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 a
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 cen-
trifuging 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 Eko-
pillar scintillation counter. The results are expressed as
the percentage $^{51}$Cr activity and not corrected for elu-

ESTIMATION OF BLOOD LOSS IN FAEces Faeces were col-
lected for periods of 10 to 14 days and pooled into
cartons which fitted the well of a plastic phosphor coun-
ter. The radioactivity of the faeces was measured and com-
pared 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, associ-
ated vitamin B$_12$, or folic acid deficiency states were
excluded. Three of the patients selected for autotrans-
fusion 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.
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 (T½) 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 T½ $^{51}$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 T½ $^{51}$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 T½ $^{51}$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 T½ $^{51}$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 autotransfused 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...
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 ⁵¹Cr-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 Witts, 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 Witts (1961).

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REFERENCES


