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## Iron Deficiency in Children in Sydney

by

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### Abstract

*Results of prospective studies of over 2,000 children with nutritional iron deficiency anaemia in Sydney are presented. The epidemiological aspects were also investigated in a study of 1500 well children, aged 6 — 36 months, attending Baby Health Centres in Sydney and the incidence of iron deficiency anaemia was found to be low (3%). Iron deficiency anaemia was common in children admitted to hospital with acute infections and diarrhoea (20%) and was clinically unsuspected in two-thirds. Because of inadequate iron prophylaxis the incidence in prematures was high (30%). Another group, recently arrived migrant children, also had a high incidence of anaemia (25%). There was circumstantial evidence linking anaemia and childhood morbidity. Matched patients awaiting elective minor surgery had a low incidence (3%) of iron deficiency anaemia, similar to the data published in out patients in Surabaya.*

*The average daily iron intake in children under 12 months of age was below 6mg., significantly less than the 10mg./day recommended by the*

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*American Board of Paediatrics. Iron intake of poorer children, derived mainly from iron-enriched cereals, was higher than in their wealthier counterparts. Children with significantly less iron but a more varied diet tended to have higher haemoglobin levels. It seems unlikely that iron fortification by a single dietary item will provide the solution to paediatric iron deficiency. Poverty or poor social ratings did not predispose to higher incidence of anaemia, and neither did multiparity, iron deficiency in the mother or the order of the child in the family.*

*No positive correlation could be shown between normal haemoglobin levels ( $12.2 \pm 2.2$  gm per 100 ml) and the iron content of the diet. As normal haemoglobin levels do not preclude underlying iron deficiency, another series of studies was undertaken with the aim of detecting iron deficiency without anaemia. The results with fragiligran technique in children without anaemia showed significant differences in two clinical trials where other haematological indices did not change after iron medication.*

*Precise information about recommended modes and dosage of iron therapy and prophylaxis will be presented. Oral iron is the treatment of choice. Iron prophylaxis is indicated in children at risk (prematures, those of multiple births and exchange transfused children) preferably after the second month. Parenteral iron therapy and blood transfusion have little place in management of paediatric iron deficiency.*

*The main aim of iron prophylaxis should be institution of public health measures to provide guidance and parental education for an adequate caloric and nutritionally varied diet in the first 12 months of life.*

The problem of iron malnutrition in paediatrics is world-wide. It increases in communities where inadequate iron intake is aggravated with blood loss associated with intestinal infestation. The condition is usually unrecognized clinically, until the haemoglobin is below 7.0 gm per 100 ml. There is even a division of opinion whether iron deficiency anaemia is of any significance in clinical practice. Whether an association exists between unsuspected iron deficiency anaemia and childhood morbidity is not yet resolved. To answer this, it would be necessary to delineate the iron deficiency state as distinct from iron deficiency with anaemia.

The purpose of this communication is to review the experience with iron deficiency anaemia at the Royal Alexandra Hospital for Children in Sydney over a 12 year period and to provide some information on the methods of assessment of iron deficiency without anaemia.

### Patients and Results

The results are based on investigations of 1,600 children (Lovric et al., 1965; Lovric 1968) with proven (nutritional) iron deficiency anaemia, between 5 months and 3 years of age (Fig. 1). About one child in eight in this age group admitted to hospital had iron deficiency anaemia (haemoglobin below 10.0 gm. per 100 ml. with a microcytic, hypochromic blood film). The condition was unsuspec-

ted in two thirds when haemoglobin levels were between 6 and 9.5 gm. per 100ml. (Fig. 2). There was a particularly high incidence of anaemia in two groups, those with birth weights below 2.5 Kg and not having iron prophylaxis from the third month, and children of recent migrants, where the daily iron intake was low, frequently below 5 mg per day.

This high incidence of iron deficiency anaemia in hospital practice raised the question as to its frequency in healthy children. Thus, 1,500 well children, representative of all social strata in Sydney, were investigated (Lovric, 1970; Lovric et al., 1972). Information was obtained about their daily dietary pattern, and the daily iron intake calculated.

Data on healthy children revealed that between 6 and 12 months of age this averaged 6 mg. per day in the poorer children, compared with 5.3 mg. in their wealthier counterparts (Fig. 3). Nevertheless, the incidence of iron deficiency anaemia was identical and infrequent (3%). It is of interest that in the poorer children, the main source of food iron was derived from iron enriched cereals, but this did not contribute to higher haemoglobin values.

The pattern of iron intake and nutrition was different in various ethnic groups (Fig. 4). Australian born children had the highest iron

intake, which was mainly cereal derived. However, their haemoglobin levels were lower than those of children from the United Kingdom who had a lower iron intake.

Other factors which could contribute to the development of anaemia were examined. It has frequently been suggested that poverty, poor social rating, multiparity, iron deficiency in the mother, and the order of the child in the family might all predispose to the subsequent development of anaemia in otherwise healthy children. The results showed this not to be the case in the Sydney community (Table I and Fig. 5). However, with the total iron intake below 5 milligrammes per day, there was a greater incidence of iron deficiency anaemia.

This investigation showed that haemoglobin values within the normal range ( $12.2 \pm 2.2$  gm. per 100 ml.) were a poor index of possible underlying iron deficiency, and comparison of iron intake and haemoglobin levels revealed no correlation. (Figs. 6 and 7).

The relationship, if any, which exists between iron deficiency anaemia and associated childhood morbidity is not clear. No direct evidence suggesting such linkage. Fig. 8 shows that children with iron deficiency anaemia admitted to hospital electively, (as for routine minor surgical procedures) had the same incidence of anaemia as healthy children out-

side hospital practice (3%). On the other hand, children with acute illnesses admitted to hospital had a high incidence of iron deficiency (20%), with anaemia usually unsuspected. Results from Fig. 9 demonstrates this point, when comparing haemoglobin levels of matched hospital patients and healthy children; the mean haemoglobin value for hospital patients was 10.6 gm. per 100 ml., compared with 12.0 gm. per 100 ml. for healthy children. The main reason for this difference is the prevalence of iron deficiency anaemia in hospital practice. Considering it takes many months to develop iron deficiency, it is possible that the anaemia made these children more ill during intercurrent illnesses, finally requiring their admission to hospital. This does not imply that iron deficient children have a higher frequency of infection and other illnesses - there is no present evidence to support that contention.

With this circumstantial evidence linking iron deficiency anaemia and childhood morbidity, the question of detecting iron deficiency before anaemia developed became pertinent. Customary studies such as serum iron levels and latent iron binding capacity were not useful, particularly in children with intercurrent illness, where these values are usually depressed. Routine examination of bone marrow iron stores were not practical. The fragiligraph technique

was developed (Lytton et al., 1971) to assess the significance of developing microcytosis and hypochromia as a result of iron deficiency, even in the absence of anaemia. With proven iron deficiency anaemia the fragiligram angles were always less than  $55^\circ$  (Figs. 10 and 11).

Another fragiligraph study was undertaken on haematologically normal children in hospital, aged 6 to 36 months (Lammi and Lovric, 1973). Following initial investigations, including fragiligraph studies, the patients were randomized in a double blind manner and given either iron therapy or a placebo. Three months later investigations were repeated. Response could be evaluated with the fragiligraph and this showed a significant change only with iron medication. Other haematological parameters did not change. In the group having iron therapy there was a significant weight gain. It was concluded that fragiligram testing was useful in the detection of underlying iron deficiency without the presence of anaemia. A similar investigation gave identical results in children with congenital cyanotic heart disease (Lovric et al., 1972).

### Discussion

A full term infant has sufficient iron stores to increase the red blood cell mass in the first 4 months. It has been calculated that for every kilogram gain in weight, about 40

milligrams of iron are required for positive iron balance. Thus, assuming that only about 10% of the dietary iron is absorbed, 6 milligram of elemental iron daily would seem to be the minimal requirement in the first year of life. Children at risk are those with greater iron needs. These include prematures, "small for dates", post exchange-transfusion infants and those of multiple births. From the second year of life growth rate slows to about 2.5 kilograms per year, and iron requirements decrease to about 0.3 milligrams per day. This is the main reason for the low incidence of iron deficiency in children after the second year.

Unfortunately, estimations of optimal iron requirements vary considerably (Burman, 1973); it seems likely that a diet containing less than 5 milligrams of iron per day in the first year of life will lead to anaemia, as shown in many migrant children in Sydney.

With more than 6 milligrams of iron in the diet, and particularly with adequate calories together with a varied food intake, iron deficiency anaemia is unlikely (Figs. 3 and 4). Normal haemoglobin levels ( $12.2 \pm 2.2$  gm. per 100 ml.) are obtained with varying levels of iron intake. Fig. 6 illustrates that there is no difference in iron intake in healthy children (with haemoglobin) levels above and below 11.0 gm. per 100 ml. In Fig. 7, similar conclusions

were reached comparing children with haemoglobin levels above the mean with those below. The problem in the past has been in considering iron deficiency anaemia purely as the result of deficiency of iron. It should be regarded as an example of malnutrition in general, with iron one of the lacking nutrients. For example, by increasing the iron intake from one source (cereals) this did not contribute to higher haemoglobin levels. There is preferential absorption of iron from mixtures of animal and vegetable foods, compared to absorption of iron from vegetables alone. Layrisse et al. (1973) concluded that fortification of food with iron was likely to be effective only in the presence of adequate animal protein in the diet. From a nutritional point of view, the solution to inadequate iron intake will not be solved by iron prophylaxis alone. There is considerable difficulty in estimating iron needs and utilization, with iron intake as the sole criterion. Equating iron intake with "standard" nutrition and hopefully providing prophylactic iron in excess of the calculated requirements will not eliminate iron deficiency. Thus, children in Sydney with an average iron intake of only 5.3 milligrams per day and well below the 10 milligrams of elemental iron per day recommended in 1969 by the American Academy of Pediatrics, rarely have anaemia, probably because their

iron was largely derived from fresh meat and eggs and only 20% from cereals. It is difficult to achieve a daily iron intake of 10 milligram per day in a 12 month old child without iron supplementation. From the data shown, iron fortification, either as medicinal iron or iron enriched food, cannot be advocated as the solution to the problems of iron deficiency.

When inadequate nutrition is accompanied by excessive intestinal blood loss, it is to be expected that iron deficiency anaemia will be more frequent and severe. The average blood loss from the gut of a normal infant is 0.6 ml. per day; this may be doubled during mild diarrhoeal illnesses (Elian et al., 1966). If diarrhoea occurs frequently, iron deficiency will inevitably develop. In addition, heavy intestinal infestation with ancylostoma, strongyloides or necator contribute to excessive blood loss. Aboriginal children admitted to the Royal Alexandra Hospital for Children have a high incidence of iron deficiency anaemia, often caused by an association of recurrent diarrhoea, strongyloides infestation and high carbohydrate diet low in protein. Thus, apart from correcting malnutrition, effective public health measures (e.g. sanitation) play a part in prevention of iron deficiency in children.

The varied mechanisms leading to anaemia in a particular child should be considered prior to iron therapy.

In the affluent Sydney community the main problem has been parental ignorance about the need for a proper, varied diet. Too frequently it is assumed that canned baby foods and adequate milk intake provide optimal nutrition. From the caloric angle this is certainly true, but many minerals including iron and some heat labile vitamins (e.g. folic acid) may be lacking from all autoclaved food. In fact, the detection of iron deficiency anaemia will inevitably demonstrate other nutritional problems in the family and instructions about changing the pattern of family nutrition should be part of the management.

With a low index of clinical suspicion it is clear iron deficiency anaemia leads to very few symptoms and signs, even with haemoglobin levels below 6.0 gm. per 100 ml. Iron deficiency anaemia is uncommon outside hospital practice, both in Sydney and Surabaya (Untario and Pitono, 1972). Does this condition then have any significant clinical implications? Evidence reviewed by Elwood (1973) from study of adults strongly refutes such a suggestion. Secondly, could detection of iron deficiency without anaemia predict the development of anaemia in any particular child? Could it either be detrimental to the child's progress? These are questions to which there are no answers yet. Apart from linking anaemia and childhood morbidity in a rather cir-

cumstantial way, there is no direct evidence that iron deficiency limits growth and performance. However, it is often observed that a child with iron deficiency anaemia associated with intercurrent illness appears more ill than a similar patient without anaemia. It is probable that, during the progression of anaemia, developing over many months, erythrocyte adaptive mechanisms compensate for the reduction in circulating red cell mass. There is an implied improved oxygen delivery to the tissues in uncomplicated iron deficiency anaemia related to increased generation of organic phosphates in the red cells. This is usually proportional to the severity of the anaemia, causing a shift in the oxygen dissociation curve to the right. During acute illness, in particular when this is associated with dehydration or acidosis, the generation of the organic phosphates in the red cell will be temporarily curtailed. This leads to lowered oxygen delivery to the tissues and anaemia may suddenly become symptomatic and a patient with a minor illness may appear more severely ill. It is unlikely that iron therapy in any form will improve the clinical state of such a child with any rapidity. Rather, correction of the dehydration and acidosis will lead to regeneration of erythrocyte phosphate in a matter of hours and thus restore the compensatory adaptation to anaemia.

Uncomplicated iron deficiency anaemia always responds to oral iron therapy. At the Royal Alexandra Hospital for Children in Sydney, it has been common practice to treat children with a liquid iron preparation (Elixir Ferrous Gluconate) in a dose of 6 milligrams of elemental iron per kilogram of body weight daily.

It has been found advantageous to give this with liquid feedings other than milk 2 or 3 times per day. This has generally been well tolerated. In order to prevent iron deficiency in children at risk, iron prophylaxis in the dosage of 2 mg. of elemental iron per kg. of body weight daily, is used over a period of three to four months from the age of two months. With this form of management no failures have been observed to date, but some failures were noted with oral colloidal iron therapy. For a number of reasons, intra-muscular or intravenous iron therapy has very little place in the management of iron deficiency anaemia in children in Sydney, although iron depots may have advantages in areas where parasitic infestations are endemic.

There is no evidence that parenteral iron therapy will produce a faster or better response. Finally, parenteral iron has many, some potentially serious, side effects.

There is virtually no indication for blood transfusion in nutritional iron deficiency anaemia of childhood based solely on low haemoglobin levels and moreover stored blood for transfusion has a low concentration of erythrocyte organic phosphates.

Whilst a transfusion with this blood will improve the colour and haemoglobin level, tissue anoxia may not be corrected as the stored blood binds oxygen more avidly (left-shifted oxygen dissociation curve) for some hours.

#### Acknowledgements

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total iron deficiency

001

SYDNEY METROPOLITAN AREA ( CHILDREN AGED 6 - 36 MONTHS )				
Suburb rating	Number of children	Mean haemoglobin	Below 9.0 weekly ( % )	Iron deficiency anaemia
1 - 2	45	12.3	2	-
3	130	11.6	17	9
4	310	12.5	19	2
5	340	12.4	34	4
6 - 7	145	11.7	54	15
8	30	12.9	53	1
TOTAL	1000	12.9 (+ 2.1)	29	31

TABEL 1 : Haemoglobin distribution and incidence of iron deficiency anaemia in various social strata. The lower the suburb number, the higher the arbitrary social rating.

TABLE 1

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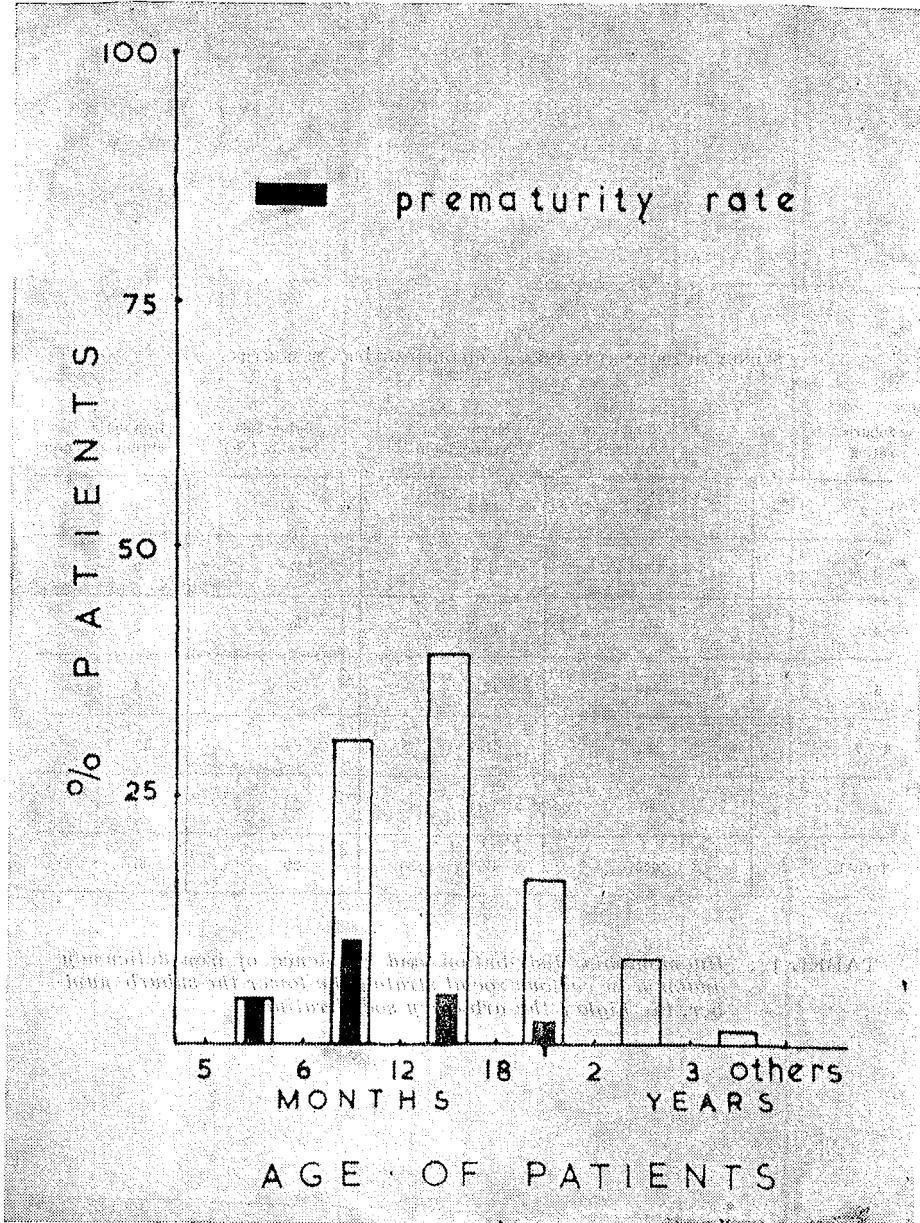


FIG. 1 : Age distribution of patients, including prematurity rates.

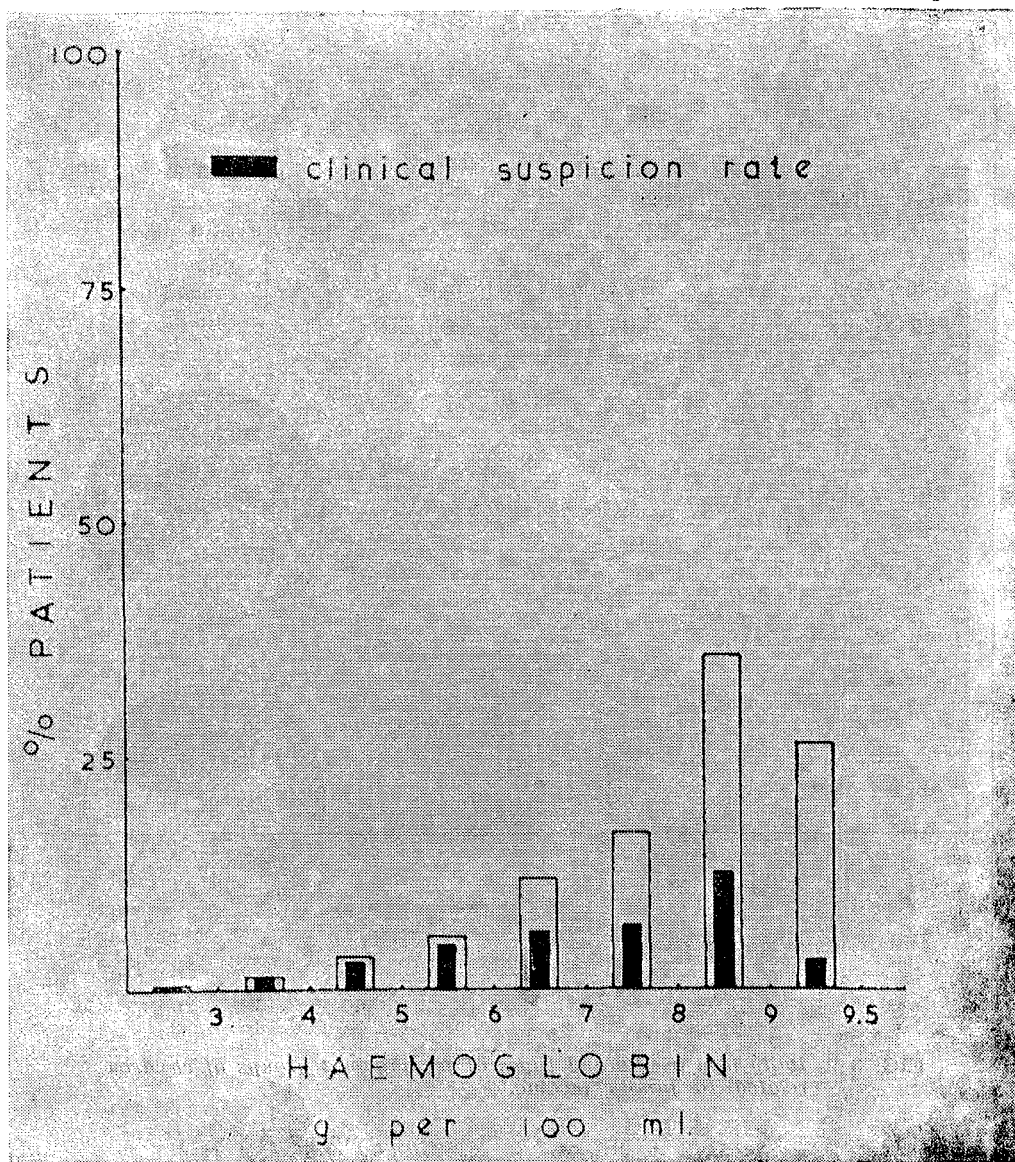


FIG. 2 : *Distribution of patients according to severity of anaemia and clinical suspicion rate.*

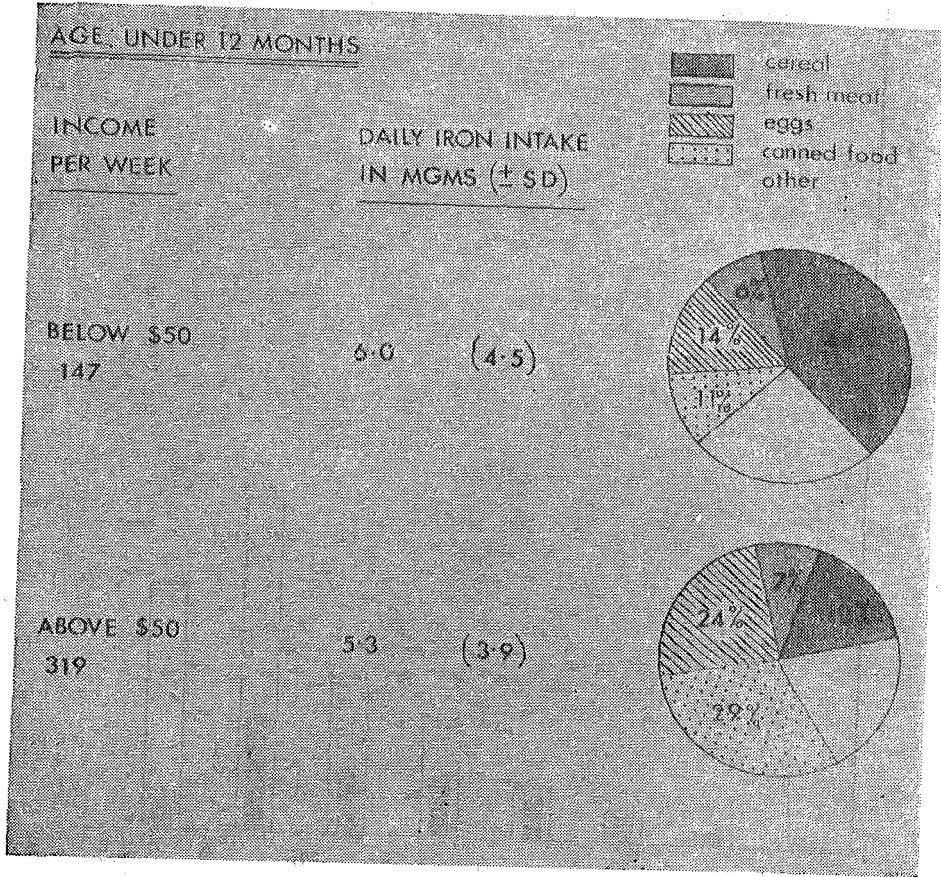


FIG. 3 : Daily iron intake and types of feeding in 2 groups of children related to family income.

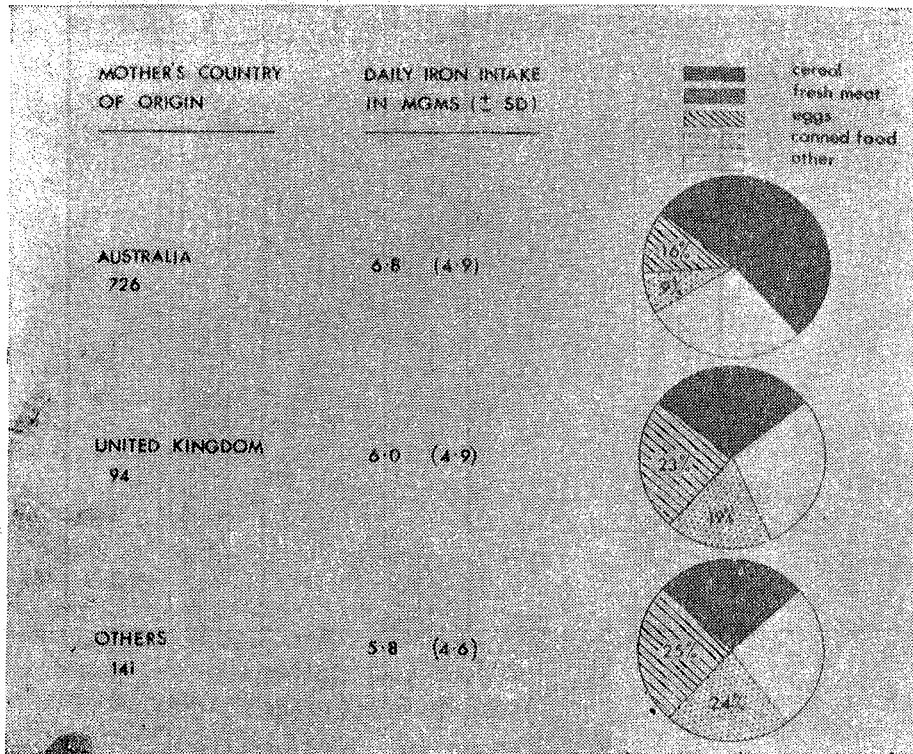


FIG. 4 : Daily iron intake and types of feeding in various ethnic groups

... of iron intake ...

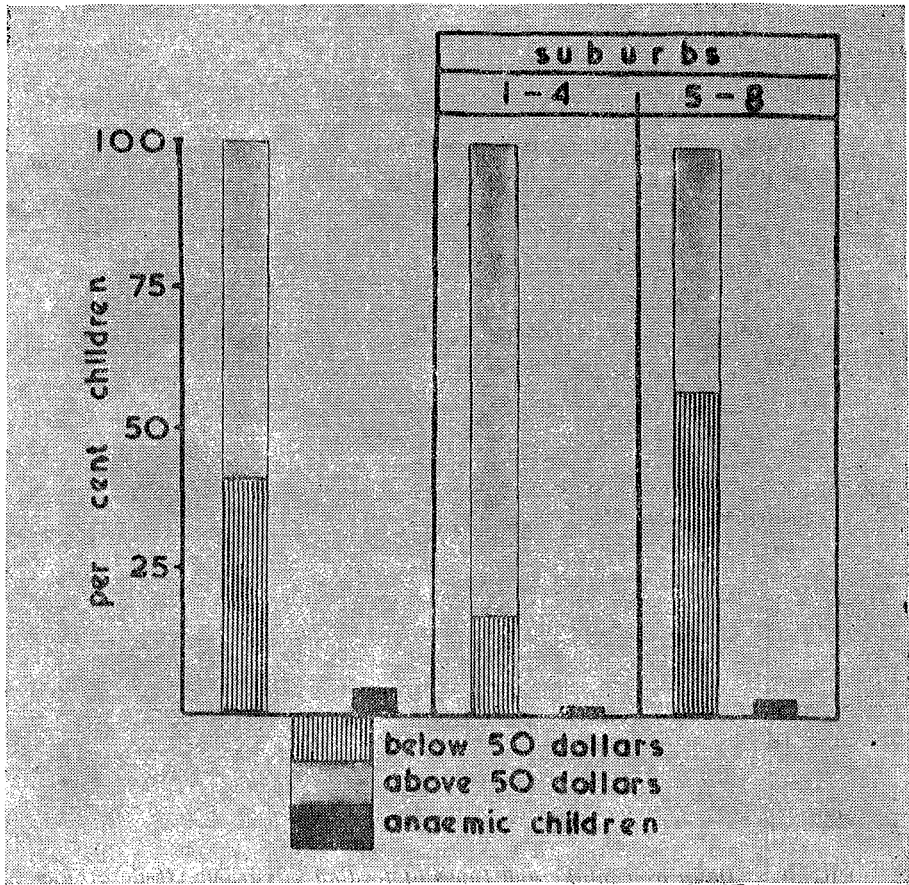


FIG. 5 : Incidence of anaemia is not significantly different in lower social ratings or in poorer families.

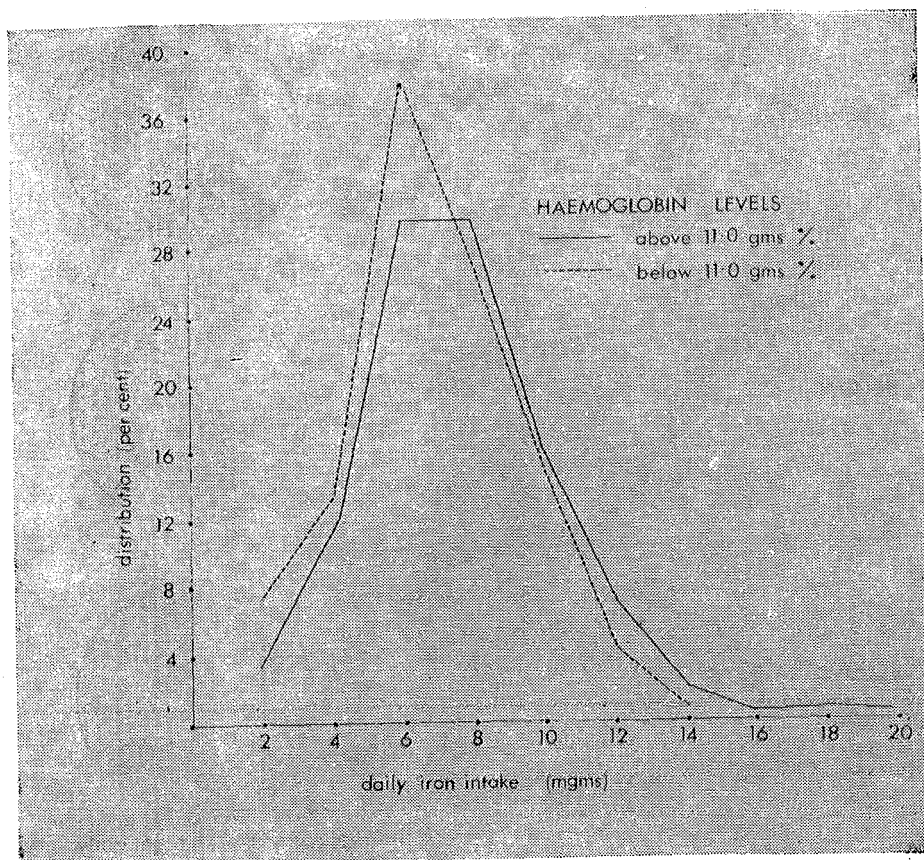


FIG. 6 : Haemoglobin values above and below 11.0 gm. per 100 ml. in relation to daily iron intake.



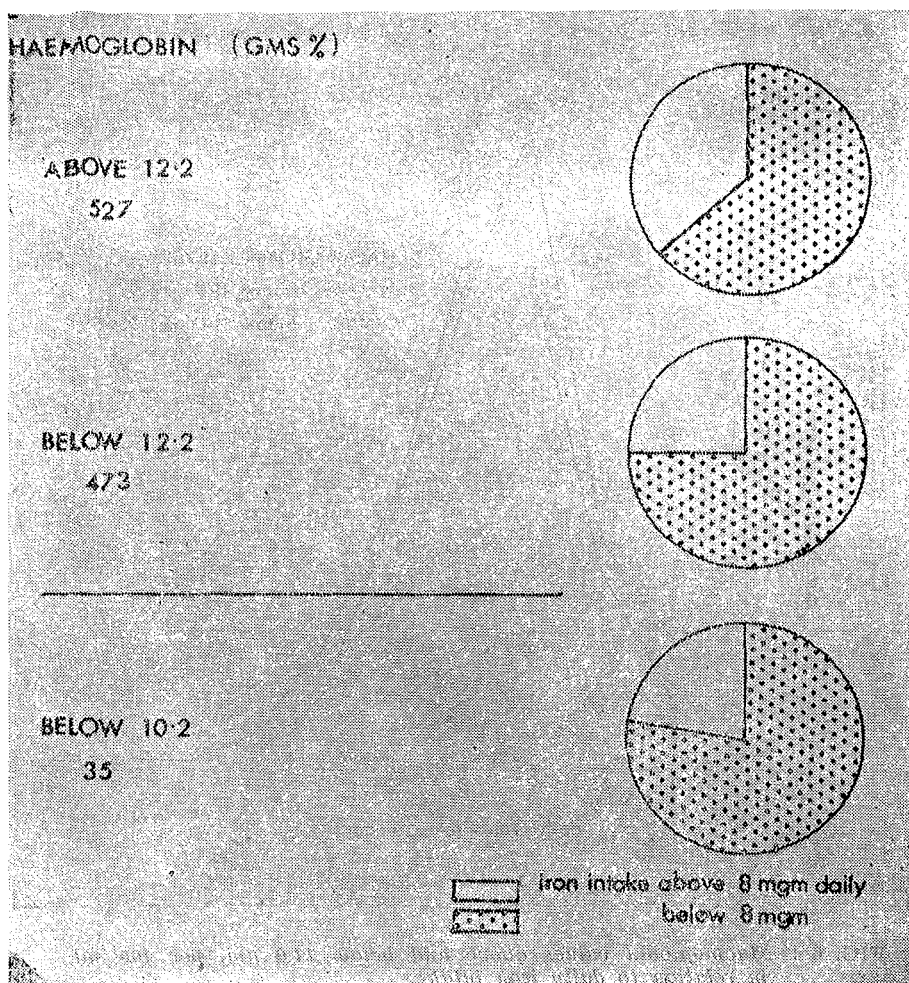
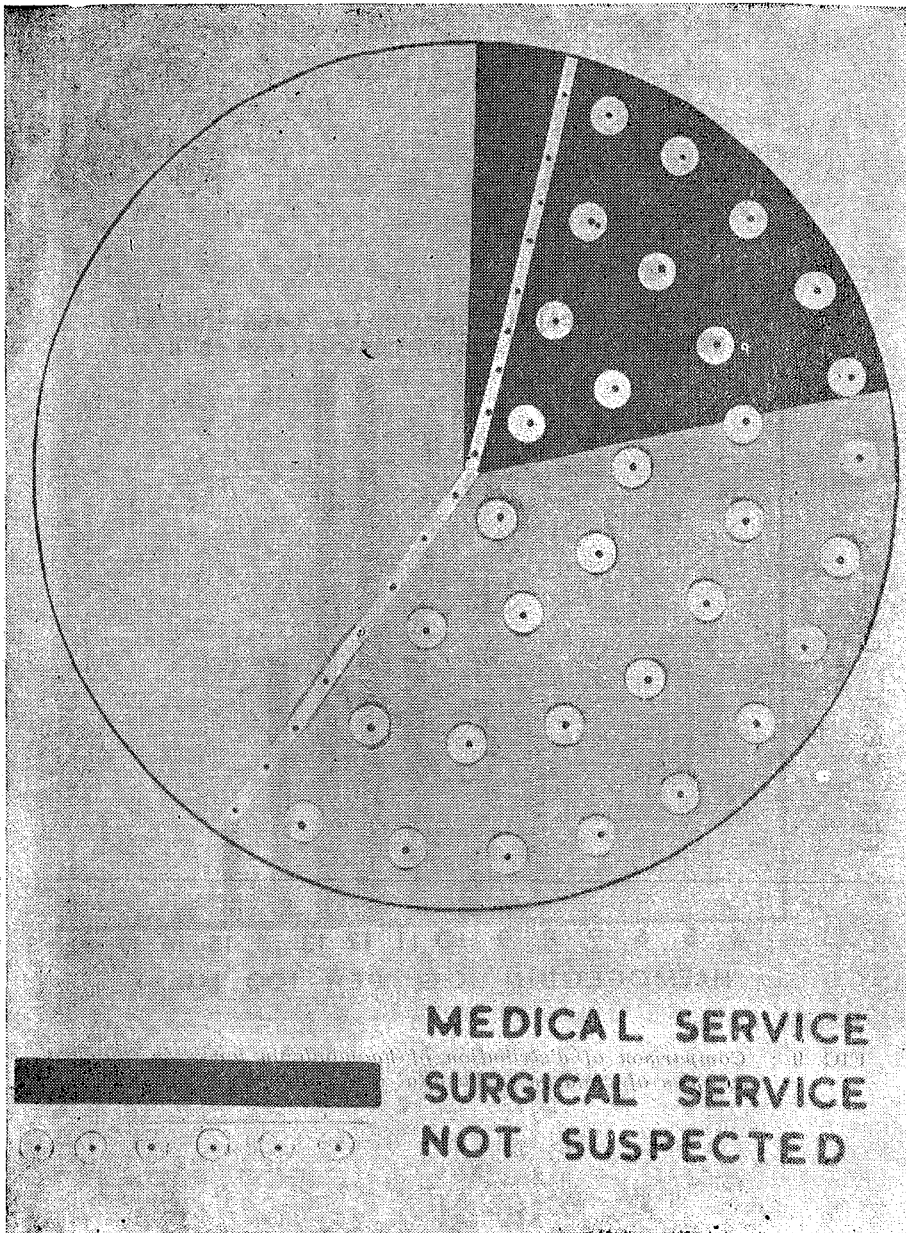


FIG. 7 : Haemoglobin value in relation to daily iron intake : open areas, above 8 mg./day; dotted areas, below 8 mg./day.



**FIG. 8 :** Admission rate to medical and surgical services in indicated. The 2 services have equal number of patients at the Royal Alexandra Hospital for Children.

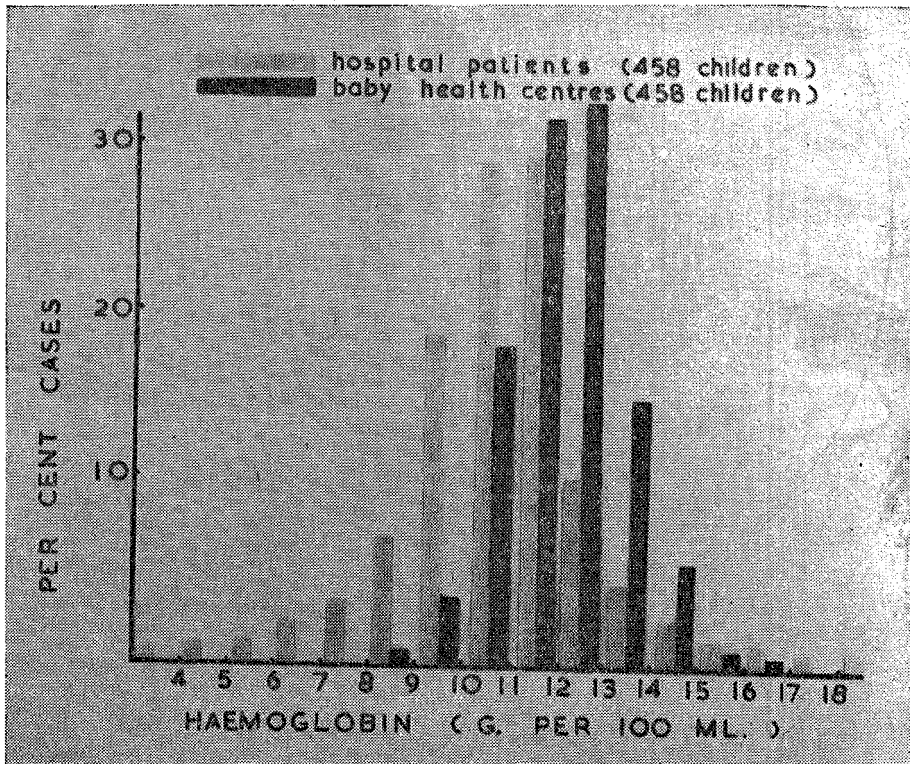


FIG. 9 : Comparison of distribution of haemoglobin levels in matched samples of children in hospital and baby health centres.

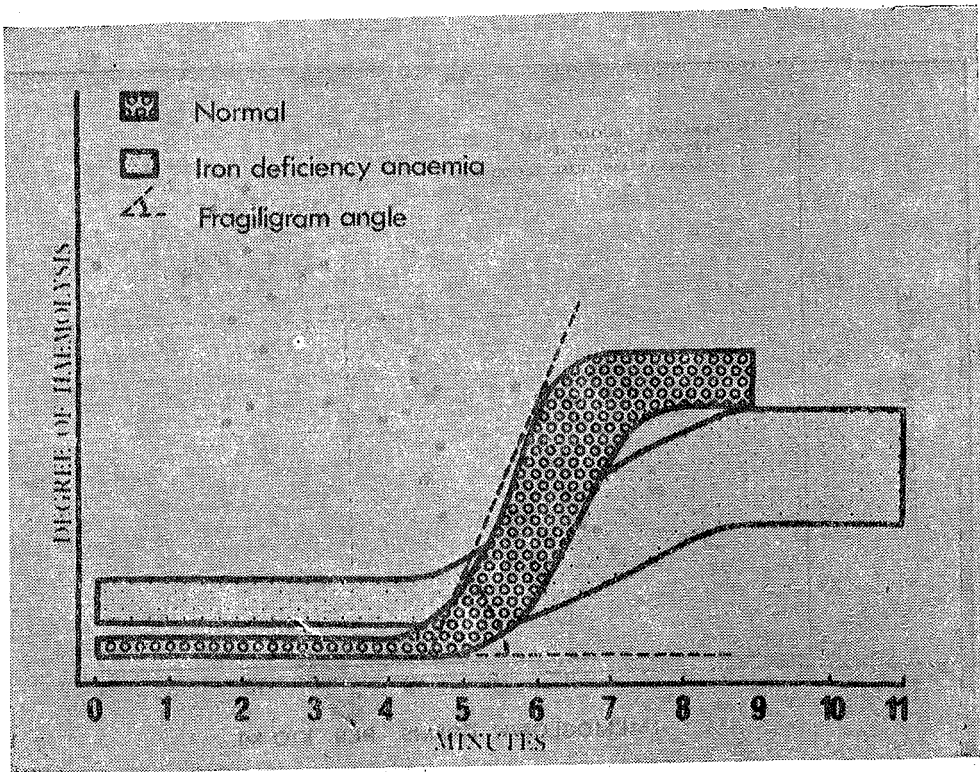


FIG. 10 : Fragiligram profiles of normal children compared to those with iron deficiency anaemia. Fragiligram angles are determined by drawing a tangent along the straight section of the recorded graph and measuring the tangent abscissa angle.

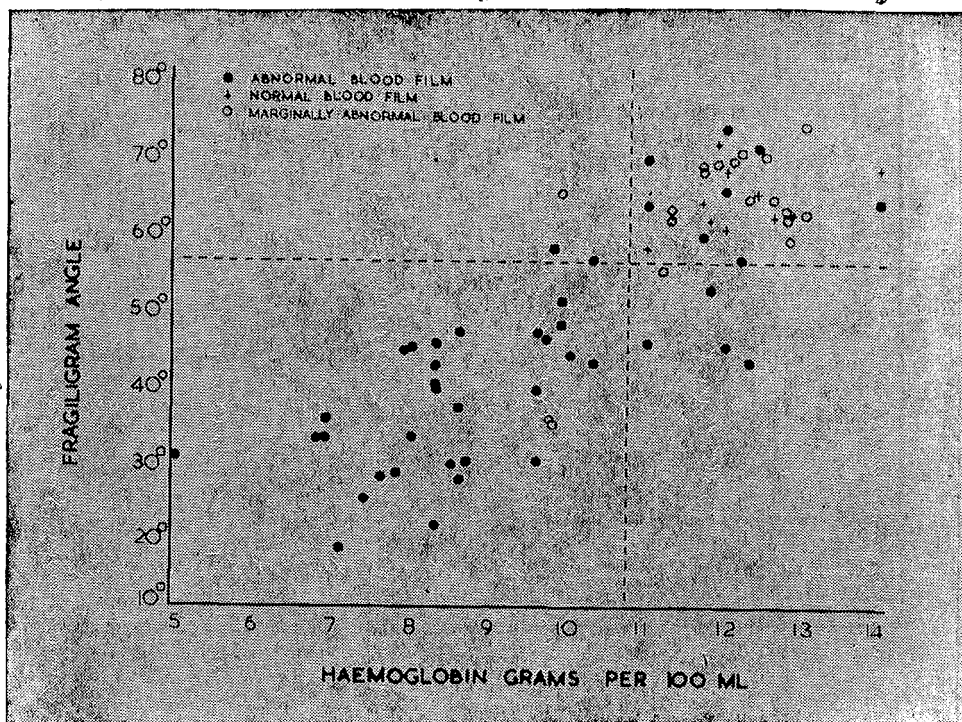


FIG. 11: Plot of fragiligram angles against haemoglobin values and assessment of blood films.