Thromboembolism after Starr valve replacement

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One hundred and six patients who left hospital after Starr-Edwards ball valve replacements have been followed for a period of 6 months to 4 years. All patients were maintained on oral anticoagulant therapy so that a prothrombin ratio of approximately 1.7:1 was attained. Four patients suffered minor nose bleeds. During the period of follow-up there have been 4 patients who have suffered embolic phenomena, one of which proved fatal. The site of thrombus formation in the fatal case was the left atrium and not the prosthetic valves.

The relatively low incidence of embolic and haemorrhagic complications can be added to the satisfactory immediate and late function of the valves themselves. Minor leaks have developed around 7 per cent of surviving aortic valve replacements but no mitral or tricuspid valve shows evidence of regurgitation. No case of valve failure has occurred.

The operative mortality of valve replacement has today dropped to a level that depends largely on the state of the patient's myocardium at the time of surgery and the pulmonary vascular resistance. Interest is, therefore, being increasingly directed towards the late complications of valve replacement, a study made difficult by the fact that individual cardiac units frequently change their valve replacement technique. When a new valve is introduced, there is a gradation over two years from enthusiasm to doubt and then to abandonment or modification of the original valve. This has been true of homografts, heterografts, and prosthetic valves and applies to the series reported here.

At St. Thomas' Hospital we elected to use Starr valves only for valve replacements, starting with the last of the models with the Silastic ball and metal strut valve in 1965, and changing to the cloth-covered valve with a metal ball when that became available in January 1968. Starr-Edwards ball valve prostheses have been used in all patients requiring valve replacement except for 3 young patients who had homograft and autograft replacements. This series is not therefore selected, as many homograft series are, where the worst risk and most ill patients receive prosthetic valves because of the shorter length of time required for their insertion compared with homografts.

The long-term complication of prosthetic valve replacement that causes most concern

is thromboembolism, which can in this series be assessed easily because it deals with the last 4 years only and because the type of valve was changed only once. Long-term evaluation is not therefore loaded with complications due to the early and less satisfactory models which produced the often quoted statement from Starr's early series that half his late deaths in isolated mitral valve replacement were due to thromboembolism (Starr, Herr, and Wood, 1967). In this series a diagnosis of embolism was made if there had been any symptom or sign that could possibly be interpreted as embolic. In this way it was hoped to include every possible embolus.

One hundred and six patients who had undergone Starr valve replacement form the basis of this study. The details of the surgical procedure are shown in Table 1.

Anticoagulant management of patients after Starr valve replacement

All patients in this series who have Starr valve replacements are given oral anticoagulants which are continued indefinitely. Phenindione was used in the early part of this series, but the coagulation laboratory changed the Hospital anticoagulant to warfarin in 1966, and phenindione is now only used when a patient is unable to take warfarin. The patients who were originally on phenindione have, however, continued to take that drug.

The first dose of warfarin is given 4 days after operation, the loading dose varying from 2.5-15 mg. depending upon the clinical state of the patient, taking into account in

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TABLE 1 *Starr valve replacement, St. Thomas' Hospital, January 1965–April 1969*

Single valve replacement	77
Aortic valve	46
Mitral valve	31
Double valve replacement	22
Aortic and mitral valves	14
Mitral and tricuspid valves	7
Aortic and tricuspid valves	1
Triple valve replacement	7
Total	106

particular the estimated level of arterial perfusion and venous congestion of the liver before and after operation. The prothrombin time is measured before giving the loading dose. If it is already raised, as it often is in jaundiced patients, 2.5 mg. warfarin is still given because in jaundice a prolonged prothrombin time does not seem to prevent thrombosis on prosthetic valves (see discussion).

Subsequently the prothrombin time is determined each day for the first week and the appropriate dosage of warfarin prescribed by the clinical haematologist. The aim has been to maintain a prothrombin ratio of 1.7, which is approximately equivalent to a prothrombin index of 60 or a prothrombin level of 30 per cent. The dose of warfarin may have to be increased when antibiotics are stopped, and again when the patient becomes active. At the time of discharge from hospital, anticoagulant requirements have usually stabilized. Routine tests are carried out at the laboratory nearest the patient's home.

No undue difficulty has been experienced in the maintenance of anticoagulant therapy. All patients who may possibly need prosthetic valves are told beforehand of the importance of continuing anticoagulant therapy for an indefinite period and the dangers of suddenly discontinuing it.

Management during pregnancy Three patients became pregnant, two after mitral valve replacement and one after an aortic valve replacement. The last had a therapeutic abortion and the first two proceeded to term and produced normal infants. They were maintained on oral anticoagulant therapy until the first stage of labour, when fresh frozen plasma was used to restore the prothrombin time to normal. Anticoagulation was then maintained with 10,000 units of heparin intravenously 6-hourly. One patient had a caesarean section, after which a small haema-

toma developed in the abdominal wound. This was the only complication in the 3 patients.

Incidence of bleeding Among these 106 patients, 4 patients have recorded nose bleeding on one occasion each. Three of these episodes were minor and were reported on routine visits to the anticoagulant clinic. One patient required admission to hospital but did not need blood replacement. Another patient who complained of getting easily bruised was found to have an abnormal prolongation of prothrombin time which was corrected. No patient has needed to discontinue anticoagulants because of a tendency to bleed, and there have been no other complications associated with anticoagulation.

Analysis of individual valve replacement groups

Aortic valve replacement Forty-six patients were discharged from hospital after replacement of the aortic valve (Table 2).

TABLE 2 *Aortic Starr valve replacement: 46 patients*

Duration of follow-up	
< 6 mth.	10
6 mth.–1 yr.	9
1 yr.–2 yr.	5
2 yr.–4 yr.	22
Embolism	0
Late deaths	5
Valve dehiscence	2
Arrhythmia	2
Myocardial failure	1

One-half of the patients had cloth-covered valves. They have now been followed for a period of 6 months to 4 years. Twenty-two of these have been followed for more than 2 years, 5 from 1 to 2 years, 9 for 6 months to 1 year, and 10 for less than 6 months.

Five patients have died, 2 from dehiscence of the valve from heavily calcified aortic rings, 2 from arrhythmias, and one from myocardial failure.

No patient at necropsy had evidence of thrombosis on the prosthetic valves. There has been no systemic embolism or valve failure in this group, though 7 per cent have developed minor regurgitant murmurs.

Mitral valve replacement (Table 3) Thirty-one patients were discharged home after successful replacement of their mitral

TABLE 3 *Mitral Starr valve replacement: 31 patients*

Duration of follow-up	
< 6 mth.	2
6 mth.-1 yr.	11
1 yr.-2 yr.	10
2 yr.-4 yr.	8
Embolism	1
Late deaths	2
Myocardial failure	
Serum hepatitis	

valves, one-third of the patients having had cloth-covered valves implanted. Follow-up periods varied from under 6 months to 4 years. Eight of these patients have been followed for a period of 2 to 4 years, 10 from 1 to 2 years, 11 from 6 months to 1 year, and 2 for less than 6 months. There have been 2 late deaths, one due to serum hepatitis and one from myocardial failure. At necropsy there was no evidence of thrombosis on the prosthetic valves. No patient has developed mitral regurgitation.

One patient in this group had an episode of cerebral embolism. A 32-year-old man had a silastic ball mitral valve replacement in November 1967. Two weeks afterwards he had pain in the loin, accompanied by haematuria and bacteriologically sterile urine. This could have been due to renal embolism. He developed a right-sided hemiplegia in January 1968, from which he recovered fully and is now back at full-time work. He is in sinus rhythm.

Double valve replacement This group consists of 22 patients, 14 having aortic and mitral, 7 mitral and tricuspid, and 1 aortic and tricuspid valve replacements (Table 4). They have been followed for a period of 6 to 42 months. Three have been followed for more than 2 years, 9 from 1 to 2 years, and 10 for a period of 6 to 12 months. There have been 3 late deaths in this series, 2 from myocardial failure and 1 from serum hepatitis.

TABLE 4 *Double Starr valve replacement: 22 patients*

Duration of follow-up	
6 mth.-1 yr.	10
1 yr.-2 yr.	9
2 yr.-4 yr.	3
Embolism	2
Late deaths	3
Myocardial failure	2
Serum hepatitis	1

At necropsy there was a small amount of firm, adherent antemortem thrombus on the apex of one mitral valve though the ball movement was still satisfactory.

There have been 2 cases of cerebral embolism in this group: a 53-year-old man had aortic and mitral cloth-covered valve replacements carried out in March 1968. In May he had a severe headache with vomiting. Gradually he noticed that there was some weakness of his right hand (failure to hold a cup) and his right leg let him down. He has now completely recovered from this episode. A jaundiced 39-year-old man had mitral and tricuspid silastic valve replacements in September 1967. In the postoperative period his jaundice intensified, with a serum bilirubin level of 30 mg./100 ml. Four weeks later while still jaundiced he developed loss of speech with a right hemiparesis. There was noticeable recovery within 24 hours and now he has residual slurring of speech only.

Triple valve replacement Seven patients had aortic, mitral, and tricuspid valve replacement (Brambridge *et al.*, 1969) (Table 5). Follow-up period ranged from 18 months to 3 years.

TABLE 5 *Triple Starr valve replacement: 7 patients*

Duration of follow-up	
18 mth.-3 yr.	
Embolism	1
Late deaths	1 (embolism from LA)

There has been one late death 5 months after operation due to multiple embolic episodes.

A 35-year-old woman had a silastic ball triple valve replacement in April 1967. When seen in the outpatient clinic two months later she could walk easily and lie flat. Her condition was recorded as 'absolutely marvellous'. A week later she was admitted with a history of abdominal pain and in June she had a cerebrovascular accident leading to hemiplegia. She was recovering from it satisfactorily, but then in August had an attack of *grand mal*, became unconscious, and died five days later. At necropsy the giant left atrium was found to contain much thrombus but the prosthetic valves were free of thrombus. There were infarcts in the cerebellum and in the spleen.

Discussion

Anticoagulants are necessary after prosthetic valve replacement for at least a year. The role of anticoagulants in reducing the formation of thrombi on prosthetic valves is convincing, as the incidence of embolic phenomena is high in series where anticoagulants were not used. Gadboys from the Mount Sinai Clinic in a mixed series has reported the incidence of embolism to be 5 per cent when anticoagulants were used and 44 per cent when they were not (Gadboys *et al.*, 1967). Effler reported an incidence of embolism of 23 per cent after mitral valve replacement if anticoagulants were not used (Effler, Favaloro, and Groves, 1965). An incidence of 42 per cent was reported from Starr's unit by Herr (Herr *et al.*, 1965), and of 24% from the Massachusetts General Hospital (Akbarian *et al.*, 1968). This incidence is not, however, comparable with modern series because the earlier and less satisfactory models of Starr valves were being used.

In a larger series from the Mayo Clinic, an embolism rate after single or double valve replacement of 5.5 per cent was reported, a little more than half of which were fatal. There were 3 cases of embolism out of 18 after triple valve replacement, all of which were fatal (Duvoisin *et al.*, 1968). No mention is made of the site of origin of emboli in the fatal cases which may have been the atrial wall rather than the valve itself, as occurred in one of our patients.

For these reasons anticoagulants have been used throughout the St. Thomas' series. The risk of haemorrhage caused by the use of anticoagulants has, however, to be taken into consideration in adopting this course. In some 800 patients discharged from the Mayo Clinic after valve replacement with a Starr prosthesis, 4 deaths were attributed to bleeding caused by anticoagulants (Duvoisin *et al.*, 1968).

At St. Thomas's we maintain a prothrombin ratio of 1.7 rather than 2.3 which was advocated by Gadboys, and the risk of haemorrhage is consequently less. There were 4 episodes of nasal bleeding. Three patients reported it during routine follow-up visits. One needed admission to hospital, but the bleeding was not severe enough to require blood transfusion. Except for the necessity for regular blood tests, there was no significant anticoagulant problem for the patients in this series.

Embolic episodes occurred after discharge

from hospital in 4 patients and in 1 case the episode proved fatal: in this case, the source of embolism at necropsy proved to be the left atrial wall and the prostheses were free of any thrombus. Of the other 3, 2 have completely recovered and the third has slight slurring of his speech. All embolic episodes in this study have occurred within the first 6 months, which is in keeping with the findings of Starr and Gadboys that this is the period of maximal risk.

The patient who had an embolus while he was still jaundiced deserves special comment. We have noticed thrombus formation in patients dying of hepatic failure in the immediate postoperative period, in spite of the fact that the prothrombin time was prolonged 2 to 5 times the control level without the use of anticoagulants. It is possible that the prolongation of the prothrombin time seen in jaundiced patients with hepatic failure is due to a different factor from the one affected by anticoagulant therapy which prevents thrombus formation on the prosthetic valves.

Pregnancy is not contraindicated for patients on anticoagulants after Starr valve replacement. Three patients in this series became pregnant, one had a therapeutic abortion, and two had normal full-term infants. In the United Kingdom therefore, where pathological services for control of anticoagulant therapy are within easy and free reach of all patients, the use of prosthetic valve replacement can carry only a small risk of thromboembolism.

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