

# Value of serum ferritin estimation in sickle cell anaemia

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**SUMMARY** In a group of 35 children with sickle cell anaemia serum ferritin concentration ranged from 70 to 2460  $\mu\text{g/l}$  (mean 367, median 180  $\mu\text{g/l}$ ). This was significantly higher than the ferritin levels (range 8-101, mean 34, median 30  $\mu\text{g/l}$ ) in a group of 63 normal control children of the same age group. 30 (86%) of the sickle cell children showed serum ferritin levels greater than 101  $\mu\text{g/l}$ , and 2 (6%) levels greater than 1000  $\mu\text{g/l}$ . 7 of the patients had not been transfused before this study. Their serum ferritin levels were all raised and showed a significant correlation with age but not with haemoglobin level. In the remainder of the patients the serum ferritin bore no significant correlation with age, haemoglobin level, or number of units of blood transfused. 2 children with HbSC disease had levels within the control range. Since patients with sickle cell anaemia have an increasing chance of long survival, we suggest that serial estimations of their iron status be made by means of serum ferritin assay in order to determine which patients are accumulating excessive iron.

Sickle cell disease is one of the commonest hereditary haemoglobinopathies. Because of better understanding of the nature of haemoglobin S and the realisation that patients with sickle cell anaemia may lead relatively normal lives with Hb levels between 7.0 and 9.0 g/dl, regular blood transfusions are no longer used in the management of these patients. However, blood transfusion may be necessary for complications such as an 'aplastic' or 'sequestration' crisis.

Among the hazards of blood transfusion is accumulation of iron. Patients with haemolytic anaemia may also become iron loaded because of excess iron absorption. It may now be possible to reduce iron overload even in patients receiving regular blood transfusion by using continuous subcutaneous desferrioxamine (Propper *et al.*, 1976; Hussain *et al.*, 1976, 1977). We assessed the iron status of a group of children with sickle cell anaemia living in London by means of the serum ferritin assay in order to see how many of these patients accumulate excessive iron.

## Subjects and methods

Thirty-seven children with sickle cell disease (35 HbSS and 2 HbSC) attending the sickle cell clinic at King's College Hospital were studied (Table). One

or more transfusions had been given to 28 of those with sickle cell anaemia because of (a) unexplained low Hb interfering with normal activities (persistent Hb level  $<5.0-6.0$  g/dl), (b) major operation planned, (c) severe infection (e.g. pneumonia, meningitis, and septicaemia), (d) gross bone infarction, (e) aplastic and sequestration crises and severe haematuria. The 2 patients with HbSC disease had not been transfused. The total units of blood received by each patient were ascertained from hospital notes; no accurate record of their transfusional state was known before referral. Blood for serum ferritin estimation was obtained from capillary samples collected at the time of routine Hb estimation. All patients were regularly receiving oral folic acid

Table Clinical and laboratory findings in the children with sickle cell disease and the control subjects

Subjects	n	Age (years) (range, mean)	Sex	Hb (g/dl) (range, mean)	Total no. units of blood received (range, mean)	Serum ferritin ( $\mu\text{g/l}$ ) (range, mean)
Sickle cell disease	37 (35 HbSS, 2 HbSC)	1-15	19 M	5.6-12.3	0-17	70-2460
		9.5	18 F	7.9	4	367
Control	63	1-15 7.7 (5)	31 M 32 F	11.7-14.7 12-9	0	9-101 34

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(5 mg/day) and oral penicillin (125 mg bd for those younger than 6 years, and 250 mg bd for those over 6).

At the same time 63 normal children, selected from a group referred to paediatric outpatient clinics at the Royal Free Hospital, were studied as controls (Table). They included children with bed-wetting, chronic abdominal pain, screaming attacks and those coming for routine developmental assessment and minor operations (circumcision, hernia repair etc.). Blood for serum ferritin was obtained from the residuum of blood taken for other investigations. None of the controls was known to have received iron or blood transfusion before the study and none was anaemic or had evidence of an inflammatory or blood disease. The method used for serum ferritin estimation was that of Addison *et al.* (1972).

## Results

Serum ferritin concentration in the group of 63 control children ranged from 8–101  $\mu\text{g/l}$  (mean 34  $\mu\text{g/l}$ , median 30  $\mu\text{g/l}$ ). In the 35 patients with sickle cell anaemia it ranged from 70 to 2460  $\mu\text{g/l}$  (mean 367  $\mu\text{g/l}$ , median 180  $\mu\text{g/l}$ ) (Fig.). This was significantly raised compared with the control group ( $P < 0.001$ ). In the 2 patients with HbSC disease, serum ferritin was 70 and 80  $\mu\text{g/l}$  (within the control range). 30 (86%) of the patients with sickle cell anaemia had serum ferritin levels  $>101 \mu\text{g/l}$ , while 2 (6%) had levels  $>1000 \mu\text{g/l}$ .

Seven patients with sickle cell anaemia had not been transfused. Their serum ferritin levels ranged from 102  $\mu\text{g/l}$  to 290  $\mu\text{g/l}$ , and correlated significantly ( $r = 0.8$ ,  $0.05 > P > 0.02$ ) with their age but not

with their Hb level. In the remaining patients with sickle cell anaemia there was no significant correlation between serum ferritin and age, Hb level, or the total number of units of blood transfused. Indeed, 2 of the patients with raised serum ferritin levels were only one year old (Fig.). One of these infants had had only one unit of blood transfused while the other had had only two, even though serum ferritin levels were 300 and 200  $\mu\text{g/l}$ , respectively.

## Discussion

This study shows that the mean serum ferritin levels of patients with sickle cell anaemia are higher than in control children of the same age group, confirming the results of two earlier studies. Siimes *et al.* (1974) found raised serum ferritin levels in 14 children in San Francisco with sickle cell anaemia of similar age to those in our study, and the median value in our patients was similar to theirs. On the other hand, serum ferritin values in our study were lower than those found by Peterson *et al.* (1975) in a group of 27 patients in New York with sickle cell anaemia aged from 12 to 40. In contrast to that study, however, we found no significant correlation between serum ferritin concentration and number of units of blood transfused.

Serum ferritin is now known to reflect mainly reticuloendothelial iron stores. Part of the rise in serum ferritin in sickle cell anaemia may be due to the presence of increased iron in the reticuloendothelial cells because of the excessive breakdown of Hb and subnormal circulating mass of Hb. This mechanism alone cannot explain the very high serum ferritin levels found in some of the patients. The most obvious source of the excess body iron is transfused blood.

The lack of correlation between serum ferritin and the total number of units of blood transfused in our patients may be due to the fact that the transfusion record of some of the patients before referral was unknown. The difference in our results and those of Petersen *et al.* (1975) may be the difference in age and transfusion policy. Blood transfusion raises the red cell mass and simultaneously suppresses the formation of HbS. These are two desired effects, and routine use of blood for treating these patients has been widely accepted in the past. Better understanding of the nature of this disease showed that patients with sickle cell anaemia are well adapted to the low steady state Hb level and do not require routine blood transfusion (Serjeant, 1974). This reduces the risk of iron overload from transfusion but continuous severe anaemia may predispose to excessive gastrointestinal absorption of iron. The contribution of iron absorbed

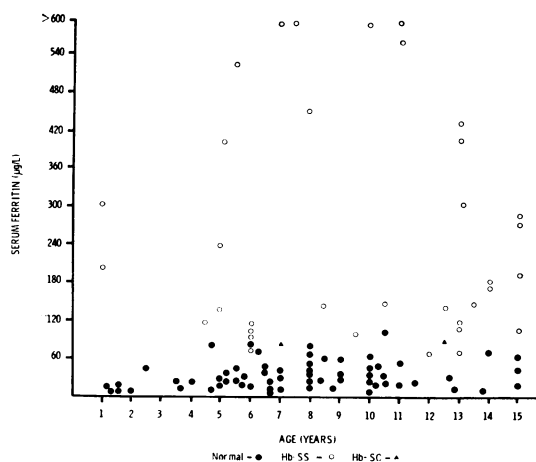


Fig. Relationship between serum ferritin levels and age.

through the gastrointestinal tract to iron overload in thalassaemia major is well known (Erlandson *et al.*, 1962), although it can be alleviated by introduction of hypertransfusion regimens. In our patients, in contrast to those of Peterson *et al.* (1975), much of the iron overload may have come from absorbed rather than transfused iron.

Patients with sickle cell anaemia have an increasing chance of surviving into late adulthood, if they survive the high risk period of childhood and early adult life (Serjeant, 1974). The severity of the disease appears to lessen with advancing age but occasional blood transfusion may still be required (Serjeant, 1974). Peterson *et al.* (1975) found that serum ferritin levels were higher than normal in patients with sickle cell anaemia even in those with absent marrow iron stores. They explained this phenomenon on the assumption that much of the iron storage pool may be sequestered in areas of previous infarction. Bone marrow aspiration may not clearly indicate iron status in these patients and has the additional disadvantage of being painful. It is still debatable whether patients with sickle cell anaemia and absent bone marrow iron will benefit from iron administration (Lincoln *et al.*, 1973; Petersen *et al.*, 1975). It has been suggested that the increase in Hb concentration after iron administration to iron-deficient patients with sickle cell disease increases morbidity by increasing the number of vaso-occlusive episodes (Peterson *et al.*, 1975). Thus, the exact role of iron excess and deficiency in the morbidity and mortality of sickle cell disease is still not clear but we suggest that the serum ferritin assay is useful for serial measurements of iron status in patients with sickle cell anaemia in order to detect those most at risk from iron overload.

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