

Red cell survival in patients with aortic valve disease¹

M. H. YACCOUB,² K. ROGERS, AND P. CROSSLAND TAYLOR

From the London Chest and Brompton Hospitals and Middlesex Hospital Medical School

The increased destruction of red cells after some corrective cardiac procedures has been recognized (Neill, Farman, Sigler, and Bahnsen, 1961; Sayed, Dacie, Handley, Lewis, and Cleland, 1961; Verdon, Forrester, and Crosby, 1963; Gehrman and Loogen, 1964; Marsh, 1964; Reed and Dunn, 1964; Stevenson and Baker, 1964). Despite increased haemolysis, anaemia is not always present, since a normal bone marrow is capable of increasing red cell production six or seven times in response to a sustained demand. Red cell survival in a chronic haemolytic state may be reduced from 120 to 20 days, but the bone marrow may be able to maintain a normal red cell count in the peripheral blood. Anaemia results only when red cells are destroyed faster than they can be produced by the bone marrow (Fig. 1). An

estimation of red cell survival using radioactive chromium (⁵¹Cr) tagged cells can detect small increases in the rate of red cell destruction (Mollison, 1956). This technique has been used to study the red cell survival in various forms of aortic valve disease and after the insertion of valve prostheses.

PATIENTS AND METHODS

Three groups of patients with aortic valve disease were studied. They were patients with severe aortic regurgitation, patients with calcific aortic stenosis with a gradient of 50 mm. Hg or more across the aortic valve, and patients after the insertion of McGoon's aortic valve prostheses; the last group consisted of eight patients, four of whom had clinical evidence of residual aortic regurgitation.

The method used was originally described by Ebaugh, Ross, and Emerson (1953). Red cells, 10 ml., were tagged with ⁵¹Cr using a total dose of 35 μ c. Autogenous cells were used except in patients studied during the first three months after operation when cross-matched fresh cells were used, as it has been shown that red cell survival is shortened by mechanical trauma during cardio-pulmonary bypass (Frey and Schmidt-Mende, 1963). Fresh cells have been shown to have a normal survival after transfusion in the absence of haemolytic factors (Mollison, 1956). The tagged cells were injected into the patient, and samples of blood were taken twice a week for six weeks. The residual radioactivity in the red cells was measured, corrected for radioactive decay, and plotted against time on semilogarithmic paper. The time taken for the radioactivity to drop to 50% of the original level ($T_{\frac{1}{2}}$ ⁵¹Cr) is an index of the rate of destruction of the red cells as well as of the rate of elution of ⁵¹Cr from the cells. As the latter is constant, $T_{\frac{1}{2}}$ ⁵¹Cr can be taken as a measure of red cell survival. The true red cell survival can be determined by correcting for the amount lost by elution. According to the formula given by Read, Wilson, and Gardner (1954), this may be expressed

$$\text{as corrected } T_{\frac{1}{2}} = \frac{T_{\frac{1}{2}} \text{ elution} \times T_{\frac{1}{2}} \text{ } ^{51}\text{Cr}}{T_{\frac{1}{2}} \text{ elution} - T_{\frac{1}{2}} \text{ } ^{51}\text{Cr}}$$

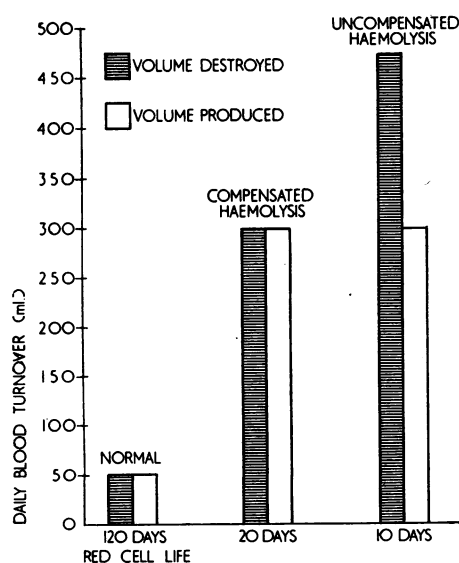


FIG. 1. Balance between red cell production and destruction under different conditions.

¹ Presented at the meeting of the Society of Thoracic Surgeons, October, 1964

² Present address: Brompton Hospital, London

The average life span or mean cell life of the red cell population may be determined using the formula given by Donohue, Motulsky, Giblett, Pirzio-Biroli, Viranuvatti, and Finch (1955)

$$\text{Mean cell life} = \frac{100}{\text{red cells destroyed per day (\%)}} \\ = \text{corrected } T_{\frac{1}{2}} \text{ Cr} \times 1.43.$$

To relate experimental mean cell life to normal life span, the destruction rate may be calculated as normal mean life (120 days)

experimental mean cell life.

In this paper $T_{\frac{1}{2}} {}^{51}\text{Cr}$ is used as an index of red cell survival.

RESULTS

Table I shows the red cell survival in the three groups of patients studied. All the patients had a normal $T_{\frac{1}{2}} {}^{51}\text{Cr}$ except those with evidence of residual aortic regurgitation after the insertion of McGoon valve prostheses, who had a slightly shortened red cell survival; none of these patients had clinical evidence of haemolysis. The red cell

TABLE I
RED CELL SURVIVAL IN PATIENTS WITH AORTIC VALVE DISEASE
(as apparent ${}^{51}\text{Cr}$ red cell half life)

Diagnosis	Case No.	$T_{\frac{1}{2}} {}^{51}\text{Cr}$ (days)
Aortic regurgitation	1	25½
	2	26
	3	25½
	4	25½
	5	24
	6	24
Calcific aortic stenosis ..	7	27½
	8	27
	9	27
	10	27
	11	25½
After insertion of McGoon prosthesis	12*	22
	1	25
	3*	23
	5	23½
	13*	23
	6*	21
	14	27½
	15	24

Normal range of $T_{\frac{1}{2}} {}^{51}\text{Cr}$ = 23½ to 27 days.

* Cases with clinical evidence of residual aortic regurgitation.

survival in case 12 was studied both in the immediate post-operative period and 10 months later (Fig. 2). The marked shortening of the red cell survival in the immediate post-operative period can be explained by the fact that his own cells were used for the estimation within two months of operation.

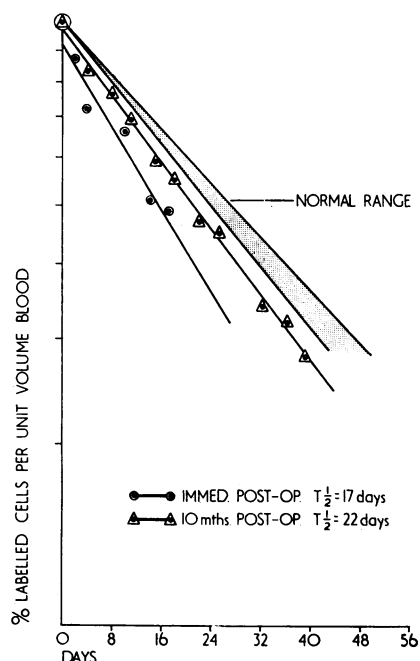


FIG. 2. Case 1. Post-operative red cell survivals of case 12.

DISCUSSION

Mechanical destruction of red cells resulting in haemoglobinaemia and haemoglobinuria can occur after strenuous exercise taken in the upright lordotic posture and not when the back is bent (Gilligan and Blumgart, 1941). This is thought to be due to kinking of blood vessels causing an abrupt change in the direction of blood flow when the back is hyperextended in association with a rapid circulation rate (Dacie, 1962). This suggests that turbulence can produce abnormal haemolysis. Our studies have shown that the red cell survival was not affected by the turbulence of aortic regurgitation nor by the fast turbulent flow of blood through the rough disorganized valves in calcific aortic stenosis.

Mechanical haemolytic anaemia after aortic valve replacement has recently been described (Gehrmann and Loogen, 1964; Marsh, 1964; Reed and Dunn, 1964; Stevenson and Baker, 1964). The mechanism of this condition is not known. Abnormal turbulence, chemically induced haemolysis, direct damage to the erythrocytes by coming in contact with the surface of the prosthesis or by being crushed between the rigid valve housing and the ball in a Starr-Edwards prosthesis are

possible factors. The normal red cell survival in our patients with a competent McGoon prosthesis suggests that the presence of teflon within the circulation does not *per se* cause destruction of red cells. The shortened red cell survival in patients with residual aortic regurgitation after insertion of a McGoon prosthesis suggests that destruction of red cells is produced by a jet of blood playing against the teflon prosthesis. This is supported by the fact that all the reported cases of haemolytic anaemia after aortic valve replacement had residual aortic regurgitation. The two patients described by Gehrman and Loogen (1964) developed severe haemolytic anaemia and jaundice which coincided with the sudden onset of aortic regurgitation a few months after aortic valve replacement using a Hufnagel tricuspid dacron prosthesis. The cases of haemolytic anaemia following the insertion of a Starr-Edwards aortic prosthesis, reported by Marsh (1964) and Stevenson and Baker (1964), had signs of residual aortic regurgitation. In the patient described by Reed and Dunn (1964) the correction of residual aortic regurgitation after insertion of a Starr-Edwards prosthesis did not stop the abnormal haemolysis, and the patient died of renal failure. After the second operation there was no evidence of aortic regurgitation; however, there was significant aortic obstruction evidenced by a systolic gradient of 40 mm. Hg across the aortic valve. At necropsy it was found that with the ball in the open position the aorta was severely obstructed with very little clearance for blood flow around the ball.

The only other condition known to produce mechanical haemolysis is the correction of endocardial cushion defects using a patch of teflon for the repair of the atrial septal defect (Sayed, Dacie, Handley, Lewis, and Cleland, 1961; Neill *et al.*, 1961; Sigler, Forman, Zinkham, and Neill, 1963; Verdon *et al.*, 1963). This is thought to be due to a jet of blood produced by residual mitral regurgitation being driven against the bare teflon patch. In the patient described by Sayed *et al.* (1961), covering the bare area of teflon with pericardium led to an immediate cessation of haemolysis.

The present study of red cell survival suggests that an increase in the rate of destruction of red

cells after open heart surgery occurs only when the presence of a prosthesis is associated with a persistent haemodynamic defect. This is supported by the fact that in all the reported cases of mechanical haemolytic anaemia following cardiac surgery there was evidence of persistent valvular obstruction or regurgitation after the insertion of prosthetic material for the repair of cardiac defects.

SUMMARY

The red cell survival in patients with aortic valve disease was studied using ^{51}Cr -tagged red cells. All the patients studied had normal red cell survival except those with evidence of aortic regurgitation after the insertion of a McGoon prosthesis, who had a slightly shortened red cell survival. This is probably caused by the turbulent blood flow playing against the prosthesis.

REFERENCES

- Dacie, J. V. (1962). Haemolytic mechanisms in health and disease. *Brit. med. J.*, **2**, 429.
- Donohue, D. M., Motulsky, A. G., Giblett, E. R., Pirzio-Biroli, G., Viranuvatti, V., and Finch, C. A. (1955). The use of chromium as a red-cell tag. *Brit. J. Haematol.*, **1**, 249.
- Ebaugh, F. G., Jr., Ross, J. F., and Emerson, C. P. (1953). The use of chromium 51 as an erythrocyte tagging agent for determining the survival of transfused and autotransfused erythrocytes. *J. clin. Invest.*, **32**, 563.
- Frey, K. W., and Schmidt-Mende, M. (1963). Chrom 51 zur Bestimmung der Erythrozytenlebenszeit nach Herzoperationen unter Anwendung der Herz-Lungen-Maschine und bei hämolytischen Anämien. *Arzneimittel-Forsch.*, **17**, 258.
- Gehrman, G., and Loogen, F. (1964). Mechanische hämolytische Anämie nach Implantation künstlicher Aortenklappen. *Dtsch. med. Wschr.*, **89**, 625.
- Gilligan, D. R., and Bumgart, H. L. (1941). March haemoglobinuria; studies of clinical characteristics, blood metabolism and mechanism, with observations on three new cases, and review of literature. *Medicine (Baltimore)*, **20**, 341.
- Marsh, G. W. (1964). Intravascular haemolytic anaemia after aortic valve replacement. *Lancet*, **2**, 986.
- Mollison, P. L. (1956). *Blood Transfusion in Clinical Medicine*, 2nd ed. Blackwell, Oxford.
- Neill, C. A., Farman, E. N., Sigler, A. T., and Bahnsen, H. T. (1961). Presented at thirty-first annual meeting of Society of Paediatric Research Program, Atlantic City, New Jersey, May 4.
- Read, R. C., Wilson, G. W., and Cardner, F. H. (1954). The use of radioactive sodium chromate to evaluate the life span of the red blood cell in health and certain hematologic disorders. *Amer. J. med. Sci.*, **228**, 40.
- Reed, W. A., and Dunn, M. (1964). Fatal hemolysis following ball valve replacement of the aortic valve. *J. thorac. Surg.*, **48**, 436.
- Sayed, H. M., Dacie, J. V., Handley, D. A., Lewis, S. M., and Cleland, W. P. (1961). Haemolytic anaemia of mechanical origin after open heart surgery. *Thorax*, **16**, 356.
- Sigler, A. T., Forman, E. N., Zinkham, W. H., and Neill, C. A. (1963). Severe intravascular hemolysis following surgical repair of endocardial cushion defects. *Amer. J. Med.*, **35**, 467.
- Stevenson, T. D., and Baker, H. J. (1964). Haemolytic anaemia following insertion of Starr-Edwards valve prosthesis. *Lancet*, **2**, 982.
- Verdon, T. A., Forrester, R. H., and Crosby, W. H. (1963). Hemolytic anaemia after open-heart repair of ostium-primum defects. *New Engl. J. Med.*, **269**, 444.