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Red cell survival after homograft replacement of the aortic valve

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Red cell survival was studied in 21 patients following homograft replacement of the aortic valve. Autologous cells labelled with ^{51}Cr were used. The $T\frac{1}{2}$ ^{51}Cr varied between 24 and 34 days, with only one patient below the normal limit of normal variations. The absence of haemolysis was confirmed by other haematological studies, including estimation of reticulocytes, serum lactic dehydrogenase, and urinary haemosiderin. Haptoglobin levels were low in most of the patients studied. In contrast to prosthetic valves there was no haemolysis in patients with regurgitation around or through the homograft valve.

Intravascular haemolysis has been described after aortic valve replacement using a mechanical prosthesis. This applies to ball valves (Marsh, 1964; Reed and Dunn, 1964; Andersen, Gabrieli, and Zizzi, 1965; Yacoub and Keeling, 1968) and valves constructed of flexible fabric in the form of leaflets made of different materials (Gehrmann and Loogen, 1964; Yacoub, Rogers, and Crossland-Taylor, 1965; Yeh, Ellison, and Wright, 1965; DeCesare, Rath, and Hufnagel, 1965; Rubinson, Morrow, and Gebel, 1966; Schade, Rowe, Young, Lockey, and Clatanoff, 1967). The degree of haemolysis depends on the type of prosthetic valve and its competence (Schade *et al.*, 1967; Yacoub and Keeling, 1968). Homograft aortic valves have established themselves as alternatives to mechanical prostheses (Ross, 1962; Barrett-Boyes, Lowe, Cole, and Kelly, 1965; Hocksema, Titus, Giuliani, and Kirklin, 1966; Ross and Yacoub, 1969). One of the main advantages of aortic homograft valves is the absence of thromboembolic complications, which are one of the major hazards of prosthetic valves in spite of an adequate anticoagulant regime (Brandenburg, 1965; Mulder, Mazzei, and MacAlpin, 1966; Fraser and Waddell, 1967). This paper reports the study of haemolytic

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TABLE

HAEMATOLOGICAL INVESTIGATIONS BEFORE AND AFTER HOMOGRAFT REPLACEMENT OF THE AORTIC VALVE

Sex/ Age	Pre-operative		Months after operation	EDM	$T\frac{1}{2}$ ^{51}Cr	Post-operative		Reticulocytes	LDH	Operation
	Hb (g./100 ml.)	P.C.V.				Hb (g./100 ml.)	P.C.V.			
M 62	13·7	41	5	Yes	25	14·3	42	1.6	490	Homograft
M 42	14·8	42		Yes	25½					
M 37			18	Yes	26	14·6	43	2·1	530	Homograft
M 46	12·3	35	24	Yes	26½	14·3	41	0·6	360	Homograft
M 55	14·0	42	9	Yes	29½	16·3				Homograft
M 49	15·3	44	24	Yes	30	16·3	49	1·0	600	Homograft
F 29	14·6	42	9	Yes	31	13·3	39	0·8	520	Homograft
F 52	13·6	41	12	Yes	32½	15·2	45			Homograft
M 55	15·4	43	12	Yes	33	15·3	45		530	Homograft
F 44				Yes	34				700	Homograft
M 20	15·7	46	3	No	26	15·4	45	3·4		Homograft
M 50	16·6	48	12	No	27	15·7	48	1·2	410	Homograft
F 53	13·1	38	18	No	28				370	Homograft. Mitral valvotomy
M 61	13·6	41	12	No	28	15·2	45	1·6	740	Homograft
F 59	15·1	43	15	No	28½	15·3	45	0·8	350	Homograft. Mitral valvotomy
M 49	14·4		24	No	28½	15·6	46	2·0	600	Homograft. Mitral valvotomy
M 26	13·6	41	24	Yes	29½	16·6	46	0·6	460	Homograft
M 48	15·6	44	18	No	30					Homograft
F 51	12·9	39	6	No	31	14·3	41	0·2		Homograft. Mitral valvotomy
F 48	13·6	41	8	No	33	12·6	40	0·4		Homograft. Mitral valvotomy

EDM = early diastolic murmur. LDH = lactic dehydrogenase.

phenomena in 21 patients following the insertion of a homograft in the subcoronary area.

PATIENTS AND METHODS

The patients studied (Table) included 15 men and six women with an age range of 20 to 62 years.

Twelve patients had calcific aortic stenosis, while dominant aortic regurgitation was the main lesion in the remaining nine. Mitral valve disease requiring either valvotomy or annuloplasty in addition to aortic valve replacement was present in six patients; 11 patients had developed early diastolic murmurs following the operation. The investigation of haemolytic phenomena was undertaken after periods ranging from four months to two years after operation.

The haematological values were determined by standard methods (Dacie and Lewis, 1963) and the ^{51}Cr red cell survival time by labelling autologous cells and reinjecting these into the patient under study. Serum haptoglobin levels were obtained by the colorimetric method described by Owen, Better, and Hoban (1960) in eight patients of the present series and in a further 20 in whom homograft replacement of the aortic valve was performed.

Lactic dehydrogenase was measured using routine biochemical techniques.

RESULTS

These are set out in the Table and in Figures 1 and 2. The pre-operative levels of haemoglobin, packed cell volume, and reticulocytes were all within the normal range. The post-operative levels were virtually unchanged in all patients. The lactic dehydrogenase levels were not raised post-operatively and the $T\frac{1}{2}$ ^{51}Cr varied between 24 and

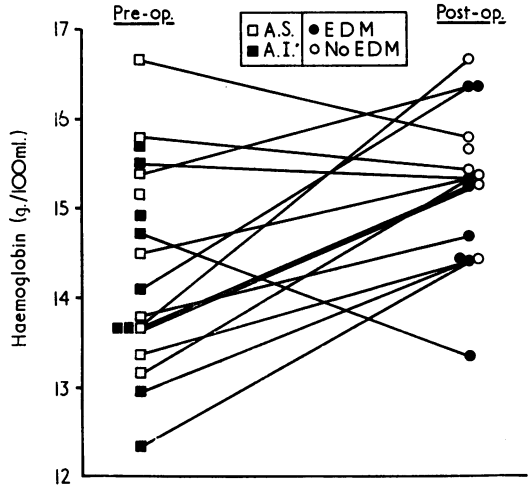

FIG. 1. *Haemoglobin levels before and after homograft replacement of the aortic valve showing no significant change.*

34 days, with only one patient below the lower limit of normal variation.

The haptoglobin levels were below the lower limit of normal in all but one patient, but there were no other parameters of intravascular haemolysis present; *i.e.*, $T\frac{1}{2}$ ^{51}Cr normal, no haemosiderinuria, no reticulocytosis, and a normal lactic dehydrogenase level.

DISCUSSION

Aortic valve replacement is an effective means of correcting stenosis or regurgitation. Prosthetic and

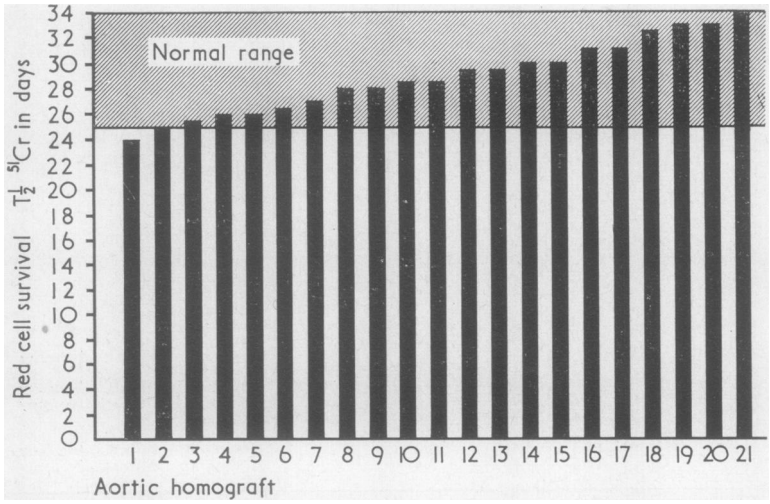

FIG. 2. *Red cell survival expressed as $T\frac{1}{2}$ ^{51}Cr in 21 patients following homograft replacement of the aortic valve.*

homograft aortic valves have been in clinical use since 1962 and mechanical disruption of the red cells is a well-recognized hazard of the use of an artificial valve. Haemolysis sufficient to cause anaemia is produced by regurgitation through or around the prosthesis and has been reported with valves made of Dacron (Gehrmann and Loogen, 1964), Teflon (Rubinson *et al.*, 1966), and silicone rubber impregnated Teflon fabric (Schade *et al.*, 1967) in addition to the ball-valve prostheses (Marsh, 1964; Reed and Dunn, 1964; Pirofsky, Sutherland, Starr, and Griswold, 1965). Leaflet valves have a high late failure rate (Braunwald and Morrow, 1965) and are now seldom used; the most widely used prosthetic valve is that originally described by Starr, Edwards, McCord, and Griswold (1963).

Previous studies (Andersen *et al.*, 1965; Yacoub and Keeling, 1968) have shown that aortic ball valves will produce a chronic intravascular haemolysis even if functioning normally, but this is not severe and usually does not produce a significant anaemia. It does, however, increase the rate of clearance of the haptoglobin/haemoglobin complex from the serum and leads to deposition of haemosiderin in the liver and kidneys. The possible effects of these changes have recently been discussed (Yacoub and Keeling, 1968).

The present study shows that homograft aortic valves do not produce haemolysis even if there is regurgitation (Fig. 3), and this is probably due to the central flow characteristics with minimal turbulence as compared with a ball valve prosthesis (Fig. 4).

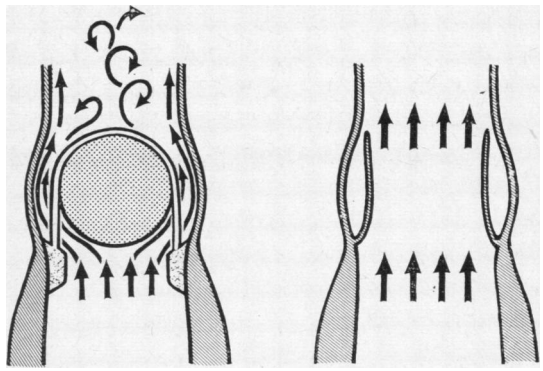

FIG. 4. *Comparison between the flow characteristics of a homograft valve and a ball valve prosthesis, showing the turbulent free flow through the homograft valve.*

The low levels of the serum haptoglobins observed are probably due to impaired liver synthesis and an increase in the fractional catabolic rate and do not in these cases reflect the degree of haemoglobin transport or stabilization.

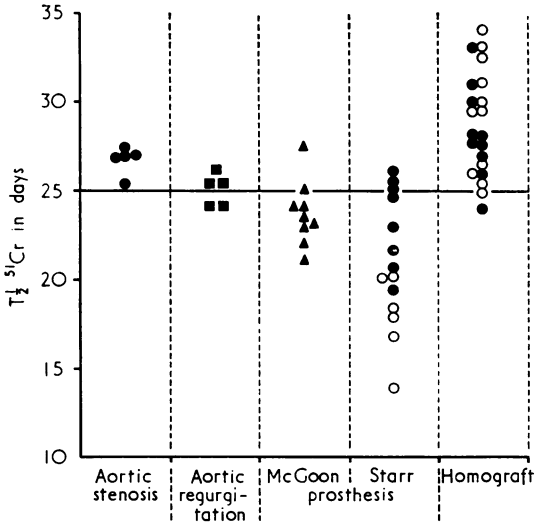

FIG. 3. *Red cell survival expressed as $T\frac{1}{2}$ ^{51}Cr in patients with aortic stenosis, aortic regurgitation, and after the insertion of a McGoon prosthesis* (*Yacoub* et al., 1965), *a Starr prosthesis* (*Yacoub and Keeling*, 1968), *and a homograft* (*present series*).

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