Third heart sound after mitral valve replacement

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Seven patients have been described who developed a third heart sound in association with a paravalvar leak around a Starr-Edwards mitral valve prosthesis.

These patients had all had the mitral valve cusps, chordae tendineae, and part of the papillary muscles excised. The presence of a third heart sound in them supports the concept of Potain (1900) that the third heart sound arises by vibrations in the ventricular wall being caused by its resistance to rapid distension. The normal mitral valve structures are not necessary for the production of a third heart sound.

Patients who have had valve replacement operations provide a unique opportunity to study the genesis of both normal and abnormal heart sounds. In particular, where valvar or paravalvar regurgitation has occurred after mitral valve replacement, there has been speculation about the part played by the mitral valve mechanism in the production of the third heart sound (Hultgren and Hubis, 1965; Dayem and Raftery, 1966; Fleming, 1969; Marshall and Gibson, 1969; El Gamal and Smith, 1970).

Absence of a third heart sound in patients with a Starr-Edwards prosthesis in place of the mitral valve, but with paravalvar leak, has been put forward as evidence that the third sound is dependent upon the presence of an intact mitral valve mechanism for its production (Ikram, Makey, and Bliss, 1969; Willerson *et al.*, 1970). However, Gianelly, Popp, and Hultgren (1970) and El Gamal and Smith (1970) have shown third heart sounds to be present after the mitral valve has been removed, and similar cases have been reported by Marshall and Gibson (1969). These cases all had homograft or heterograft aortic valves replacing the diseased mitral valve, so that valve leaflets were present, though chordae and papillary muscles were not.

We now present 7 patients, with paravalvar regurgitation around Starr-Edwards prosthetic valves in the mitral position, who have developed a third heart sound: 5 of them have had postoperative cardiac catheter studies, including left ventricular intracardiac phonocardiography.

Methods

Phonocardiograms and apex cardiograms were recorded before and after operation in each case, using techniques previously described (Coulshed and Epstein, 1963). Most patients had several phonocardiograms recorded at serial post-operative assessments.

Cardiac catheterization in the 5 patients studied was performed at varying times after operation. With Case 2 the interval was 12 months, in Case 3, it was 16 months, while in Cases 4, 5, and 7, 9 months, 5 months, and 3 months, respectively, had passed after operation. Left ventricular cineangiography was performed on each patient, and in addition intracardiac sounds and pressures were recorded from the left ventricle using a Telco micromanometer adapted for use with a Cambridge multichannel oscilloscope recorder. The micromanometer was inserted via a brachial arteriotomy. A simultaneous external phonocardiogram was recorded to aid identification of heart sounds.

Simultaneous micromanometer recordings in Case 3 had been obtained before cardiac operation with the Telco catheters introduced into the left ventricle via brachial arteriotomy, and into the left atrium by the transseptal route (Forman, Laurens, and Servelle, 1962).

Case 1 A man of 51 years in March 1967, was found to have acute mitral regurgitation, the diagnosis being based on clinical, haemodynamic, and cineangiographic findings. There was a loud pansystolic murmur at the apex, and both third and fourth heart sounds could be heard. A palpable 'A' wave accompanied the fourth sound (Fig. 1).

At operation in May 1967, the chordae tendineae of the posterior mitral valve cusp were found detached. Repair was not possible, and the valve cusps, chordae, and papillary muscles were

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excised and replaced by a No. 3 Starr-Edwards valve prosthesis.

The patient failed to do well after operation, remaining dyspnoeic at rest, with paroxysmal dyspnoea and with signs of fluid retention and increasing cardiomegaly. A moderately loud systolic murmur at the apex was accompanied by a third but no fourth heart sound.

Never fit for repeat angiography, he was operated upon again in June 1967, when exposure of the Starr-Edwards valve revealed a 2 cm gap in the suture line through which free regurgitation occurred. Closure of the gap stopped the regurgitation, and subsequent recovery was slow but uneventful.

The systolic murmur disappeared, but the third sound remained for some time, together with a rapid filling wave and 'F' peak on the apex cardiogram. These latter features are shown in Fig. 2, recorded in July 1967, four weeks after the second operation.

Case 2 A woman of 58 years had a mitral valvotomy in 1964. There was relief of dyspnoea for about a year, but then she slowly worsened, until by early 1969 her dyspnoea was again incapacitating. Signs of mitral stenosis and regurgitation were confirmed by cardiac catheterization and left ventricular cineangiography.

In November 1969 the mitral valve was replaced by a No. 3 Starr-Edwards valve. The tips of the papillary muscles were excised together with the chordae and valve cusps.

There followed a difficult postoperative course, with persisting right and left heart failure and jaundice. A pansystolic murmur audible from apex to left sternal border was noted from the earliest postoperative examination, but the prosthetic valve opening and closing sounds remained constant. A mid diastolic murmur and third heart sound became audible as the systolic murmur increased in intensity (Fig. 3). Repeat cardiac catheter studies and left ventricular cineangiography showed severe paravalvar regurgitation, and a third sound was recorded from the left ventricle during the same study, using the Telco catheter (Fig. 4).

Case 3 A man of 53 years had rapidly progressive dyspnoea over 8 months, until admitted to hospital in right heart failure. There had been no evidence of rheumatic heart disease, bacterial endocarditis, or myocardial infarction. Physical signs of gross mitral regurgitation were confirmed by left ventricular cineangiography and intracardiac phonocardiography (Fig. 5A).

At operation in September 1969 the chordae tendineae of the posterior cusp were found to be ruptured. The mitral valve and chordae were excised and replaced by a No. 4 Starr-Edwards valve. The tissues into which the valve was seated, were noted to be friable, and infiltrated with 'lipoid' material.

Initial progress was smooth, with no evidence of mitral regurgitation and no haemolysis of note, but by November 1969 a soft systolic murmur

FIG. 1 Case 1: The phonocardiogram (PCG) taken at the apex shows the pansystolic murmur (SM) and the third (S_3) and fourth (S_4) heart sounds, while the apex cardiogram (ACG) shows the early filling wave (EFW), with the tall A wave accompanying the fourth heart sound. The A/H ratio is 30 per cent.

had appeared at the apex, and six months later this had become much louder, and was accompanied by a clear third heart sound (Fig. 6), while the interval between the aortic second sound and the Starr-Edwards valve opening sound had progressively shortened (Willerson *et al.*, 1970).

FIG. 2 Case 1: The phonocardiogram after the second operation shows no systolic murmur, the A_2 to Starr-Edwards valve opening sound (SEO) time is 70 msec, and a third sound is present. The apex cardiogram shows a well-defined early diastolic filling wave with a sharp terminal F peak which accompanies the third sound on the phonocardiogram.

FIG. 3 Case 2: The postoperative PCG shows the pansystolic murmur at the apex, and the very loud opening sound is followed by a clear third sound and diastolic murmur.

Dyspnoea had returned, and there was now a severe haemolytic anaemia with persistent reticulocytosis of 8 per cent and a conspicuous rise in the serum lactic dehydrogenase.

Fourteen months after operation, cardiac catheterization and left ventricular cineangiography were again performed. Severe paravalvar

FIG. 4 Case 2: The intracardiac phonocardiogram shows a clear third sound, coinciding with the return of the first derivative (dp/dt) of the pressure record to zero. Both intracardiac and external sound recordings demonstrate the diastolic murmur after the third sound.

regurgitation was shown, while the intracardiac sound records showed the third heart sound to have returned, with characteristics almost identical to those recorded before operation (Fig. 5B).

Case 4 A woman of 51 years was diagnosed as having rheumatic mitral valve disease in 1960, and when first investigated in 1968 gave a history of progressive dyspnoea with paroxysmal dyspnoea over the preceding 5 years. Clinical findings indicated the presence of mitral stenosis and regurgitation, and cardiac catheterization with left ventricular cineangiography showed moderately severe mitral regurgitation with a heavily calcified mitral valve.

In July 1969 the valve cusps, chordae, and papillary muscles were excised and replaced with a No. 4 Starr-Edwards prosthesis. Early progress was satisfactory but slow. About 8 weeks after the operation she had an episode of acute breathlessness for which she was admitted to her local hospital. Six weeks after this she was still dyspnoeic, pale, and for the first time had a moderately loud (grade 2/3) pansystolic murmur at the apex, propagated to the posterior axillary line. A haemolytic anaemia of 9.6 g/100 ml with reticulocytosis of 8 per cent was present.

She was readmitted to hospital in March 1970, and examination confirmed the physical signs (Fig. 7) with a third heart sound recordable at the apex. She was febrile, and, though blood cultures were negative, staphylococci were cultured from her sputum. Because of the possibility of bacterial endocarditis she was given intravenous antibiotics for 6 weeks.

Cardiac catheterization including intracardiac phonocardiography (Fig. 8) and left ventricular cineangiography confirmed the presence of severe paravalvar regurgitation. Repeat cardiectomy in June 1970 showed non-epithelialization around one-quarter of the valve circumference, through which regurgitation had occurred. The patient did not survive the operation.

Case 5 A man of 54 years after rheumatic fever in early life, developed mitral stenosis, which in 1960 necessitated closed mitral valvotomy. This gave only temporary relief of symptoms, and left him with signs of combined mitral stenosis and regurgitation.

After preliminary investigation and haemodynamic studies, mitral valve replacement was carried out in April 1970 using a No. 4 Starr-Edwards valve. The postoperative course was complicated by staphylococcal endocarditis, after which he slowly worsened, with increasing evidence of left and right heart failure. There was now a loud pansystolic murmur heard at the cardiac apex and as far round as the right scapular angle. A third sound could be heard, though the opening and closing sounds of the Starr-Edwards valve were unvaryingly normal (Fig. 9).

Cardiac catheterization in September 1970 showed higher pulmonary artery and left atrial pressures than before valve replacement, and left ventricular cineangiography showed severe regurgitation to the left atrium. Intracardiac left

ventricular phonocardiography (Fig. 10) showed only a soft systolic murmur, but a loud third sound and a short but intense diastolic murmur.

At the second open heart operation in October 1970, the surgeon found a 2 cm gap posteriorly, where the stitches holding the valve in place had cut out from the mitral annulus. The gap was closed, and initial recovery was rapid, coinciding with loss of the third sound. Unfortunately the patient contracted a fungal endocarditis and died six months later. Permission for necropsy was not granted.

Case 6 A woman of 45 years, known to have had heart disease since rheumatic fever at the age of 9, began to complain of increasing dyspnoea when aged about 40. When seen, she was recovering from an attack of pulmonary oedema. The physical signs indicated that mitral regurgitation was the dominant lesion.

Cardiac catheterization confirmed the diagnosis, and open heart operation was advised. In March 1966, the mitral valve was replaced with a No. 4 Starr-Edwards prosthesis, the mitral valve cusps and chordae having been excised.

One month after the operation she had an attack of nocturnal dyspnoea, and though a soft (grade 1/3) systolic murmur was heard at the apex, it was not thought that regurgitation past the valve was significant. The sounds of the Starr-Edwards valve opening and closing were loud and consistent, and there were no added sounds.

Two months after operation the apical systolic murmur was still present, and now a distinct third heart sound and short mid diastolic murmur were easily heard.

Four months after operation she was having more paroxysmal dyspnoea and signs of severe tricuspid regurgitation. Though with intensive therapy she improved slightly over the next few months, she was never well enough for reinvestigation, and eventually she again deteriorated, and died a year after operation. The systolic murmur and the short interval from the aortic second sound to the Starr-Edwards opening sound are shown in Fig. 11.

Necropsy showed the valve to be functioning normally, but paravalvar channels were present at three sites around the valve, where the sutures were not covered by endothelium. There was no intracardiac thrombus. The aortic, pulmonary, and tricuspid valves were normal, though the tricuspid ring was dilated.

Case 7 A woman of 51 years was found to have rheumatic heart disease during pregnancy when she was 30 years old. Increasing dyspnoea, with bronchitis and attacks of nocturnal dyspnoea, had been present from the age of 48 years.

The physical signs were those of mitral stenosis and regurgitation, and the diagnosis was confirmed by right and left heart catheter studies and left ventricular cineangiography.

At operation in July 1968, the valve cusps, chordae, and papillary muscles were excised and a

FIG. 5 Case 3: The preoperative record (A) shows from above downwards the intra-left atrial sound, intra-left ventricular sound, and external sound. The loud systolic murmur in the atrium contrasts with its softness in the ventricle, where the third sound and diastolic murmur are both loud. The post-operative record (B) still shows the intra-left ventricular third heart sound coincident with that recorded externally, and almost exactly the same as was recorded before mitral valve replacement.

Note the diastolic pressure gradient across the prosthetic valve.

The preoperative pressure records were obtained from the Telco intracardiac transducers. Statham P23Db external transducers produced the postoperative pressure curves.

No. 2 Starr-Edwards mitral prosthesis was inserted. Slight aortic and tricuspid regurgitation were both noted. The postoperative period was marked by severe right ventricular failure, and by a prolonged postcardiotomy syndrome which responded only to steroid therapy.

By April 1969 she had intractable right ventricular failure, and attempts to withdraw steroid therapy resulted in more fever, chest pain, and pericarditis. Repeat right and left heart catheter studies in June 1969, with left atrial and ventricular cineangiography showed no obvious thrombus in either chamber or on the valve, but a high, persistent diastolic gradient from left atrium to ventricle was present. This obstruction to flow from atrium to ventricle necessitated further surgical exploration, and in February 1970 the

- No. 2 valve was excised and replaced by a No. 4 prosthesis. Though no major clot was present, a thin layer of thrombus extended across the sewing ring into the lumen of the No. 2 prosthesis.

Recovery from the second operation was immediate, but she had to be kept on the steroids. Seven weeks after operation, she began to deteriorate and a soft systolic murmur was found at the apex. Signs of right ventricular failure returned. A mid diastolic murmur was heard at the apex, and a third heart sound was recorded on the external phonocardiogram. In April 1970, further catheter studies with left ventricular cine-angiography revealed considerable paravalvar regurgitation. No significant diastolic gradient was present, but intracavity phonocardiography from the left ventricle showed both a third heart sound and a diastolic murmur (findings exactly as in Case 2, Fig. 4).

- She underwent operation for the third time in May 1970. There was no healing around the posterior half of the No. 4 valve ring, leaving a gap through which regurgitation had occurred. She did not survive this operation. In retrospect it seems probable that the lack of healing around the prosthesis was caused by the prolonged steroid therapy.

Discussion

- Doubt may exist about the precise mode of production of the third heart sound vibrations, but it is generally accepted that they coincide with the end of the early rapid filling of the ventricle, and with the 'F' peak of the apex cardiogram.

- There are two main theories regarding the genesis of the third heart sound. Firstly, it is produced by vibrations of the left ventricular wall itself, due to limitation of filling by the elastic resistance of the wall which causes a sharp check to distension: this view was initially put forward by Potain (1900) and more recently by Crevasse *et al.* (1962). Secondly, the sound develops in the mitral valve complex due to elongation of the ventricle, and tension of the valve structures, at the end of the early rapid filling phase of the ventricle, as has been suggested by Dock, Grandell, and Taubman (1955), Nixon (1961), and Fleming (1969); or by early mitral valve closure, as was suggested by Gibson (1907) and Thayer (1909). This latter view is certainly not correct, as Fleming (1969) showed that in patients with mitral regurgitation, the mitral valve was not closed at the time of the third sound, while Gianelly *et al.* (1970) showed similar findings when homograft valves in the mitral position became incompetent.

Nevertheless, it has been suggested that an intact mitral valve apparatus is necessary for

FIG. 6 Case 3: (A) Phonocardiogram 2 months after operation. There is no systolic murmur, and the A_2 -SEO time is 140 msec. No third sound is present. (B) Phonocardiogram 8 months after operation. There is now a pansystolic murmur, and the A_2 -SEO time is 100 msec. (C) Phonocardiogram 10 months after operation. A pansystolic murmur is now present, the A_2 -SEO time has shortened further to 80 msec, and a third sound is now present, A_2 - S_3 time being 130 msec.

the production of a left ventricular third sound. Fleming (1969) showed that the third sound of mitral regurgitation was abolished by successful replacement of the mitral valve by a Starr-Edwards prosthesis, deducing from this that a normal valve mechanism was necessary

FIG. 7 Case 4: The phonocardiogram from the position of V_3 (4L), where the systolic murmur is not loud. The A_2 -SEO interval was 80 msec, and the S_3 occurs at the end of a clear EFW on the apex cardiogram.

both for a third sound and the 'F' wave of the apex cardiogram to be present, the latter representing retraction of the apex at the end of early ventricular filling. He thought that the Starr-Edwards valve did not obstruct flow into the left ventricle, on the grounds that the early diastolic filling wave reappeared on the apex cardiogram. However, our own records in patients with normally functioning Starr-Edwards valves, in addition to demonstrating the abolition of previously present third sounds, show very poor early filling waves, and no visible 'F' waves on the apex cardiogram. In 4 of the patients reported here (Cases 3, 4, 6, and 7) the third heart sound reappeared, having been abolished by operation. Each of these patients had undergone successful mitral valve replacement, but later developed paravalvar mitral regurgitation. The other three patients (Cases 1, 2, and 5) who had mitral Starr-Edwards valve replacements, all had paravalvar regurgitation from the immediate post-operative period, and did not lose their third heart sounds. Five patients (Cases 1, 3, 4, 5, and 6) were found to have recordable 'F' waves on the apex cardiogram, coincident with the third sound.

Ikram *et al.* (1969) reported three patients with severe paravalvar regurgitation where Starr-Edwards valves had been inserted because of mitral valve regurgitation, and in none of these patients was a third sound or a mid diastolic murmur recorded after operation. The valve cusps, chordae, and papillary muscles had been excised from these patients, and the non-recurrence of the previously recorded third sounds and 'F' waves was taken as evidence that these structures were necessary for the production of these signs.

Dayem and Raftery (1966) and Raftery, Dayem, and Melrose (1968) showed no instances of third sounds appearing in patients with prosthetic valves, even when considerable regurgitation had been temporarily produced through the valve itself, during cardiac catheterization.

Hultgren and Hubis (1965), in an earlier review of patients with Starr-Edwards mitral valve replacements, had concluded that left ventricular third sounds did not occur in these patients because of loss of the mitral valve structure, but five years later Hultgren, with Gianelly and Popp (Gianelly *et al.*, 1970), reporting on 11 patients with homograft replacement of the mitral valve, found 4 patients with third sounds of left ventricular origin, coincident with the end of the early filling wave of the apex cardiogram.

Marshall and Gibson (1969) have also reported that with homograft replacement of

FIG. 8 Case 4: The intracardiac phonocardiogram (top line) from the left ventricle shows only a short systolic murmur, but a third sound is coincident with the third sound recorded externally. A diastolic murmur is also present in the ventricle.

the mitral valve, 11 patients developed third heart sounds with the appearance of valvar regurgitation, while El Gamal and Smith (1970) showed that a third sound and an

FIG. 9 Case 5: The postoperative phonocardiogram and apex cardiogram. The A_2 -SEO time is 60 msec, and a third sound is present; A_2 - S_3 time interval is 160 msec. The systolic and diastolic murmurs are shown; and the apex cardiogram shows a small but clear EFW, with a terminal peak just after S_3 .

abnormal 'F' wave could be seen in patients with regurgitation through an incompetent mitral heterograft, convincingly demonstrating that the attachment of chordae to valve cusps and papillary muscles is not necessary for their production.

As far as we are aware a third heart sound has never been reported in a patient with a Starr-Edwards mitral valve prosthesis, where not only have the chordae and papillary muscles been excised but also the mitral valve leaflets. In this present series of patients we have been able to demonstrate that if the paravalvar leak is sufficiently severe, the 'F' peak on the apex cardiogram will reappear as well as a third sound (Cases 1, 3, 4, 5, and 6), and in 5 patients (Cases 2, 3, 4, 5, and 7) we have shown by intracardiac phonocardiography that the third sound originates in the left ventricle, and is accompanied by a mid-diastolic murmur. Where intracardiac left ventricular sound records are taken with a Starr-Edwards valve in the mitral position without regurgitation, a diastolic murmur can be recorded, as might be expected, but there is no third sound. Fig. 12 shows the left ventricular intracardiac phonocardiogram of such a case. The diastolic murmur appears to be due to turbulent flow across the prosthetic valve, but is not usually audible externally. It may become sufficiently intense to be heard when there is severe valvar obstruction, or when there is increased flow across the valve in association with a paravalvar leak, as in the patients reported here.

Although we were able to hear a third heart sound in all but two of these patients (Cases 4 and 7), the appreciation of its presence was difficult because of the very high intensity of the immediately preceding Starr-Edwards opening sound, and this may also in part explain why the diastolic murmur of flow across the prosthetic valve is rarely heard.

Moreover, in order to include the very loud Starr-Edwards opening and closing sounds, attenuation of the phonocardiographic record may be so great as to prevent adequate recording of other sounds and murmurs, particularly those of low intensity and frequency which occur in diastole.

Our evidence therefore supports the original concept of Potain (1900) that the third sound is produced when the rapidly distending ventricle reaches a point when its distension is checked by the resistance of its wall, and the ensuing vibrations are audible as the third heart sound. It also shows that the mitral valve cusps, chordae, and papillary muscles are not necessary for the production of an abnormal third heart sound.

FIG. 10 Case 5: Shows the intra-left ventricular phonocardiogram with S_2 -SEO time as 50 msec, the A_2 - S_3 time as 150 to 170 msec. The S_3 is prolonged to about 80 msec, as is usual with intracavity recording. The diastolic murmur is well shown. The S_3 occurs at the time when the LV first derivative (dp/dt) returns to zero after its nadir.

FIG. 11 Case 6: The postoperative phonocardiogram shows the systolic murmur of the paravalvar regurgitation, the loud Starr-Edwards opening noise being followed by a third heart sound and short diastolic murmur.

The apex cardiogram shows a small but clear EFW.

FIG. 12 No paravalvar regurgitation was present in this case which is not described in the text, but shows normal intracavity recording after Starr-Edwards valve replacement. There is no S_3 , but a diastolic murmur is shown.

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Addendum

Since this paper was submitted for publication, we have seen 3 additional patients, all female, who developed severe paravalvar regurgitation after Starr-Edwards valve replacement of the mitral valve. All had audible and recordable third heart sounds, and one in particular had a palpable 'F' wave. The regurgitation was demonstrated in all 3 by left ventricular cineangiography, confirmed in 2 at operation, and in 1 at necropsy.

The sound records and apex cardiograms were similar to the records published above, making our total series number 10.

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