pulmonary resistance. The second heart sound is very loud and virtually single, and the mitral diastolic murmur is soft and short.

FIG. 2.—Postero-anterior and lateral views of the heart in Case 4 with a large left-to-right shunt and only slightly elevated pulmonary resistance. The right ventricle and pulmonary artery are enlarged and there is pulmonary plethora. Definite left atrial enlargement is seen in the lateral view.

right the pulmonary flow would be higher and the resistance lower than when the right ventricle was dominant. This was not the case, for there was no clear relationship between the cardiographic and haemodynamic findings. Further, it was anticipated that when the right ventricle dominated the

left a smaller fall of right heart pressure would occur than when the left ventricle was dominant, but we were disappointed in this also. Nevertheless we continue to use the cardiogram in the assessment of individual patients in the belief that the presence of left hypertrophy is a favourable sign.

Cardiac Catheterization

This was carried out in every case, and the data were used to estimate the size of the defect, the severity of the pulmonary vascular disorder, and the presence of associated anomalies. The size of the left-to-right shunt was expressed as the ratio of pulmonary to systemic flow.

$$\frac{\text{Pulmonary flow}}{\text{Systemic flow}} = \frac{\text{Systemic A-V O}_2 \text{ difference}}{\text{Pulmonary A-V O}_2 \text{ difference}}$$

The pulmonary arteriolar resistance was expressed in arbitrary units (Wood, 1956), and in cases where the oxygen consumption was not measured an average value for age and surface area was obtained from tables.

The results of this investigation are summarized in Table I.

TABLE I.—Haemodynamic Studies at Catheterization, at Operation, and Results

Case No.	Age	Pulmonary Artery Pressure (mm. Hg)	Pulmonary Systemic Flow Ratio	Pulmonary Arteriolar Resistance (Units)	% Fall in R.V.P.† L.V.P.	Result
<i>V.S.D. Alone</i>						
1	10	100/57	1.5	9	37	Dead
2	2½	39/12	5.0	3*	6	Alive and well
3	5	100/35	1.8	13*	65	" " "
4	5	70/20	2.0	4	9	" " "
7	7	75/55	1.1	17*	2	" " "
8	7	70/40	2.2	6*	41	" " "
10	10	83/48	2.0	6	58	" " "
11	8	120/70	2.0	9	44	" " "
12	10	60/30	2.4	3.5*	37	" " "
13	9	42/20	2.5	1.5	13	" " "
16	4½	75/40	2.7	9.5*	54	" " "
17	9	55/20	1.8	5*	8	" " "
18	25	17/5	4.5	1*	55	" " "
19	11	32/8	3.2	1.5*	31	" " "
21	13	44/8	2.6	1.5	16	" " "
<i>V.S.D. and Patent Ductus</i>						
5	3½	40/20	2.8	1*	27	" " "
14	10	110/60	2.0	20*	5	Dead
15	9	70/53	1.3	18*	—	" " "
20	3½	60/20	3.7	4.5*	28	Alive and well
<i>Two Ventricular Defects</i>						
9	2½	72/20	2.6	10*	0	Dead
<i>Single Ventricle</i>						
6	7	75/30	2.0	5	0	Alive and well

* = O₂ consumption assumed.

† R.V.P. = right ventricular systolic pressure. L.V.P. = left ventricular systolic pressure.

% fall in R.V.P. = $\frac{\text{R.V.P. \% before closure} - \text{R.V.P. \% after closure}}{\text{L.V.P.}}$

Also see text.

The pulmonary artery pressures ranged from 17/5 to 120/70, and were mostly of the order of 70/50 mm. Hg. The left-to-right shunt was large in all but three cases, the ratio of pulmonary to systemic flow ranging from 1.1:1 to 5:1, with an average of 2.4:1. The pulmonary resistance was usually only moderately elevated, but in four patients it was high. The average for all cases was 7.4 units. An infundibular gradient, usually slight, was found in nine patients and ranged from 7 to 40 mm. Hg. One patient had a 30 mm. Hg gradient at valve level. The oxygen saturation was higher in the pulmonary artery than the right ventricle in four patients, of whom two had an associated patent ductus. In two cases proved to have a ductus the saturation in the two sites was equal. The arterial oxygen saturation was always above 88%, and averaged 93%.

The pulmonary wedge pressure when determined ranged from 5 to 16 mm. Hg (measured from 5 cm. below the sternal angle).

Associated Lesions and Unusual Features

Patent Ductus Arteriosus.—The classical signs were absent, although suspicion was raised by an early diastolic murmur at the left sternal edge in two. Cardiac catheterization

FIG. 3.—Electrocardiogram of Case 19, showing dominant left ventricular hypertrophy with deep Q waves, tall R waves, only small S waves, and tall T waves in V5-V7. Slight right ventricular hypertrophy is present too.

FIG. 4.—Electrocardiogram of Case 1 showing dominant right ventricular hypertrophy with no clear evidence of left ventricular hypertrophy at all. There is a monophasic R wave in V1 with S waves across to V7 and a dominant R wave in lead aVR. There are no Q waves in V5-V7.

FIG. 5.—Post-operative electrocardiogram of Case 4 showing complete right bundle-branch block with the secondary R wave present even in V7. Well-marked T-wave inversion is present across to V5.

revealed a further rise in oxygen saturation in the pulmonary artery as compared with the right ventricle in only two, even though in another the ductus was found at operation to be large and the ventricular defect small. On x-ray examination the pulmonary artery was always at least moderately dilated. Our experience indicates that when the ductus is patent in the presence of a V.S.D., it is difficult to diagnose pre-operatively with certainty without the aid of retrograde aortography. The importance of the patent ductus in relation to perfusion is discussed below. Patency of the ductus should be suspected if there is a basal early diastolic murmur, if the catheterization data suggest a further left-to-right shunt at pulmonary artery level, or if there are any other features associated with patent ductus, as in one of our patients who had stigmata of the "rubella syndrome" (Heiner and Nadas, 1958).

Obstruction to Right Ventricular Outflow.—Nine patients were found to have infundibular obstruction at cardiomy, while another had definite valvular stenosis. In no case was the obstruction severe enough to reverse the left-to-right shunt, and the pulmonary artery pressure was elevated in all but one.

Pulmonary Valve Lesions.—Two patients had abnormal valves. In Case 5 the cusps were fused and the orifice reduced to 1 cm. in diameter. In Case 18 the cusps were adherent to the pulmonary ring, and this gave rise to pulmonary incompetence with a diastolic thrill.

Atypical Ventricular Defects

Case 6.—This boy of 7 years with a *single ventricle* was of exceptional interest, for pre-operatively all the signs were those of a straightforward ventricular defect apart from the cardiogram. This showed gross left-axis deviation with extreme clockwise rotation and absent Q waves over the left ventricle.

Case 9.—This patient, a girl aged 2½ years, had *two ventricular defects*, and pre-operatively the only hint of an associated lesion was a very large diphasic complex in lead I of the cardiogram.

Case 13.—In this girl of 9 years the defect was a low one beneath the septal cusp of the tricuspid valve, and the jet from the left ventricle was directed partly into the right atrium. Clinically the patient was unusual because she had a tall *a* wave, a widely split second sound, a very large right atrium, and the systolic thrill was near the apex.

Indications and Contraindications to Operation

In view of the known poor prognosis it is clear that all patients with a moderate-sized or large defect should be considered for surgery unless there is some contraindication. It is equally clear that the main hazard regarding closure is the presence of severe pulmonary vascular disease, because patients with this complication have a very high operative mortality and also may derive uncertain benefit if they survive. Thus the difficulty in selecting suitable cases for operation is experienced mainly in those patients who have an elevated pulmonary vascular resistance.

If the pulmonary resistance is so high as to cause an obvious right-to-left shunt with an arterial oxygen saturation below 85%, with or without cyanosis and clubbing, then closure of the defect should not be recommended. Such cases will have only a small left-to-right shunt with pulmonary flow less than 1.5 times the systemic, and the clinical features previously mentioned of a substantial shunt will be absent. The whole clinical picture, in fact, will be dominated by evidence of extreme pulmonary hypertension.

Cases less severe than this first group but with a substantially elevated pulmonary resistance (9 units or more) present the greatest difficulties in selection and a careful consideration of *all* aspects of the patient is essential. It is doubtful whether any one parameter is of overriding importance. Evidence for the presence of an appreciable left-to-right shunt with only a small or absent right-to-left shunt must be sought, so that a fall in pulmonary artery pressure after closure can be anticipated.

Case 3 can be cited as an example of a patient in this group, for she had a pulmonary artery pressure of 100/35 mm. Hg and a pulmonary arteriolar resistance of 13 units. We were encouraged to operate on her by finding a definite left ventricular thrust at the apex even though the right ventricular pulsation was prominent too, by a long loud V.S.D. murmur and thrill with a moderately loud mitral diastolic murmur, by the presence of a qR pattern in V6 even though R was monophasic in V1, and by a pulmonary flow 1.8 times the systemic. At operation a good drop in pulmonary artery pressure after closure was obtained. On the other hand, a girl of 9 with a pulmonary artery pressure of 80/40 mm. Hg and a pulmonary resistance of 14 units was thought to be unsuitable because of the following features. Clinically the left ventricle was doubtfully palpable, the V.S.D. murmur was not full length, and the thrill rather weak, there was no mitral diastolic murmur, the cardiogram showed deep S waves with no Q waves over the left ventricle, and the pulmonary flow was only 1.2 times the systemic.

The ideal case for operation is typified by Case 12. This boy of 10 years had a pulmonary resistance of 3.5 units, with a pulmonary artery pressure of 60/30 mm. Hg and a pulmonary blood flow 2.4 times the systemic. Clinically there was a quite forceful localized thrust at the apex, a loud long V.S.D. murmur with a strong thrill, and a loud long mitral diastolic murmur. The cardiogram showed a small Q, tall R, and small S in V6 with a prominent peaked T wave, and the predominant deflection in aVR was negative. On x-ray examination he had well-marked pulmonary plethora. At operation his pulmonary artery pressure dropped from 50/20 to 27/20 mm. Hg after closure of the defect.

Anaesthesia

The patients are made very drowsy by premedication, and we have found it best in children to give quinalbarbitone per rectum (4–5 mg./kg., maximum 200 mg.) with intramuscular promethazine (1.5–2 mg./kg., maximum 50 mg.) and pethidine (3–4 mg./kg., maximum 100 mg.). This allows the patient to be weighed without disturbance immediately before induction of anaesthesia by a minimal dose of thiopentone (25–50 mg.). After curarization (tubocurarine 0.5 mg./kg.) the trachea is intubated. Very light general anaesthesia is maintained with nitrous oxide and oxygen, using intermittent positive-pressure ventilation by a pulmoflator.

In the theatre a cannula is placed in a left arm vein for blood transfusion; a nylon catheter is passed from a right arm vein into the thorax for measurement of superior vena caval pressure and serves as an alternative route for intravenous therapy. Blood lost during surgery is estimated by weighing swabs and measuring suction loss, continuous balance being maintained by transfusion with citrated blood. All other intravenous fluids, including those used in manometry, are restricted to a minimum. Intermittent pethidine and tubocurarine are given as needed, with an additional dose of these two drugs before perfusion to anticipate the sudden dilution of circulating anaesthetic agents by blood from the pump oxygenator.

During the period of total bypass the lungs are held in a position of partial inflation with a mixture of helium and 20% oxygen at a steady pressure of 5–8 cm. of water to prevent pulmonary collapse.

After perfusion, ventilation is resumed with 100% oxygen until nitrous oxide is needed to maintain anaesthesia. Usually no more anaesthetic drugs are given; 18 patients spoke as soon as the endotracheal tube was removed, two others gradually returning to full consciousness in two hours. In only one instance was it necessary to reverse residual curarization.

Bronchial secretions have not been increased and aspiration has been unnecessary, but before the end of the operation a Ryle tube is passed through the nose to empty the stomach and is left in place.

Surgical Technique

Approach to the Heart and Great Vessels.—A vertical sternum-splitting incision is made, using a Gigli saw to divide the bone in the midline. The left internal mammary artery is isolated and catheterized with a fine elastic nylon tube for arterial pressure recording. After reflection of the lower pole of the thymus the pericardium is opened vertically in its full extent. Traction sutures hold the pericardium over the edges of the sternum, thus protecting the pleural cavities. A self-retaining retractor spreads the incision. Whilst the heart is being exposed the left common femoral artery is prepared for later cannulation, and through the same incision in the groin the saphenous vein is catheterized for recording pressure in the inferior vena cava.

Examination of the Heart.—Confirmation of the diagnosis is next sought by direct observation of the size of the various cardiac chambers, by palpation of the thrill invariably present, and by measurement of the pressures within the pulmonary artery and the right and left ventricles. A search is also made for any anomaly in the venous return of the heart, particularly for a left superior vena cava, which if present is temporarily occluded. A most thorough search is made for a patent ductus arteriosus, which must be ligated.

Preparations for Cardio-pulmonary Bypass

Half-inch lengths of Paul's tubing are placed around the venae cavae close to their points of entry into the right atrium and are threaded through a rubber tube to form a snare. The ascending aorta is mobilized at a point approximately 2.5 cm. above its origin so that it will later be possible to occlude it by a clamp put across it at this site. Just proximally a purse-string suture of 5/0 silk is placed through the adventitia of the aorta on its anterior aspect. At this stage heparin (3 mg./kg. body weight) is given. A stainless-steel cannula is inserted into the previously prepared site in the common femoral artery, and this is then connected to the arterial line of the pump oxygenator. Each vena cava is cannulated via separate incisions in the wall of the right atrium in the region of the appendage. The tips of the plastic catheters used are positioned to lie approximately 3 cm. beyond the snares, and they are then joined by a Y connexion to a single tube of 1.25 cm. bore which leads to the oxygenator. The caval catheters are of such a size that flow of blood around them to the heart is not obstructed, but they are known to be more than adequate to carry the flow required during bypass. Care is taken to remove all air from arterial and venous pipelines. Elective cardiac arrest (Melrose *et al.*, 1955; Gerbode and Melrose, 1958) is induced in all cases, and the arresting solution (potassium citrate 1 g. in 50 ml. of blood) is made ready at this stage.

Cardiac Bypass and the Intracardiac Procedure

Partial bypass of the heart and lungs is now begun; the clamps previously applied to the arterial and venous pipelines are removed and venous blood flows by gravity into the oxygenator, arterialized blood being returned by the pump into the femoral artery. Stay sutures are inserted into the right ventricle. A few minutes later a partial bypass is made total by tightening the snares and anchoring the snares around the venae cavae; all blood returning to the heart is thus diverted

by the oxygenator, and the heart is seen at once to become much smaller. A small incision is made in the right ventricle between the stay sutures and a low pressure sucker inserted into its cavity; the blood that is aspirated consists of the coronary venous return to the right atrium and the blood returning to the heart from the lungs. Blood sucked in this way is eventually returned to the oxygenator. A needle (18 s.w.g., 8 mm. in length) is next inserted into the lumen of the ascending aorta in the centre of the purse-string stitch, the aorta is then cross-clamped just distally, and the arresting solution injected as rapidly as possible. Within a few seconds cardiac arrest occurs, the needle is withdrawn and the purse-string suture tied to avoid later troublesome bleeding from the puncture site. The ventricular incision is now extended upwards and downwards and the interior of the right ventricle is inspected. The low-pressure sucker is placed in the pulmonary artery after securing a dry field.

The common type of septal defect which lies immediately below the crista supraventricularis can usually be readily identified and adequately displayed for precise closure if traction sutures are inserted at each end of it. The flaccid condition of the arrested heart greatly facilitates the exposure. The defect is closed in two layers by interrupted sutures of silk; care is taken to avoid damage to the leaflets of the aortic valve. When considered necessary for security the second layer of sutures are tied over a small piece of polyvinylformol ("ivalon") sponge. (A very large defect may require insertion of a patch of the same material, as in Case 6.) The rest of the septum is examined for the presence of a second defect, particularly inferiorly in its muscular part. If infundibular narrowing is present sufficient muscle is resected to ensure that there is no

FIG. 6.—Intracardiac pressures in Case 12 before (B) and after (A) closure of the ventricular septal defect. Prior to closure there is a well-marked gradient at infundibular level. After closure of the defect and infundibular resection the gradient is much reduced. Note also satisfactory fall in pulmonary artery pressure.

obstruction to the outflow tract of the right ventricle (Fig. 6). Distension of the left atrium or left ventricle must be prevented at all costs. If bronchial flow is at all great the infundibulum must be resected before closure of the defect. In the presence of an excessive reflux of blood into the left ventricle through an incompetent aortic valve care is taken to prevent distension of this chamber by direct drainage through the left atrial appendage and mitral valve.

The incision in the right ventricle is next sutured, leaving the closure incomplete centrally where the original stay sutures were inserted. The aortic clamp is released; a coronary blood flow thus begins again and the arresting solution is washed out of the myocardium. The blood that

FIG. 7.—Photograph of boy (Case 16) two weeks after operation, showing the median sternotomy scar. The chest deformity, so common in patients with a ventricular septal defect, is also well seen.

initially wells up through the incompletely sutured ventricular incision is discarded, as it is rich in potassium citrate, but after about 15 seconds the low-pressure sucker is reintroduced into the ventricle and the coronary return collected and passed on to the oxygenator. Within one to three minutes cardiac contractions begin, and, as soon as it is found that the beat is powerful enough to eject blood into the aorta against the pressure maintained in it by the pump, the sucker is withdrawn and suture of the ventricle completed. A short while later the caval snares are released and a partial bypass is re-established. The arterial

inflow from the pump is steadily reduced as the patient's heart resumes full activity and responsibility for the circulation. At this stage intracardiac pressures are measured again and compared with the initial figures in order to confirm correction of the defect.

Closure.—The catheters are withdrawn from the cavae and the atrial incisions repaired. The cannula is also removed from the femoral artery and the incision in its wall carefully repaired. Protamine sulphate (4.5 mg./kg. body weight) is now given in order to restore the clotting mechanism of the blood. Haemostasis is carefully secured before closure of the chest is begun and tubes are placed to drain the pericardial sac and the mediastinum, and if either pleural cavity has been opened this is also drained; all tubes are led through underwater seals and continuous suction is applied.

The Perfusion

The perfusion was without difficulty in all but one of these patients in whom a large patent ductus arteriosus which could not be ligated made perfusion impossible. A patent ductus is a direct route from the aorta to the open heart through the pulmonary vessels, and a high proportion of the blood delivered to the aorta is returned to the machine and fails to perfuse the patient.

A flow rate of 2.4 litres per square metre of body surface was maintained throughout the bypass, which flow allowed but little variation in arterial and venous pressures. The smallest patient received 1.2 litres a minute, the largest 4.3 litres a minute.

The average perfusion was of 39 minutes (30–68 minutes), during which time elective cardiac arrest was maintained for an average of 24 minutes (13–52 minutes).

Venous drainage was obtained by gravity, a difference of 25 cm. (10 in.) being established between the height of the operating table and that of the oxygenator. This differential was always in excess of that required, and on every occasion a screw clamp on the outflow tube had to be partially closed to maintain a normal venous pressure within the great veins. Great care was taken to adjust this clamp accurately, it being felt that such adjustment gives the least possible disturbance to vascular tone and ensures a smooth perfusion.

Return of oxygenated blood into the common femoral artery was always carried out at a line pressure of less than 200 mm. Hg. This pressure, reflecting as it does both the resistance of the cannula and that of the patient's vascular bed, can be used to measure the flow rate from the pump. As the mean pressure in the aorta is known, then the pressure created by the cannula can be determined. Previous calibration of each cannula enables an accurate measurement of flow rate to be obtained from this pressure measurement.

Oxygenation was always adequate, as was carbon dioxide removal. At no time was the rotational speed of the oxygenator excessive, and usually it was below 50 revolutions a minute. Heat loss from the oxygenator was prevented by radiant-heat lamps and the body temperature maintained within 1° C.

Removal of blood from the open heart was never a problem, cross-clamping the aorta producing an almost dry field. Blood contained in the heart at any time was removed by gentle suction and stored in a settling helix before return to the heart-lung machine. An additional high-vacuum suction was available, but blood recovered in this manner was rarely re-used. The pressure in the superior and inferior venae cavae as well as intra-aortic pressure was continuously displayed and recorded. Both the electrocardiogram and the electroencephalogram were similarly monitored.

Post-operative Care

At the conclusion of the operation the patient is carefully lifted from the operating table on to a weighing machine. After allowance for drainage-tubes and dressings his weight is compared with the pre-operative figure. The difference in weight forms a useful check on blood and fluid balance derived from swab-weighing and measurement during the operation. The patient is placed on his bed in the operating theatre and transferred to the recovery ward. An oxygen tent, adequately cooled and humidified, is placed around the head of the patient, and tubes are reconnected to drainage bottles and continuous suction at 3 cm. of Hg vacuum.

A clear record is kept, on which blood transfusion is shown balanced against drainage from pleural and pericardial cavities, and watery fluids infused are balanced against urinary output and gastric aspirations. It is our practice to limit fluid for the first 24 hours to avoid gastric distension. The Ryle tube is aspirated intermittently for the first 24 hours, should nausea or gastric distension warrant it.

Intravenously dextrose 5% with sodium chloride 0.3% is given, 400 ml. per square metre of surface area during the first 24 hours and 800 ml. per square metre during the second 24 hours. Thereafter normal diet is quite rapidly resumed.

During the first 24 hours pulse and blood pressure are charted at 15-minute intervals and the patient is turned and encouraged to cough and breathe deeply. It is found useful to introduce the younger child to an oxygen tent pre-operatively so that his post-operative surroundings are not too unfamiliar. Parents are invited to visit the children as soon as they are in the recovery ward and every few hours thereafter.

Post-operative Drugs.—If the patient has been already digitalized pre-operatively this is continued. Otherwise

digitalis is withheld unless the pulse rate is unduly rapid or the jugular venous pressure high. If heart block is present isoprenaline is administered as a suppository (2.5 mg.) should the heart rate fall below a figure at which a satisfactory blood pressure can be maintained. The precise figure cannot be stated, as the age and condition of the patient is the determining factor. In the two patients in this series who required this drug its use was continued at lengthening intervals from five-hourly for the first 48 hours. Antibiotics, consisting of penicillin, streptomycin, and chloramphenicol, are used prophylactically for the first four days. Some patients received erythromycin and novobiocin, but these drugs were not well tolerated.

Convalescence.—The patients were allowed up at the end of a week and were usually discharged from hospital at the end of three weeks. A number of patients had a rise in jugular venous pressure during the first week post-operatively, but this fell gradually during the last ten days in hospital. These children tend to be extremely active during the last week and can make a marked contrast with the pre-operative picture.

Post-operative Complications

Chest haemorrhage was a problem in only two patients. In all cases the clotting mechanism has been rapidly restored to normal; the platelets have been reduced at the end of the perfusion to an average of 60,000 c.mm., but the figure rises to normal early in the post-operative period. The usual blood loss has been less than 500 ml. In two patients the loss was over 1 litre and probably contributed to their death. Both were patients in whom a fall in pulmonary artery pressure had not been obtained, so that pressures on the right side of the heart were unusually high. It is possible that bleeding may have occurred from manometric puncture sites or the cardiac wounds.

Pulmonary Complications.—Coughing and deep breathing is not easy during the first few post-operative days, though we believe it is less difficult if the midline sternum splitting incision is used. In several of our cases expectoration of sputum has been a problem, but in only one instance was a tracheostomy required. The left lower lobe requires an especially careful watch as it is somewhat displaced by the enlarged heart, and the left main bronchus is often narrowed by the large pulmonary artery. Pulmonary oedema has not been encountered.

Infection.—Localized wound infection occurred in two patients, but in no instance was there any suggestion of infection of the blood stream.

Heart-block.—Transient heart-block has occurred in several patients during the period immediately following re-establishment of the heart-beat. Complete heart-block persisted in two patients, in one of whom the idioventricular rate was too low to support an adequate blood pressure even after intravenous isoprenaline in repeated doses of 0.1 mg. The artificial pacemaker connected directly to the ventricle maintained a satisfactory rate and blood pressure until the child's sudden death 10 hours post-operatively (Case 9). In the other patient the use of isoprenaline was satisfactory.

Surgical Pathology

Septal Defect.—In all patients the right ventricle was grossly enlarged, with a well-marked thrill best felt over the outflow tract and the base of the pulmonary artery. The right atrium was normal in size in all cases except one; in this latter instance the jet of blood passing through the defect was blowing the septal cusp of the tricuspid valve back into the atrium, producing tricuspid incompetence (Case 13). In all our patients the defect was located high up on the septum but inferior to the crista supraventricularis; the upper margin of this defect was formed by the annulus of the aortic valve, with the right and posterior aortic leaflet visible immediately beyond the rim. The lower margin of the defect was formed by the muscular interventricular septum, but often had a well-developed fibrous rim. One

patient (Case 9) had in addition a second defect in the muscular septum, and in Case 6 there was a single ventricular chamber. Excluding this last case, the size of the defect varied from 1 to 3.5 cm. in diameter.

Coexistent Patent Ductus Arteriosus.—In our first patient a patent ductus was not suspected until perfusion was started and a shunt from the systemic circulation into the pulmonary artery was encountered. Perfusion proceeded normally after ligating the duct. In all subsequent patients the left pulmonary artery was deliberately explored from inside the pericardium in order to exclude the presence of a ductus, and in this way two further undiagnosed ducts were discovered. One of these was successfully ligated, but the other, a thin-walled friable ductus 2.5 cm. in diameter, tore during mobilization and led to death (Case 15). The ductus diagnosed by aortography (Case 20) was ligated without difficulty.

Infundibular Obstruction.—This was present to some degree in nine of the cases. In all cases the obstruction was due to an irregular but generalized hypertrophy of the muscle of the outflow tract and the crista supraventricularis which appeared to be part of the generalized right ventricular hypertrophy. As much infundibular muscle was removed as was necessary to relieve the obstruction, and post-operative manometry rarely revealed a gradient or more than 10 mm. Hg.

Results

Mortality

Of the 15 patients with a ventricular defect as the sole lesion only one died. Among the four patients with an additional patent ductus, two died. A patient with two defects also died, but one with a single ventricle survived.

As previously mentioned, one of the deaths occurred on the table when it was found impossible to ligate a large ductus. The other three occurred between 5 and 36 hours after operation, and were of a similar pattern with sudden cessation of respiration after a period of restlessness and low blood pressure. None of these patients had more than a slight fall in pulmonary artery pressure after closure of the defect, and it seems possible that death was due to abrupt right ventricular failure. Two of these three had a moderate-to-large haemothorax, one of which was treated by open operation.

Reduction in Right Heart Pressures with Closure

We consider that a substantial fall in right ventricular and pulmonary artery pressure after closure of the defect is an important sign, since it indicates that much of the pulmonary hypertension was due to flow rather than to changes in the pulmonary vessels and therefore that the long-term results from closure of the defect are likely to be good. It also indicates that the defect is substantially closed and that no other lesion causing a further left-to-right shunt—such as a second V.S.D.—is present. In order to take account of changes in systemic pressure after closure we have expressed the right ventricular systolic pressure as a percentage of the left (R.V.P./L.V.P.%), and these pressures have been measured at operation in all cases. Prior to closure, R.V.P./L.V.P. ranged from 37 to 100%, with an average of 67%.

After closure of the defect the right ventricular pressure fell in 16 patients and was unchanged in 4. The extent of the fall has been expressed as R.V.P./L.V.P.% before closure minus R.V.P./L.V.P.% after closure—for example, before 100%, after 63%, fall=37%. The fall in pressure averaged 33%, with a range of 8 to 58%. Details are available in Tables I and II. A small fall in pressure does not imply a poor result if the initial pressure, as in Cases 2 and 4, is low, but otherwise it presumably indicates that considerable pulmonary vascular disease is present.

In the whole group of 20 patients whose defects were closed the R.V.P./L.V.P.% after closure was close to normal in five, slightly elevated in eight, moderately raised in three, and high in four.

TABLE II.—Operative Findings, Anatomical and Haemodynamic

Case No.	Size of Defect (cm.)	Infundibular Hypertrophy	Infundibular Gradient, mm.Hg		R.V.P. %* L.V.P.	
			Before	After	Before	After
V.S.D. Alone						
1	3×2	0	0	0	100	63
2	1.5×1.5	0	0	0	37	31
3	1.5×1	0	25	5	94	29
4	2×1	+	50	2	38	29
7	1.5×1.5	+	16	6	74	72
8	2×2	+	36	10	86	45
10	2.5×2.5	0	3	10	92	34
11	3×3	+	25	17	83	39
12	3×2	+	32	7	73	36
13	1.5×1.5	+	7	0	51	38
16	2.5×2.0	0	0	0	100	46
17	1×1	0	0	5	63	55
18	3.5×3.5	+	70	4	100	45
19	2×2	+	14	10	70	39
21	2×1.5	+	20	15	71	55
V.S.D. and Patent Ductus						
5	2×1.5	0	0	0	67	40
14	2×2	+	10	20	91	86
15	0.7×0.7	—	—	—	—	—
20	1×1	0	0	9	93	66
Two Ventricular Defects						
9	(1) 1×1 (2) 1×1	0	0	0	75	96
Single Ventricle						
6	3.5×3	0	12	14	96	96

* R.V.P.% = right ventricular systolic pressure
L.V.P.% = left ventricular systolic pressure %

Post-operative Assessment

On discharge from hospital three to six weeks after operation all the patients were active and well. The exercise tolerance was improved in most patients. This was particularly obvious in a boy of 2½ years with a huge left-to-right shunt (Case 2), who from being unable to walk more than 20 yards was able to run vigorously without distress. In one patient (Case 7) who had a very small shunt with a high resistance, and no fall in right heart pressures after closure, there was but little improvement.

The jugular venous pressure and pulse were normal in all except the patient with a single ventricle in whom a high venous pressure persisted for several weeks. The arterial pulse sometimes retained its waterhammer quality and one patient still had complete heart-block, with a rate of 90. The cardiac impulses were usually less marked after operation, but the diminution in right ventricular heave depended on the fall in right ventricular pressure obtained.

The most striking change in physical signs was, however, found on auscultation. The thrill and murmur of the ventricular defect disappeared in all patients (Fig. 1B), and in only two instances did a mitral diastolic murmur persist. In these two patients the defect appeared on other grounds to be closed, and the murmur is attributed to mild congenital mitral stenosis; one of these was the patient with a single ventricle who also had a loud apical systolic murmur possibly due to mitral incompetence. Soft or moderate ejection systolic murmurs at the left sternal edge were quite common post-operatively and probably originated in the infundibulum or pulmonary artery; they were sometimes best heard near the apex. A basal diastolic murmur persisted in four. The second heart sound remained loud and closely split in Case 7, who still had substantial pulmonary hypertension after closure, but otherwise was usually softer and was sometimes widely split from right bundle-branch block.

The electrocardiogram in most cases showed a constant and unusual pattern. There was complete right bundle-branch block with the secondary R wave persisting as far as V5-V6 together with striking T-wave inversion in all chest leads. These appearances were presumably due to the intracardiac manœuvre and the ventriculotomy (Fig. 5).

Radiological assessment is probably not very profitable so soon after surgery, but in one case there was considerable diminution in heart size, and others have shown a definite reduction in pulmonary plethora.

Indicator dye-dilution curves performed on two patients post-operatively (Cases 5 and 6) have demonstrated the absence of a left-to-right shunt. Cardiac catheterization is being deferred until a year or more after closure of the defect.

Conclusions

Our results harmonize with those of other workers in showing that closure of ventricular septal defects can be carried out in special centres as a routine surgical procedure with an acceptably low mortality in suitable cases. The indications and contraindications to operations have been outlined, but in assessing cases for operation we have experienced two main problems: first, the detection of additional lesions; and, second, in predicting whether a good haemodynamic response will result from closure.

The most important additional defect is a patent ductus, for it renders perfusion impossible. As already mentioned, this lesion was definitely diagnosed (by aortography) in only one of our four patients with it, though it was queried in one other. We suspect the diagnostic difficulty may lie in the fact that in patients with a V.S.D. the duct is virtually functionless and therefore gives rise to practically no direct signs. Support for this hypothesis is given by the absence of a thrill over the ductus at operation in three of the four patients and by the findings in Case 20. In this last patient, prior to aortography, 2 ml. of indicator dye was injected into the aorta via a retrograde arterial catheter, and no recirculation due to dye entering the pulmonary artery (Swan and Wood, 1957) was found. Further, at operation, no change in right heart or systemic pressure was noted when the duct was ligated. One patient (Case 21) was found at operation to have severe aortic incompetence, and clinically this was not diagnosed with certainty.

The other problem is that of predicting which patients will achieve a substantial fall in pulmonary artery pressure after closure. In this respect, other workers (Zimmerman *et al.*, 1957) have emphasized the importance of the actual level of the pulmonary artery pressure, but in our series this has not been helpful. We believe that the pressure must be considered in relation to pulmonary flow and that it is useful to calculate the pulmonary arteriolar resistance. However, the difficulty in young children of measuring the oxygen consumption, and also other factors, make the calculated resistance in many cases at best an approximation. It may turn out to be just as helpful to consider simply the oxygen saturation in the pulmonary artery, which has been over 80% in all our patients whose pulmonary pressure fell after closure. As mentioned earlier, it is necessary to consider all aspects in deciding for or against operation in the borderline cases with a high pulmonary resistance. No patient should be categorically denied operation if there is evidence of an appreciable left-to-right shunt, but when the pulmonary resistance is high and the unfavourable features already mentioned are present, a much higher operative mortality must be faced. It is clear from our results, however, that a number of patients who might in other centres be considered inoperable have had their defects successfully closed.

It must be emphasized that, in such a rapidly expanding field, views necessarily change fast as a result of new experience. Firm rules should not therefore be formulated until opinion has crystallized in the light of further knowledge of the problems involved.

Summary

Twenty-one patients with ventricular septal defect have been treated by open surgery using extracorporeal circulation.

The clinical features, indications for operation, surgical technique, and post-operative care are presented.

The results of surgical treatment are given and the implications of these are discussed.

We are indebted to Dr. R. E. Bonham-Carter, not only for referring many of these patients, but also for his continued encouragement and support; to Dr. J. D. James and Dr. P. B. Booth and the staff of the North London Blood Transfusion Service for their unfailing co-operation; to Professor J. V. Dacie and his colleagues in the department of haematology in the Postgraduate Medical School of London; and to the matron and nursing staff of Hammersmith Hospital. To Mr. J. R. Robson, Mr. E. Gains, Miss M. Murphy, and Mrs. E. Victor, the technical staff of the department of surgery, and to Mr. C. Lordon and the staff of the workshops of the Postgraduate Medical School we owe a special debt of gratitude.

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Natural Causes, a new play on a challenging theme by Mrs. Vera Colebrook, was given a number of performances in London last month at the Hovenden Theatre Club. The action of the play takes place in the country house of an old lady who has just suffered a cerebral haemorrhage, complicated by the onset of pneumonia. Her family doctor had previously given her a solemn promise that should she fall seriously ill he will not administer any antibiotic or other drug that may prolong her life—or, rather, “prolong her death.” On the insistence of her daughter-in-law, a well-known London consultant is called in; he advises injections of penicillin. The family doctor refuses to give these, telling the consultant of his promise and insisting that there is all the difference in the world between administering a lethal dose and withholding a life-saving drug. The old lady’s two children want their mother to die as she had lived, with dignity and without fear of mental deterioration. But her shrewish daughter-in-law desires only that her mother-in-law’s life might be prolonged for the sake of the benefits her annuity brings to the family. The Hovenden Players, directed by Miss Valery Hovenden, were completely successful in bringing out the realism of this situation. A philosophical nurse—who assumes a more pronounced Irish brogue with private cases, because “it goes down so lovely with the patients”—adds a touch of humour to the play, which is not concerned with “mercy killing” but rather with the truth or otherwise of Clough’s “Thou shalt not kill, but needst not strive officiously to keep alive.” The whole vexed problem, while remaining unsolved, is given an unexpected twist by the London consultant at the end of the play.

STAPHYLOCOCCAL INFECTION RESISTANT TO CHLORAMPHENICOL, ERYTHROMYCIN, AND NOVOBIOCIN

EFFECT OF ANTIBIOTIC COMBINATIONS ON THE EMERGENCE OF RESISTANT STRAINS

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Control of the use of antibiotics in hospital communities is imperative if we are to combat the adaptability of the staphylococcus to these agents. Until recently most hospitals in Great Britain have tried to keep erythromycin and novobiocin in reserve, to be used only for the treatment of staphylococcal infection resistant to all other antibiotics. By 1957, however, about 50% of all staphylococcal infection occurring in many hospitals was found to be resistant to penicillin, streptomycin, and tetracycline, so that erythromycin and novobiocin inevitably had to be used more extensively.

The danger of the increased use of these two drugs is obvious, since it is well recognized that staphylococci develop resistance to erythromycin and novobiocin more readily than to any other antibiotic except streptomycin (cf. Hobson, 1954; Garrod and Waterworth, 1956; Lin and Coriell, 1957). Moreover, this change occurs quite often during the treatment of staphylococcal infections with erythromycin (Thomson *et al.*, 1956) and novobiocin (Nichols and Finland, 1956), and the spread of erythromycin-resistant strains in a hospital where the use of this antibiotic is extensive may be very rapid (Lepper *et al.*, 1954).

In an attempt to combat this situation a policy for the control of antibiotics was introduced into this hospital at the beginning of April, 1958. The essential items of the policy were: firstly, abandonment of penicillin except in certain wards of the hospital, and, secondly, the use of two antibiotics in combination wherever possible and always when erythromycin or novobiocin was used.

About six months previously a cross-infection committee was appointed to investigate staphylococcal infection in the hospital and to introduce measures for its control. The effect of these measures and that of the antibiotic policy are inextricably confused. Nevertheless analysis of the antibiotic sensitivity pattern of all staphylococcal infections in the hospital throughout the year has brought to light certain facts about the emergence of erythromycin- and chloramphenicol-resistant strains which are considered worth reporting.

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