Red cell indices and serum ferritin levels in children

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SUMMARY The blood counts of 187 non-anaemic children who attended hospital with minor illnesses and who were between the ages of 12 months and 6 years were studied retrospectively. As many as 76.8% of these children were found to have MCVs below the normal adult range. A prospective study of a further 28 non-anaemic children in the same age group showed that the majority of children with low MCVs have normal haemoglobin A₂ and F levels and have serum ferritin levels within the normal adult range. These findings indicate that microcytosis is an intrinsic feature of erythropoiesis in early childhood and that in most instances this feature cannot be attributed to iron deficiency or β -thalassaemia syndromes.

Previous authors have shown that many children whose haemoglobin concentrations are within the usually accepted normal range (above 10.8 g/dl (World Health Organisation, 1959)) have a low mean corpuscular volume (MCV) and a low mean corpuscular haemoglobin (MCH) compared with normal adults (Guest and Brown, 1957; Sturgeon, 1958; Schmaier *et al.*, 1974) and have attributed these findings to a high prevalence of iron deficiency in children. The present study was undertaken to investigate the validity of this explanation. Our results clearly indicate that iron deficiency accounts for only a minor proportion of the microcytosis of childhood and that normal iron-replete children show microcytosis, their red cells being smaller the lower the age of the child.

Material and methods

SUBJECTS STUDIED

In a preliminary study, a retrospective analysis of the data from blood samples of 200 randomly selected children between the ages of 12 months and 6 years were made. Most of these children were suffering from trivial medical complaints or were having a routine blood count before planned minor surgery. Nineteen of the 200 children were excluded from the study because they had chronic diseases which might affect erythropoiesis or showed anaemia (ie, Hb <

10.8 g/dl) or were already known to have a haemoglobinopathy. As the children included in the retrospective study were drawn from a multiracial population, it is possible that undiagnosed thalassaemia syndromes, haemoglobinopathies or iron deficiency could have accounted for the high incidence of low MCVs and MCHs subsequently observed. These possibilities were investigated in a prospective study on a further 28 consecutive non-anaemic children aged between 22 months and 6 years attending an outpatient department. On these 28 children we performed blood counts, Sickledex tests, and haemoglobin electrophoresis and estimated haemoglobin A₂ and F levels. Serum ferritin levels were assayed in 20 of the 28 children.

METHODS

Blood counts were performed on a Coulter Counter, Model S, standardised with 4C Coulter Counter cell control. Serum ferritin levels were assayed using the technique of Addison *et al.* (1972). In our hands, the mean serum ferritin level in 38 non-anaemic, normal adult females was 56.6 μ g/l (range 14-148 μ g/l) and in 39 non-anaemic normal adult males was 165.4 μ g/l (range 39-340 μ g/l). The haemoglobin studies were performed using standard techniques (Dacie and Lewis, 1975).

Results

The mean $\pm$ 2 SD for the various parameters in-

vestigated in the 181 patients studied retrospectively were: haemoglobin 12.3 ± 1.7 g/dl; red cell count $4.64 \pm 0.76 \times 10^{12}/l$; MCV 78.1 ± 10.4 fl; MCH 26.6 ± 4.1 pg. The proportions of children having MCVs and MCHs below the normal adult ranges (Bain and England, 1975) of 89.5 ± 7.5 (2 SD) fl and 30.3 ± 2.6 (2 SD) pg were as high as 76.8% (Figure) and 69.6% respectively. In addition, the mean (± 2 SD) for the MCV was found to be low, with a value of $79.9 (\pm 9.0)$ fl, even when only the 67 children with haemoglobin levels above 12.4 g/dl were considered. We also found that in the entire group of 181 children studied, the mean values for the MCV and MCH increased slightly, but progressively, with age from 76.5 fl and 25.9 pg between the ages of 1 and 3 years to 79.6 fl ($P < 0.02$) and 27.4 pg ($P < 0.005$) between the ages of 5 and 6 years.

Figure Histogram of the frequency distribution of MCVs in the 181 children studied retrospectively (solid line) together with a histogram of the distribution of MCVs in an equal number of healthy adults (interrupted line).

Three of the 28 children in the prospective study were found to have a haemoglobinopathy or β -thalassaemia syndrome. The mean values for the MCV and MCH in the 25 patients without a haemoglobinopathy or β -thalassaemia syndrome in this prospective study were similar to those in the larger retrospective study, being 79.8 fl and 26.8 pg respectively. None of the 20 children in whom serum ferritin levels were assayed had a haemoglobinopathy or β -thalassaemia syndrome. Despite the high prevalence of the low MCVs and MCHs in these children only one of them had serum ferritin levels below the normal adult range of 14 to 340 $\mu\text{g}/l$ and the mean serum ferritin level in the 20 children was 42.2 $\mu\text{g}/l$ (range 12-122 $\mu\text{g}/l$). There was no correlation between MCV and serum ferritin in these children.

Discussion

The data presented here indicate that many children with low MCVs and MCHs are not iron deficient, do not have thalassaemia, a haemoglobinopathy, or other cause for microcytosis, and suggest that the production of microcytes is an intrinsic feature of erythropoiesis in childhood and that this is independent of the iron status of the child. This concept is supported by the observations that infants given 250 mg iron dextran intramuscularly at the age of 9 months still show a low average MCV of 78.9 and 82.3 fl when they reach the ages of 12 and 18 months respectively, despite the parenteral iron therapy (Sturgeon, 1958), and that although children with haemoglobin levels above 12.4 g/dl have a low mean MCV (our data) such children do not increase their haemoglobin levels after six weeks of oral iron therapy (Evans *et al.*, 1972).

The spontaneous rise in mean MCV with age, demonstrated in the present study in children between the ages of 1 and 6 years, has been shown to continue both in older children (Guest and Brown, 1957; Schmaier *et al.*, 1974) and in adults (Stenhouse and Woodliff, 1974). These findings also suggest that microcytosis is an inherent phenomenon of erythropoiesis in childhood and that there is a gradual change to the production of red cells of adult size as the child grows.

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