The life span of erythrocytes in iron-deficiency anaemia

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SYNOPSIS Red cells, derived from 13 patients with iron-deficiency anaemia, were found to have normal life span in the patients' own circulations and those of normal volunteers.

The life span of iron-deficient red cells in circulating blood is assumed by most haematologists to be normal, yet the wide variety of shape and size adopted by iron-deficient red cells suggested that this might not be so.

Using the Ashby technique for measuring red cell survival, Brown, Hayward, Powell, and Witts (1944) have shown that normal red cells survive for a normal period when transfused into an iron-deficient patient, and iron-deficient red cells survive normally when transfused into a normal person (Kaplan and Zuelzer, 1950).

However, Rasch, Cotton, Griggs, and Harris (1958), using ^{51}Cr -tagged iron-deficient red cells, reported a decreased red cell survival in 14 iron-deficient infants and, using the same method, Verloop, Van der Wolk, and Heier (1960) found a shortened life span in five out of six patients with iron-deficiency anaemia.

In view of these results, a further investigation of this problem was undertaken and the survival of iron-deficient red cells was studied, using the blood from 13 iron-deficiency patients.

METHODS

MEASUREMENT OF LIFE SPAN OF ERYTHROCYTES (^{51}Cr) The method of labelling the erythrocytes was that described by Veall and Vetter (1958). The blood was added to an anticoagulant mixture in a universal container, 15 to 20 ml. of blood to 3 ml. of acid citrate dextrose. After centrifuging the supernatant plasma was removed and 2 to 3 ml. of this was added to 100 ml. sterile saline; the remainder of the plasma was discarded. Then 100 μC . ^{51}Cr was added to the packed cells. The red cells were left at room temperature for 30 minutes before washing twice in the plasma-saline. The washed red cells were finally resuspended in plasma-saline to make a total volume of 18 to 20 ml.; the ^{51}Cr -labelled red cells were injected intravenously, and the 100% sample was taken at 15

minutes. One more sample was taken at 24 hours, and the activity of all samples was estimated on an Ekco pillar scintillation counter. The results are expressed as the percentage ^{51}Cr activity and not corrected for elution.

ESTIMATION OF BLOOD LOSS IN FAECES Faeces were collected for periods of 10 to 14 days and pooled into cartons which fitted the well of a plastic phosphor counter. The radioactivity of the faeces was measured and compared with the activity of appropriate standards, prepared from the patients' own blood in similar cartons. From these standards the radioactivity/volume of faeces was related to millilitres of the patients' blood.

ESTIMATION OF SERUM IRON Two methods were used (Bothwell and Mallet, 1955; Ramsay, 1954).

CLINICAL MATERIAL

The 13 patients were considered to have uncomplicated iron-deficiency anaemia. Patients with disseminated malignancy, renal and hepatic failure, infection, associated vitamin B_{12} , or folic acid deficiency states were excluded. Three of the patients selected for autotransfusion were bleeding from the gastro-intestinal tract and continued to do so throughout the study. The criteria used to substantiate the diagnosis of iron-deficiency anaemia were as follows:

A haemoglobin estimation of less than 11.5 g./100 ml. in women and 13.5 g./100 ml. in men (Dacie, 1956); a mean corpuscular haemoglobin concentration of less than 32%; a typical blood film of iron-deficiency anaemia; a serum iron level of less than 60 μg ./100 ml. a good response to iron therapy.

Table I represents the data collected to satisfy the above criteria. All the blood films showed the changes found in iron deficiency—anisocytosis, poikilocytosis, and hypochromia. Because of the uniformity of these findings they are not included in Table I. A serum bilirubin estimation was carried out in each case and the highest level was 0.3 mg./100 ml. Bogomolow's screening test for urobilinogen in the urine was negative in each case.

The survival of iron-deficient red cells from 10 patients

TABLE I
CLINICAL FINDINGS IN CASES OF IRON-DEFICIENCY ANAEMIA

Case No.	Sex	Age	Clinical Cause	M.C.H.C. (%)	Serum Iron (μ g./100 ml.)	Occult Blood in Stools	Hb (g./100 ml. before treatment)	Treatment	Period between Hb Estimations (weeks)	Hb (g./100 ml. after treatment)
1	M	50	Post-gastrectomy	29	24	—	10.3	Oral iron	2	12.0
2	F	45	Undiagnosed	28	13	—	11.4	Intravenous iron	5	14.5
3	M	20	Duodenal ulcer		43	+	6.9	Oral iron	4	14.5
4	F	70	Undiagnosed gastrointestinal bleeding	27	10	+	6.8	Oral iron	4½	12.9
5	F	31	Menorrhagia	27	11	—	7.5	Oral iron	12	10.2
6	F	47	Undiagnosed	26	33	—	7.3	Oral iron	4	11.1
7	F	38	Undiagnosed	25	41	—	6.7	Oral iron	6½	13.8
8	F		? poor diet	26	31	—	8.4	Intramuscular iron	6	11.5
9	F	46	Undiagnosed	28	19	—	10.9	Oral iron	2	12.4
10	F	37	Undiagnosed gastrointestinal bleeding	27	16	+	8.1	Oral iron	3	10.7
11	F	17	Gastrointestinal bleeding from aspirin	27	56	+	7.1	Oral iron	6	11.5
12	M	41	Gastrointestinal bleeding, undiagnosed	30	53	+	10.8	No treatment		
13	M	62	Post-gastrectomy	26	24	—	8.8	Intramuscular iron	2	10.9

was studied in the circulation of 10 non-anaemic volunteer patients. The normal precautions for preventing the transmission of infection and for cross-matching were observed.

RESULTS

In three cases the life span of ^{51}Cr -tagged iron-deficient red cells was measured in the patients' own circulation; in three cases, both in the patients and in a normal volunteer; and in the remaining seven cases in normal volunteers only (Table II).

The 50% chromium survival time ($T_{1/2}$) of tagged iron-deficient red cells in the patients' own circulation (Table II, column 1) varied between 25 and 30 days (with a mean of 26.8 days). The $T_{1/2}$ ^{51}Cr of the tagged iron-deficient cells in normal recipients was between 25 and 32 days (mean 28 days) (Table

II, column 2), with two exceptions where the $T_{1/2}$ ^{51}Cr was abnormally short. In these two instances the initial drop of ^{51}Cr activity was within the normal range (Figs. 1 and 2), and, when the slope of the initial drop was projected to cut the 50% line, the $T_{1/2}$ ^{51}Cr was 23 and 28 days respectively. But at approximately 18 days the amount of radioactive chromium remaining in the blood decreased rapidly to reach background in 28 and 25 days respectively.

In one instance it was possible to repeat the survival, using the same recipient, 82 days after the first experiment (Fig. 3). The patient had had the iron deficiency corrected by this time and Hb was 15.2 g./100 ml. The $T_{1/2}$ ^{51}Cr was three days and all radioactivity had disappeared from the recipient's blood in 11 days.

Serological tests performed both before and after this cross-transfusion showed no demonstrable incompatibility between donor cells and recipient's serum. In addition, the recipient's serum was screened against a cell panel of known antigenic pattern, but no antibody could be detected.

ESTIMATION OF BLOOD IN FAECES Three auto-transfused patients had occult blood in the stools. In only one of these could any significant amount of radioactivity be found in the faeces after the injection of the ^{51}Cr tagged red cells intravenously; the amount lost in this instance was estimated as 1.7 ml./day. This amount of blood loss would not alter the ^{51}Cr survival in the blood to any significant degree.

DISCUSSION

The results obtained in this investigation show that the life span of iron-deficient red cells in the circulation

TABLE II

LIFE SPAN OF ^{51}Cr -TAGGED IRON-DEFICIENT RED CELLS

Case No.	Apparent Half-time (days)	
	Patient to Patient	Patient to Recipient
1	30	26
2	30	32
3		32
4		21 ¹
5		17 ¹
6		26
7		27
8		29
9		25
10	25	27
11	25	
12	26	
13	25	
Range	25 to 30	25 to 32
Mean	26.8	28

¹Results due to incompatibility and not included in the range or mean.

FIG. 1. The Cr survival, uncorrected for chromium elution, of red cells of patient No. 4 in a normal recipient on the first occasion. The continuous line represents the actual findings, the interrupted line the projection of the slope of the original rate of destruction.

FIG. 2. The Cr survival, uncorrected for chromium elution, of red cells of patient No. 5 in a normal recipient. The continuous line represents the actual findings, the interrupted line the projection of the slope of the original rate of destruction.

FIG. 3. The Cr survival, uncorrected for chromium elution, of red cells of patient No. 4 in the same recipient, 82 days after the first transfusion of ^{51}Cr -labelled erythrocytes (see Fig. 1).

is normal, both in the iron-deficient patient and in the normal circulation.

In the two instances where cross-transfusion resulted in an abnormally short survival in the recipient, the pattern of the survival suggested that incompatibility developed in the recipient to the donor's cells after transfusion and in one case a subsequent survival study showed that this was the most probable explanation.

Although no conventional tests could define this incompatibility, either before or after these studies, similar phenomena have been reported by Mollison (1959), Loutit, Mollison, and Young (1943), and Jandl and Greenberg (1957), and may be encountered in about 30% of cases where a small amount of homologous blood is transfused into normal recipients (Mollison, 1959).

From these studies, survival of red cells in iron-deficiency anaemia would appear to be normal, but it has been shown that the plasma iron turnover in this anaemia is normal or increased (Bothwell, Callender, Mallett, and Wits, 1956). Pollycove (1959) deduced that in iron-deficiency anaemia where the mean red cell haemoglobin is reduced, this turnover must represent a daily haemoglobin production of above normal limits and, therefore, increased daily red cell production. If the survival of red cells in the peripheral blood is normal, then

some red cells must be destroyed in the marrow before reaching maturity in the peripheral blood. This hypothesis of 'ineffective erythropoiesis' has been discussed by Wits (1961).

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