SURGICAL REPAIR OF RUPTURED SINUS OF VALSALVA

BY

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Successful operations to repair ruptured congenital aneurysms of the sinus of Valsalva have been made possible only by the introduction of hypothermia and extracorporeal circulation. The earliest successful operations were reported by Morrow *et al.* (1957), Lillehei *et al.* (1957), McGoon *et al.* (1958), Cooley (1960), Spencer *et al.* (1960), and Lippschutz and Wood (1960). By 1962 Szveda and Drake had repaired two, and Dubost *et al.* (1962) had reported on the largest series of eight cases. Altogether these reports include 27 patients, three of them operated on under hypothermia and the remainder with extracorporeal circulation, profound hypothermia being used in three of

the cases of Dubost. Surgical correction of this lesion in six patients therefore seemed worthy of report, especially as two of these cases were complicated by coexisting atrial septal defects.

Possible causes of aneurysmal dilatation of the aortic sinuses include a congenital aetiology, bacterial infection, syphilis, and cystic medial necrosis. The condition has been well reviewed by Jones and Langley (1949), Oram and East (1955), and Gibbs and Harris (1961). Our six cases are considered as being of congenital origin, and the other types of aneurysm will not be discussed.

FIG. 1

FIG. 2

FIGS. 1 and 2.—Case 1. Aortogram demonstrating the aneurysm projecting into the right atrium and jetting into the right ventricle.

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Anatomical terminology of the aortic sinuses has caused confusion in the past, and the most frequently observed convention now describes them as left and right coronary, and non-coronary or posterior. Sawyers *et al.* (1957) found 37 cases of congenital sinus rupture in the literature; aneurysmal change involved the right sinus of Valsalva in 26 and the non-coronary (posterior) sinus in 11. The left coronary sinus is least often affected, but may be involved alone, or together with other sinuses; Micks (1940) reported a case of his own, and cited three from the literature in which all three sinuses were abnormal.

The embryology of congenital sinus of Valsalva aneurysms has been investigated by Jones and Langley (1949) and by Edwards and Burchell (1957), and the latter believe that the basic lesion is a defect between the aortic root and the heart. This fault appears to be a lack of continuity between the elastic media of the aorta and the annulus fibrosus due either to a lack of fusion or to later separation. A similar defect may occur below the valve ring, giving rise to a ventricular septal defect, and the two lesions may coexist.

Unruptured sinus of Valsalva aneurysms are rarely diagnosed, but may be demonstrated by aortography (Falholt and Thomsen, 1953). Micks (1940) described a case in which pressure from the aneurysm caused atrioventricular block. Important complications are aortic incompetence and bacterial endocarditis, and as the latter is often the cause of rupture it may be difficult to decide whether the aneurysm has been due to infection or whether it is a congenital lesion complicated by infection. Rupture of a congenital aneurysm is the most frequently noted complication. Rupture may occur in the absence of infection, and Davidsen *et al.* (1958) have noted 17 such cases. Of the 27 cases described in the literature to date in which operation has been carried out, adequate data of the site of rupture are available in 22. The site of rupture was in the right atrium in 13, the right ventricle in eight, and the left atrium in one.

The present series of six patients consists of two women aged 25 and 56 and four males aged 6, 24, 39, and 59. Details of the individual cases are here presented.

Case Histories

Case 1

A woman aged 56 had had "heart disease" diagnosed in childhood but was symptom-free until the age of 55. Since then moderately severe dyspnoea has been present and she was referred for surgery as a case of ductus arteriosus.

Examination.—She was of normal build, with a collapsing pulse and B.P. 210/90. A 7-cm. systolic wave was present in the jugular pulse. The heart was clinically enlarged, and left and right ventricular impulses were palpable. On auscultation a loud continuous murmur was heard, of maximal intensity at the third left interspace parasternally.

Investigations.—The electrocardiogram showed nothing of note; chest x-ray examination revealed cardiac enlargement (C.T.R. 66%) with pulmonary plethora. Cardiac catheterization showed a left-to-right shunt at atrial level. A retrograde aortogram demonstrated a saccular aneurysm of the right coronary sinus communicating with the right atrium (Figs. 1 and 2).

Operation was carried out in September, 1959, under surface hypothermia (31° C.). With caval occlusion and clamped aorta and pulmonary artery the right atrium was opened and a cylindrical aneurysm 2.5 by 1.5 cm. was seen. There was a perforation at the tip opening above the septal leaflet of the tricuspid valve. A fossa ovalis atrial septal defect was also present. The aneurysm was ligated at the base and removed, and the septal defect was sutured (Fig. 3). The post-operative course was uncomplicated.

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When last seen (November, 1961) the patient was symptom-free and leading an active life. No murmurs could be detected, and x-ray examination showed resolution of her pulmonary plethora and diminished heart size (C.T.R. 58%); blood pressure 160/105.

Fig. 3.—Case 1. Operation photograph showing open atrium and saccular aneurysm secured at base by ligature.

Case 2

This patient was a woman aged 25. At 21 a murmur was found at an antenatal examination during the fourth month of her second pregnancy. She was symptom-free, but had had a previous examination, when x-ray films revealed no abnormality. She was first seen by us at this time, and the signs suggested a diagnosis of a ruptured sinus of Valsalva, which was confirmed by catheterization. Mild dyspnoea developed in her last trimester, but she underwent a normal delivery. Some disability persisted, and this increased in severity at the age of 23. At 25 she was readmitted for operation.

Examination.—She was of average build, the venous pulse was normal, her arterial pulse was collapsing, with a B.P. of 145/65. The apex impulse was left ventricular and a parasternal thrill was present. On auscultation there was a continuous murmur at the site of the thrill and a delayed apical diastolic murmur. In the pulmonary area a split second sound was noted, and in the aortic area a distinct loud diastolic murmur had developed since she was first seen at 21.

Investigations.—The electrocardiogram indicated biventricular hypertrophy, and x-ray examination showed plethora and slight cardiac enlargement (C.T.R. 52%). Catheterization suggested a shunt at low right atrial and at ventricular levels. An aortogram showed aortic incompetence and a sinus aneurysm leaking into the right ventricle.

Operation was carried out in October, 1959, using extracorporeal circulation and potassium arrest, and the right atrium was explored. A tubular aneurysm 2 cm. long extended from the right coronary sinus into the atrium with its orifice at the angle of the tricuspid valve, thus "jetting" into the ventricle. An aortic valve cusp was partially prolapsed through the aneurysm and a small fossa ovalis atrial septal defect (2 by 2.5 cm.) was present. The aneurysm was excised, competence of the aortic valve was restored, and the atrial septal defect was sutured.

Post-operative Course.—A soft aortic diastolic murmur was the only abnormality on auscultation after surgery until a pyrexia developed. Evidence of bacterial endocarditis appeared, and this murmur became louder and then a continuous murmur reappeared. The infection eventually responded

to methicillin, but it was thought that the repair had broken down. Two years later she was symptomatically much improved, working full-time, and able to climb three flights of stairs. The x-ray picture showed decreased plethora and a smaller heart, and her blood-pressure was 135/85. A continuous murmur remained, softer than that present before operation.

Case 3

This man, aged 24, was discharged from the Forces A1 at the age of 23 and a murmur was first noted on a routine examination a few months later. He was referred to his local hospital, where investigations, including catheterization, suggested a diagnosis of a ruptured sinus of Valsalva. Two months later he was readmitted with bacterial endocarditis and treated with a six-weeks course of penicillin. His only disability was mild dyspnoea, of gradual onset and present before his recent infection.

Examination.—He was of average build, with sinus tachycardia and a collapsing pulse; B.P. 115/40. A 12-cm. systolic jugular venous pulse was present. The heart was enlarged, with distinct left and right ventricular impulses. On auscultation a loud continuous murmur at the left sternal border and a delayed apical diastolic murmur were heard.

Investigations.—The electrocardiogram showed right axis deviation, partial right bundle-branch block, and left ventricular dominance in the chest leads. Chest x-ray examination showed plethoric lung fields and cardiac enlargement (C.T.R. 62%). Catheterization previously had shown a left-to-right shunt at atrial level. Retrograde aortography showed an aneurysm of the right aortic sinus communicating with the right atrium.

Operation was carried out in May, 1960, under hypothermia at 30° C. A saccular aneurysm 2 by 0.75 cm. was presenting in the right atrium. It was calcified in places and perforated. No other lesions were present. The aneurysm was tied and removed. The post-operative course was uneventful. In February, 1961, he was at work without symptoms. No significant murmurs were present and x-ray examination showed reduction of the heart size to 53% C.T.R.

Case 4

This man, aged 39, had a questionable history of rheumatic fever at 14, when a murmur was noted. He was symptom-free and very active until an attack of nocturnal dyspnoea at 38 occurred after strenuous physical exertion during the day. He recovered from this and remained well until four months prior

FIG. 4

FIG. 5

FIGS. 4 and 5.—Case 4. Aortogram demonstrating the aorto-right-ventricular communication.

to operation, when a similar episode occurred. This attack was followed by congestive cardiac failure and he was referred as a case of persistent ductus arteriosus.

Examination revealed sacral and ankle oedema with hepatic enlargement and a 14-cm. systolic wave in the jugular venous pulse. The blood-pressure was 130/60 and a left ventricular apex beat was palpable in the mid-axillary line. On auscultation a loud continuous murmur was present at the left sternal edge and a delayed apical diastolic murmur was heard.

Investigations.—The electrocardiogram showed left ventricular hypertrophy. Chest x-ray examination showed gross plethora and cardiac enlargement (C.T.R. 68%). Catheterization was not carried out. An aortogram revealed an aneurysm of the right coronary sinus communicating with the right ventricle below the pulmonary valve (Figs. 4 and 5). After intensive treatment for his failure with only limited success, he was referred for surgery.

FIG. 6.—Case 4. Drawing from operation, showing the right-ventriculotomy and the stages in excision and prosthetic repair of the sessile ruptured aneurysm in the right ventricle.

Operation was carried out in March, 1961, using extracorporeal circulation. The right ventricle was incised and a 2-cm. long tubular aneurysm with two rupture holes could be seen projecting into the ventricle. A small ventricular septal defect was also present. The aneurysm was sutured and removed and the septal defect was patched (Fig. 6).

Post-operatively a massive diuresis occurred in the first three days following surgery, and after a slow recovery he was discharged with no signs of failure and a blood-pressure of 140/80; the only remaining murmur was a soft aortic diastolic bruit.

Case 5

This patient was a man aged 59. A murmur was first noted at the age of 32 and he was asymptomatic until six months before admission. He was then woken by nocturnal dyspnoea, and his effort tolerance was thereafter reduced. Three further episodes of nocturnal dyspnoea occurred subsequently.

Examination showed him to be of normal build with a collapsing pulse, blood-pressure 200/30, and frequent ectopic beats. The venous pressure was normal. The apex beat was left ventricular, and auscultation elicited a pulmonary ejection sound and a loud continuous murmur over the mid-sternum.

Investigations.—The electrocardiogram varied; intermittent right bundle-branch block and a varying pacemaker were present. X-ray examination showed plethoric lung fields and a C.T.R. of 60%. Catheterization revealed a left-to-right shunt at ventricular level, and a pressure gradient at the pulmonary valve (R.V.P. 100/0, P.A.P. 50/10). Aortography showed a grossly dilated pulmonary artery and a ruptured sinus aneurysm entering the right ventricle.

Operation was carried out in February, 1962, using extracorporeal circulation and hypothermia to 30° C. The right ventricle was opened. A "wind-sock"-shaped aneurysm projected from the posterior non-coronary cusp into the right ventricle immediately beneath the pulmonary valve. Calcification was present surrounding both the orifices of the aneurysm and the adjacent pulmonary valve cusp, causing pulmonary incompetence. The aneurysm was excised and the sutured base was reinforced with a patch of pericardium (Fig. 7).

The post-operative course was uneventful except for transient atrial flutter. On discharge the blood-pressure was 140/90.

Pulmonary systolic and faint diastolic murmurs were present but the continuous murmur had disappeared. Two months after discharge this man died in a prolonged paroxysmal tachycardia at another hospital. Necropsy showed complete repair of the sinus rupture.

Case 6

This patient was a boy aged 6. A murmur was found at the age of 3, when dyspnoea was first noted. He was moderately disabled.

Examination.—A boy of frail build with a prominent upper chest; blood-pressure 120/60, and venous pressure normal. Apex beat was biventricular, and auscultation revealed the following: basal ejection and immediate diastolic murmurs, left parasternal pansystolic and diastolic murmurs, and a delayed apical diastolic murmur. The electrocardiogram was right ventricular. Radiographs showed plethoric lung fields with a C.T.R. of 74%. Catheterization revealed a left-to-right shunt at ventricular level with a 3:1 flow ratio. A clinical diagnosis of ventricular septal defect and aortic incompetence was made.

In August, 1962, an exploratory atriotomy, using extracorporeal circulation and hypothermia to 30° C., revealed the orifice of a coronary sinus aneurysm into the atrium. The right ventricle was then opened and an infracristal ventricular septal defect 2.5 by 3 cm. was found and repaired with a patch. The orifice of the ruptured sinus was approached through the tricuspid valve and closed by direct suture. After closure of the ventricle free aortic regurgitation was apparent; the aorta was then opened and the deformed valves were repaired.

FIG. 7.—Case 5. Operation photograph showing right-ventriculotomy and saccular aneurysm held by tissue forceps.

Clinical Findings

The presence of the ruptured sinus of Valsalva in the above cases became manifest either by the onset of dyspnoea or by the detection of a murmur. In the two older patients a murmur was known to have been present for at least 25 years. In the four younger patients routine examination several years prior to the diagnosis of ruptured

sinus of Valsalva had not revealed any evidence of heart disease. The detection of a murmur preceded symptoms and first suggested the diagnosis in two of the younger patients, whereas the onset of dyspnoea was the presenting complaint in the remainder. Bacterial endocarditis occurred in one patient after the diagnosis of ruptured sinus of Valsalva had been confirmed by cardiac catheterization. Thus infection did not cause rupture in any of these patients, and in four there was no precipitating cause. Rupture was associated with pregnancy in one patient and followed strenuous effort in another, a man who was suffering from severe congestive failure when first seen. The remainder had mild-to-moderate dyspnoea on effort at the time of surgery.

Clinical findings were similar in all six patients. A wide pulse pressure was present, and cardiac enlargement was chiefly left ventricular, although a right ventricular impulse could often be felt as well. On auscultation there was a loud continuous murmur at the left sternal border in all cases, a delayed apical diastolic in three, and an aortic diastolic bruit in two. The venous pressure varied; it was normal in three cases and raised, with a prominent systolic wave, in three.

The E.C.G. patterns varied; left or biventricular hypertrophy was usually present. Chest x-ray examination invariably showed pulmonary plethora and cardiac enlargement. The catheter findings in five cases are detailed in Table I. In two cases the shunt occurred at atrial level, in one case it appeared at both atrial and ventricular levels, and in two cases it was confined to the ventricle. The shunts were not large except in the case of the child with an associated ventricular septal defect. The pulmonary pressure was raised without any increase of pulmonary vascular resistance in four cases.

TABLE I.—Catheter Findings in Five Cases

Case No.	O ₂ Saturations (%)				Pulmonary/ Systemic Flow Ratio	P.A. Pressures	P.V.R.
	S.V.C.	R.A.	R.V.	P.A.			
1	75	84	84	84	1.6:1	36/5	1.7 units
2	73	77	85	84	2:1	30/10	1.0 unit
3	63	82	82	84	2:1	50/25	1.0 "
5	64	64	81	81	2:1	50/10	1.5 units
6	75	77	89	89	3:1	52/30	—

Operative Findings and Technique

Surgery was performed with surface cooling in two cases and with extracorporeal circulation in four. In four of the cases the aneurysm had ruptured into the right atrium.

TABLE II.—Operative Details in Six Cases

Case No.	Sex and Age	Ruptured Sinus	Chamber of Entry	Associated Defects	Method
1	F 56	Right	R. atrium	A.S.D.	Hypothermia
2	F 25	"	" " (+R.V.)	A.S.D., A.I.	By-pass
3	M 24	"	"	—	Hypothermia
4	M 39	"	" ventricle	V.S.D.	By-pass
5	M 59	Posterior	"	P.I.	"
6	M 6	"	" atrium	V.S.D., A.I.	"

P.I.=Pulmonary incompetence. A.I.=Aortic incompetence.

and in the other two into the right ventricle. The findings at operation are summarized in Table II. In three of the cases with aorto-atrial fistulae the aneurysm presented a "wind-sock" appearance, measuring 2 to 2.5 cm. in length and 0.75 to 1.5 cm. in diameter. In the child this tubular appearance was not present. The ruptured orifice was small, measuring 3 to 5 mm. at the tip of the cylindrical

aneurysm, and presented just above the septal leaflet of the tricuspid valve. In two cases the opening of the aneurysm lay so close to the valve that the jet projected into the right ventricle. In these four cases of aorto-atrial fistulae two also had central foramen ovale atrial septal defects, one had free aortic incompetence due to prolapse of an aortic cusp into the aneurysm, and one had an associated ventricular septal defect with aortic incompetence.

In the two cases with aorto-right-ventricular fistulae the aneurysms had double perforations projecting high into the outflow tract. In one a small ventricular septal defect was present, and in the other pulmonary incompetence was found. In the latter case calcification surrounded the orifice of the aneurysm, and the adjacent pulmonary valve cusp was heavily calcified and deformed.

The surgical approach to a ruptured sinus of Valsalva is conditioned by its position. If it can be determined that the leak is into the right atrium the lesion can be handled by circulatory occlusion under 30° C. hypothermia obtained by surface-cooling. This was done in two out of our six cases, and might have been done in a third but for the fact that the rupture was assumed to be into the right ventricle when in fact there was a jet projecting from the atrium through the tricuspid valve into the diaphragmatic aspect of the right ventricle. Aneurysms opening into the ventricle require extracorporeal circulation because the lesion is more complex and requires more time for repair.

The procedure used in exposing and repairing the aorto-atrial aneurysm is a routine one employed in right atriotomy. Our own preference is for a transverse fourth-space incision to expose the atrium, which is opened longitudinally after vena caval clamping, and allowing the heart to beat itself empty. Aortic clamping is necessary to prevent back-flow of blood from the aorta through the ruptured sinus.

For ventricular aneurysms a vertical chest incision allows a better exposure of the right ventricle, and when full perfusion has been established a transverse incision is made in the ventricle 1–2 cm. below the pulmonary valve sinuses. When visualized, the aneurysm usually presents as a white or yellowish bulge or wind-sock with a narrow neck 5–6 mm. wide and small perforations at its apex. It balloons readily with each systole and provides a well-marked jet. In the two cases with aorto-ventricular aneurysms the sac was wider and shorter than those that occurred in the aorto-right-atrial fistulae.

The procedure for repair consisted in excising the sac if it was degenerate or calcified but leaving some margin to assist in the application of sutures. A long narrow sac could be transfixed and oversewn by one or two sutures; a wider one required closure by patching. Any defect more than 0.75 cm. in diameter is likely to be under undue strain with simple suture, and a double layer of pericardium used as a patch and held in place with six to eight stitches has proved satisfactory. The one case of aorto-atrial rupture without a tubular aneurysm was repaired by direct suture of the orifice.

The coexisting atrial septal defects occurring in two cases were repaired by direct suture, and associated ventricular septal defects required patching for closure.

When repair is complete, the aortic clamp is released to test for any leakage and if satisfactory the heart is closed and the circulation restored in the usual manner.

The actual surgery is not difficult if the means of exposure are adequate, and with our limited experience it would appear that aneurysms rupturing into the atrium are

more often of the wind-sock variety and easier to repair than ventricular ones.

Post-operative Course.—This was relatively uneventful in four patients (Cases 1, 3, 4, and 5). (An immediate and dramatic post-operative diuresis occurred in the one patient (Case 4) in failure at the time of surgery.) In all four the continuous murmur disappeared and the heart decreased in size with concomitant reduction of pulmonary plethora on x-ray film. In the two earlier cases the patients became symptom-free and returned to work; no murmurs were heard when they were last examined. Two more recent cases were left with slight aortic and pulmonary incompetence respectively, but symptomatically the results were excellent. Unfortunately, one of these patients (Case 5) died during a prolonged attack of tachycardia three months after operation. One patient (Case 2) had an incomplete repair owing to post-operative bacterial endocarditis. This infection caused a partial breakdown of the repair and the return of a continuous murmur. However, a smaller pulse pressure and heart size support her affirmation of improvement in effort tolerance. The sixth case has only recently been repaired and it is too early to assess the results of surgery.

Discussion

The symptomatology of this condition has been fully described by Oram and East (1955). It is of interest that none of our patients suffered from any chest pain, discomfort, or general collapse such as commonly occurs at the time of rupture. Two had initial nocturnal dyspnoea with an ensuing remission of symptoms for some months before severe disability recurred. This sequence is well known in this condition, but the gradual onset and slow increase of dyspnoea shown by three of our cases is not so well recognized in sinus rupture. This more benign course may be related to the small shunt. Davidsen *et al.* (1958) stated that patients with ruptures of 8–12 mm. died within two months, whereas those with perforations of 5–6 mm. survived for longer than one year. Our three cases with mild disability had aorto-atrial ruptures of 3–4 mm. with flow ratios of 2:1 at catheterization. Two of the more severely disabled cases had aorto-ventricular ruptures 5 and 7 mm. in size, and the third had an aorto-atrial defect 7.5 mm. in diameter. Physical effort has precipitated rupture according to many authors: McGoon *et al.* (1958) repaired one that followed indirect trauma, and Szweda and Drake (1962) reported a case in which rupture had occurred during a pregnancy five years earlier. This last case resembles one of ours, observed from the time of rupture in the fourth month of pregnancy until operation four years later.

Clinically the most frequent error in diagnosis of this syndrome is to attribute the signs to a persistent ductus arteriosus, and two of our cases were referred with this diagnosis. In one of these the misapprehension had been supported by mistaking a massive jugular systolic pulsation for a Corrigan arterial pulse. The combination of ventricular septal defect and aortic incompetence may present difficulty in differentiation from a ruptured aortic sinus, both clinically and on catheterization.

The venous pulse has not proved of value in identifying the site of rupture in these six patients. It would be expected that the aorto-atrial defects would have the most marked systolic venous pulsations. This was not so, for the most prominent venous pulse-wave was present in one case with an aorto-ventricular shunt, and in two aorto-right-atrial defects there was no elevation of the venous pressure

at all. The results of catheterization may be misleading in locating the site of rupture when the aneurysm projects into the right atrium at the tricuspid valve, with jetting into the ventricle. Oxygen determinations then suggest an aorto-ventricular fistula. This mistaken impression may be reinforced by aortography, and the exact location of the aneurysm may be determined only at operation. Nevertheless retrograde aortography is the investigation of most value in this condition (Figs. 1, 2, 4, and 5). The aneurysmal aortic sinus is well delineated and associated aortic incompetence can be detected. If a true aorto-ventricular fistula is present it usually opens into the outflow tract of the ventricle; if contrast medium appears in the inflow area it is more probable that a sino-atrial aneurysm is present. Aortography is also of value in the detection of the other lesions that may mimic a ruptured aortic sinus clinically. The investigation has proved misleading in only one case where a ruptured sinus was suggested clinically, by catheterization and aortography. However, at surgery the lesion was found to be a communication between a dilated coronary artery and the right ventricle.

Coexistent ventricular septal defects occur in 25% of cases with aneurysms of the right coronary sinus (McGoon *et al.*, 1955), but associated atrial septal defects have not been reported previously. In the two cases of atrial septal defects associated with aorto-atrial aneurysms there were no features in the examination, E.C.G., chest x-ray picture, or cardiac catheter which distinguished these cases from the aorto-atrial aneurysms without such septal defects. Cardiac catheterization demonstrated the presence of a left-to-right shunt at atrial level, but as the aortic sinus was shown by aortography to enter the right atrium, the shunt was assumed to be due only to the aorto-atrial communication.

Acquired deformities may follow aneurysm formation as in one of our cases of calcific pulmonary incompetence. This suggested long-standing irritation by the adjacent aneurysm that presumably occupied this position for many years before rupturing.

Recent surgical experience supports previous pathological evidence in finding the right coronary sinus to be the one most often affected by aneurysmal change. Sawyers *et al.* (1957) have stated that aneurysms of the posterior sinus usually rupture into the right atrium, whereas those of the right sinus tend to rupture into the right ventricle. This association has been suggested as a diagnostic guide when aortography reveals the affected sinus but fails to define the point of rupture. As the choice of operative technique may be determined by this, our limited experience provides an interesting contrast. Of the two posterior sinus aneurysms one ruptured into the ventricle, and three of the four right sinus aneurysms opened into the atrium.

Surgery is indicated in the majority of patients with this syndrome. Even the mildest of our cases, symptom-free when rupture was detected accidentally, developed symptoms within a few months. Despite the presence of an atrial septal defect in two of these cases the sudden additional shunt following rupture produces a load for which the heart is not prepared. This is reflected by the appearance of symptoms, increased heart size, and some rise of pulmonary pressure with a relatively small shunt. Other than heart failure, the risks to which these patients are exposed include bacterial endocarditis, free aortic incompetence, and heart-block. For these reasons surgery is recommended for cases with mild disability, and it is a matter of urgency in the more severe cases in which failure is already present.

Summary

Ruptured sinus of Valsalva aneurysms in six patients have been investigated and then repaired under extracorporeal circulation or hypothermia. The clinical and anatomical features and investigations are described and are compared with cases recorded in the literature. The operative techniques are also described.

The investigation of greatest value in the diagnosis and anatomical location of this lesion is retrograde aortography.

In two of these six cases atrial septal defects were found, an association not previously reported. In three of the patients the presentation was atypical in that it was of gradual onset. One patient died two months after operation.

Four of these patients were under the care of Dr. D. Evan Bedford and Dr. Walter Somerville. We are grateful to them for permission to publish these cases and for their help in writing this report. We are also grateful to Dr. C. B. Matheson, who referred one patient and provided us with follow-up data.

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REFERENCES

- Cooley, D. A. (1960). *Amer. J. Cardiol.*, **6**, 605.
 Davidsen, H. G., Fabricius, J., and Husfeldt, E. (1958). *Acta med. scand.*, **160**, 455.
 Dubost, C., Blondeau, P., and Piwnica, A. (1962). *J. thorac. cardio-vasc. Surg.*, **43**, 421.
 Edwards, J. E., and Burchell, H. B. (1957). *Thorax*, **12**, 125.
 Falholt, W., and Thomsen, G. (1953). *Circulation*, **8**, 549.
 Gibbs, N. M., and Harris, E. L. (1961). *Brit. Heart J.*, **23**, 131.
 Jones, A. M., and Langley, F. A. (1949). *Ibid.*, **11**, 325.
 Lillehei, C. W., Stanley, P., and Varco, R. I. (1957). *Ann. Surg.*, **146**, 459.
 Lippschutz, E. J., and Wood, L. W. (1960). *Amer. J. Med.*, **28**, 859.
 McGoon, D. C., Edwards, J. E., and Kirklin, J. W. (1958). *Ann. Surg.*, **147**, 387.
 Micks, R. H. (1940). *Brit. Heart J.*, **2**, 63.
 Morrow, A. G., Baker, R. R., Hanson, H. E., and Mattingley, T. W. (1957). *Circulation*, **16**, 533.
 Oram, S., and East, T. (1955). *Brit. Heart J.*, **17**, 541.
 Sawyers, J. L., Adams, J. E., and Scott, H. W. (1957). *Surgery*, **41**, 26.
 Spencer, F. C., Blake, H. A., and Bahnson, H. T. (1960). *Ann. Surg.*, **152**, 963.
 Szweda, J. A., and Drake, E. H. (1962). *Circulation*, **25**, 559.

GAMMA-GLOBULIN FOR PREVENTION OF RUBELLA IN PREGNANCY

BY

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A national survey conducted in Britain by the Ministry of Health and General Register Office (Manson *et al.*, 1960) showed that for women who had rubella in the first 12 weeks of pregnancy in 1950-3, the risk of malformation in live-born infants was 15.8%, compared with 2.3% in controls. The risk of abortion or stillbirth was also higher in the rubella series—9.5% compared with 4.8%. Audiometric examination of a sample of the children at the age of 3-5 years in the survey showed that 30% of those whose mothers had rubella in the first 16 weeks of pregnancy had severe congenital perceptive deafness, though in half these the defect was unilateral (Jackson and Fisch, 1958). Similar estimates for the risk of foetal malformation after maternal rubella have been reported from the United States (Siegel and Greenberg, 1960), Australia (Pitt, 1961), and Sweden (Lundström, 1962); a recent report from New Zealand (Liggins and Phillips, 1963) put it rather higher. Passive immunization is the only means at present available for protecting pregnant women who have been exposed to infection from this considerable hazard.

Lundström *et al.* (1961) summarized the attempts that have been made to assess the prophylactic effect of convalescent serum, convalescent gamma-globulin, and pooled gamma-globulin in rubella. Very few studies have been adequately controlled or large enough to give statistically significant results. Trials in children with normal gamma-globulin by Landon *et al.* (1949) in New York and by Grayston and Watten (1959) in Taiwan provide the best evidence of protection. It is probable that only three batches of gamma-globulin were used in these trials, however, and Korns (1952) has shown that results may vary from batch to batch. Convalescent serum and gamma-globulin prepared from convalescent serum have not been shown to be better than normal gamma-globulin, or even as good. There is little evidence that any form of passive immunization will protect adult women from rubella, let alone protect the foetus.

In England and Wales gamma-globulin prepared by the Blood Products Laboratory of the Lister Institute from the

pooled plasma of normal adult donors by the method of Kekwick and Mackay (1954) is distributed to doctors by public health laboratories. Gamma-globulin was made available in 1954 for women exposed to rubella in early pregnancy. Since 1961 the British product has been supplemented from France and Holland. Several attempts were made in 1954 and 1955 to arrange controlled trials in children and in adults, but in only one was the subsequent attack rate high enough to allow any conclusion to be drawn. This trial was in five wards at the Fountain Hospital, London, in November, 1954, where the patients were exposed to infection. Ninety-four children, selected at random from 183 who had no past history of rubella, were each given 250 mg. of gamma-globulin from 46 different batches. The distribution of the 16 cases that subsequently occurred (see Chart) suggests that the globulin

Cases of rubella in patients given gamma-globulin and in uninoculated controls.

gave protection. Excluding patients with illnesses that began within three days of inoculation, only 2 out of 91 (2.2%) were attacked compared with 10 out of 88 (11.4%) controls (difference ÷ standard error = $9.2 \div 3.7 = 2.5$).

The ethical and practical difficulty of arranging a properly controlled trial of gamma-globulin for rubella prophylaxis in pregnant women is almost insuperable. For want of better evidence, an attempt has therefore been made in this paper to see what conclusions can be drawn from an analysis of the results reported by doctors in practice who have used gamma-globulin for the protection of their patients. As these patients were subjected to very