IRON DEFICIENCY ANAEMIA IN ADULTS: PREVALENCE AND PREVENTION

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Prevalence Studies

Between 1930 and 1940 Davidson and his colleagues studied the prevalence of anaemia in Aberdeen. The subjects of this early work were not random samples of the population but volunteers from the poorest classes in the community. It is difficult to compare their results with those of later workers because of selection and differences in methods of haemoglobinometry and in definition of anaemia but they did demonstrate that iron deficiency anaemia was common in adult women in the poorer classes in North East Scotland (Davidson, Fullerton, Howie, Croll, Orr and Godden, 1933; Davidson and Fullerton, 1935). When anaemia was defined as a haemoglobin of less than 85%, (Haldane) 16% of adolescent girls and no less than 45% of adult women were found to be anæmic. Anaemia was rare in men and usually associated with organic disease. Thus age and sex were clearly defined as important etiological factors. Davidson and Fullerton (1938) concluded that poor dietary intake of iron, together with the demands of reproductive life, led to the high prevalence of iron deficiency anaemia in the women they investigated. A later study in Edinburgh gave similar results (Davidson, Donaldson, Lindsay and McSorley, 1943).

In 1943 the Medical Research Council carried out a detailed study of haemoglobin levels in Great Britain (Medical Research Council, 1945). It was not possible to examine a true random sample of the population but testing was planned to cover as many social groups as possible at all ages. Sixteen thousand individuals were tested and detailed questionnaires were completed providing data on health, diet, occupation, marital state and social condition. Haemoglobin levels as a whole were rather higher than the previous Aberdeen figures, which may have been due to the different methods of selection. It was concluded that haemoglobin levels were low in a considerable proportion of subjects, especially in children below the age of five years, pregnant women and persons at the lower economic levels, and that this could be prevented by raising the dietary intake of iron.

Apart from some studies in adolescents and the elderly, few general surveys were done after the war until Kilpatrick and Hardisty (1961) studied a random sample of an industrial community, the Rhondda Fach in South Wales. Their population included 300 miners and ex-miners, 300 non-miners, aged between 35-64 years, and 200 postmenopausal women between 55-64 years. They found the mean haemoglobin concentration of the men to be 14.9 g./100 ml. and that of the women to be 13.3 g./100 ml. Three per cent of the men, 18 in number, were found to have a haemoglobin of 12.5 g./100 ml. or less, and of these 14 had a mean corpuscular haemoglobin concentration (MCHC) of 31% or less. Fourteen per cent of the women, 25 in number, had a haemoglobin concentration of 12.0 g./100 ml. or less and 22 of them had an MCHC of 31% or below. Iron deficiency was thus by far the commonest cause of anaemia in this community. Although there was no clear fall in haemoglobin concentration with age there was a progressive fall of MCHC with age. Kilpatrick (1961) studied a sample of people over the age of 15 years living in Wensleydale, an agricultural area in the northern part of Yorkshire. The results of examining 182 men and 230 women in this district are summarised in Table 1. The criteria of anaemia are those used in the Rhondda survey.
TABLE 1
PREVALENCE OF ANAEMIA IN WENSLEYDALE (182 men; 230 women)

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>15—24</td>
<td>3.4%</td>
<td>28.0%</td>
</tr>
<tr>
<td>25—34</td>
<td>0.0%</td>
<td>23.0%</td>
</tr>
<tr>
<td>35—44</td>
<td>2.9%</td>
<td>24.0%</td>
</tr>
<tr>
<td>45—54</td>
<td>8.3%</td>
<td>12.0%</td>
</tr>
<tr>
<td>55—64</td>
<td>8.0%</td>
<td>12.5%</td>
</tr>
<tr>
<td>65—74</td>
<td>20.0%</td>
<td>21.0%</td>
</tr>
<tr>
<td>75</td>
<td>25.0%</td>
<td>21.0%</td>
</tr>
</tbody>
</table>

Fry (1961) reported anaemia cases in his general practice in South London seen over a five-year period. His patients were investigated only if they presented clinical signs of anaemia. He found an annual incidence of 17.5 per thousand, but had he examined a sample of his practice this figure would undoubtedly have been higher. He confirmed that iron deficiency anaemia was the commonest type.

Of surveys of selected age-groups, there have been several to determine the prevalence of anaemia in young men. Leonard (1954) using the copper sulphate method for estimating haemoglobin concentration examined 4,221 recruits aged 18 to 20 entering the Royal Air Force. Fifty were found to be undoubtedly anaemic as they had a haemoglobin concentration of less than 12.0 g./100 ml. He examined these 50 men thoroughly and found that 49 had iron deficiency anaemia. In two of these men the anaemia was presumed to be due to bleeding from the gastro-intestinal tract but in the remaining 47, no obvious cause for the anaemia was discovered and he regarded them as having idiopathic iron deficiency. Brumfit (1960) examined 2,000 Royal Army Medical Corps recruits aged 17 to 21 years and found 1.1% to have a haemoglobin concentration of less than 12.0 g./100 ml. He compared these recruits with 1,000 trained men of an airborne division and in these found only 0.1% to have a haemoglobin concentration of less than 12.0 g./100 ml. Elwood, Withey and Kilpatrick (1964), in a study of 505 boys and 621 girls aged 14 years in 9 secondary modern schools in Cardiff, found that 12 boys (2.4%) and 25 girls (4.0%) had haemoglobin concentrations of 12.5 g./100 ml. or less and 12.0 g./100 ml. or less respectively. In children of this age in Cardiff anaemia was thus not a serious problem.

So far as the elderly are concerned Hobson and Blackburn (1953) took a 1 in 30 random sample from the food office register in Sheffield of men and women who had reached pensionable age (65 for men and 60 for women).

Only those living alone or with their spouses were selected. There were 177 men aged between 66 and 85 and 246 women aged between 61 and 87; the mean haemoglobin concentrations of these two groups were 14.4 g./100 ml. and 13.8 g./100 ml. respectively. They considered any person with a haemoglobin below 11.7 g./100 ml. to be anaemic and they found 9 men (5.1%) and 16 women (6.5%) who met this criterion. Of these, 8 men and 13 women were iron deficient. If 12.5 g./100 ml. were to be taken as the criterion then 23 men and 37 women were anaemic. Parsons, Withey and Kilpatrick (1965) examined a random sample of elderly people in Swansea consisting of 208 individuals over the age of 65. Ten men (12%) had a haemoglobin concentration less than 12.5 g./100 ml. and 18 women (15.7%) less than 12.0 g./100 ml. In 8 men and 13 women the MCHC was less than 31% indicating iron deficiency.

Semmence examined 256 people in general practice (101 men and 155 women); of these, 5 men (5%) and 20 women (13%) had haemoglobin concentrations below 12.0 g./100 ml. In all 5 men a cause was found; 2 had carcinoma, 1 leukaemia, 1 pernicious anaemia and 1 bleeding duodenal ulcer. In the women a poor diet was considered to be an important factor. Women living alone had significantly lower haemoglobin concentrations than those not living alone, but this did not apply to the men. Hobson and Blackburn (1953), on the other hand, found the haemoglobin concentration to be lower in men living alone.

Iron Metabolism

In the normal non-anaemic adult about 3 g. of iron is present in the body as circulating haemoglobin. About 1 g. is present either as haemosiderin or ferritin and this functions as an iron store which can be mobilised for haem synthesis if necessary. Smaller amounts of iron are found in compounds serving specialised functions such as myoglobin or tissue enzymes.

The newborn baby derives about 300-400 mg. of iron from its mother by transfer across the placenta, most of this taking place in the later weeks of pregnancy. All the additional iron necessary for the immense demands of haemopoiesis in infancy and childhood, together with that necessary to build up adequate reserves for adult life, must be derived from the diet and it seems clear that the amount obtained in this way is not always adequate. Even when adolescence is reached with enough iron to maintain a normal haemoglobin
level, storage iron may be depleted. The maintenance of a normal haemoglobin concentration in adult life depends on the adequacy of the total body iron pool and this in turn depends on a favourable balance between intake and loss from the pool.

Hypochromic anaemia in this country is almost invariably due to iron deficiency. It is characterised by a reduction in the number of circulating red cells together with a reduction in their haemoglobin content. In addition to a haemoglobin concentration below normal the MCHC is decreased and the blood film shows the presence of pale mis-shapen red cells. Fry (1961) found that the red cells in 84% of anaemic men and 95% of anaemic women in his Beckenham practice were hypochromic. In the Rhondda Fach survey carried out by Kilpatrick and Hardisty (1961) 18 anaemic men and 25 women were found of whom 14 men and 22 women had an MCHC of 31% or less. Serum iron concentration is low in iron-deficiency anaemia and there is an increased amount of iron binding protein. The bone marrow is usually devoid of haemosiderin and the developing red cells are poorly formed.

The early stages of iron deficiency may not show all these phenomena. Reduction of serum iron levels and a low saturation of the iron-binding protein may be found before the haemoglobin level has fallen below accepted normal limits and reduced marrow haemosiderin may also be a feature of pre-anaemic iron deficiency. It has been suggested that this sideropenic state may, itself, give rise to symptoms which can be corrected by the administration of iron. The relationship of the symptoms of anaemia to haemoglobin level has never been fully investigated and this we are now attempting to do in a controlled manner by means of a questionnaire administered before and after treatment with iron. Reduced activity of several iron-containing enzymes in the tissues has been demonstrated in iron-deficient animals by Beutler and his co-workers and it appears that this may occur before anaemia is manifest (Beutler, 1964). The only similar observation in man is a deficiency of cytochrome oxidase activity in the buccal mucosa of some iron-deficient patients (Jacobs, 1961). Whether the symptoms of the sideropenic state are related to enzyme deficiencies is debatable. Beutler, Larsh and Gurney (1960) carried out a well controlled double-blind trial of iron therapy in non-anaemic women suffering from chronic fatigue and found that iron had a significant effect in relieving symptoms in those with evidence of sideropenia, such as a low serum iron concentration or a reduction in marrow haemosiderin.

Anaemia develops when the amount of iron available for haemoglobin in the bone marrow is inadequate and this only occurs when the storage iron of the body has been depleted. There is some information on the iron balance of normal subjects but a great deal more data is required. Excretion of non-haemoglobin iron from the body is small and loss from urine, faeces and skin has been estimated at about 0.5 to 1 mg. per day (Moore, 1964). In women iron loss through menstruation varies considerably between individuals but is about 10 to 40 mg. per month. Iron intake depends on the amount in the diet and the proportion absorbed. The National Food Survey Committee (1963) showed that the mean daily iron intake in persons from different types of household varied from 11 to 18 mg. per day and individual variations must presumably be much greater than this. The proportion of food iron absorbed is 5 to 15% to normal subjects, the mean being 6.5% (Moore, 1964). These figures indicate that about 0.5 to 2.7 mg. iron per day are being added to the body pool while 0.5 to 1 mg. per day in men and 0.8 to 2.3 mg. per day in women is being lost. These approximations only apply to normal persons in whom there is no special demand for iron, either physiological or pathological.

Although theoretical considerations indicate that the common iron-deficiency anaemia in adults must be due to inadequacy of iron stores resulting from a negative iron balance the precise aetiology remains obscure. It is usually assumed that blood loss is an important factor causing iron depletion but the loss is often difficult to measure or even to detect. Bannerman, Beveridge and Witts (1964) have shown that even when occult bleeding from the gastrointestinal tract is detected it is common for no cause to be discovered. Fry (1961) could find no obvious reason for iron deficiency in 53% of men with anaemia and in 87% of anaemic women in his general practice. Only in 22% of anaemic men and in 7% of anaemic women was there a clear source of blood loss such as peptic ulceration or carcinoma. Poor diet, excessive menstruation and repeated pregnancies are often suggested as causes of iron deficiency in women but although these factors are undoubtedly important precise data are not usually obtainable in individual cases.
Information about iron in the diet is usually derived from questionnaire surveys rather than by actual analyses, and the validity of such surveys has been criticised (Lambert, 1964). There is no certainty that the diets recorded by the National Food Survey (1963) in this country represent the normal household diet when a survey is not being conducted; it is well recognised that people are unreliable when questioned about their dietary habits. Despite these qualifications some interesting facts emerge from the survey. The average consumption of iron per person per day in the United Kingdom is 14.2 mg, and this shows little variation between geographical regions. Dietary iron intake is highest in childless households but in households with children the average intake falls as the number of children increases. In families with four or more children the average daily intake is only 11.2 mg. This is found in all social classes.

A number of factors influence the amount of iron absorbed from the food. Studies of food containing radioactive iron show a different degree of availability from different foodstuffs (Moore, 1964). Absorption is decreased when the meal has a large bulk or when phytates or phosphates are present in large quantities, and achlorhydria may have a significant effect in reducing absorption (Goldberg, Lochhead and Dagg, 1963). The proportion of iron absorbed from the intestine is increased considerably in subjects with iron deficiency anaemia by a homeostatic mechanism the nature of which is not fully understood.

The evaluation of iron loss from the body by menstruation is of use only if precise measurements are made. The subjective assessment of menstrual loss by women is notoriously unreliable even when questioning is extended to the number of pads used, presence of clots etc. A recent survey of sanitary towels (Consumer Association, 1964) showed that different brands vary in their power to absorb blood from 0.05 fl. oz. (1.4 ml.) to 2.5 fl. oz. (71 ml.) per towel. Thus estimation of the number used is of little value. In our hospital, patients referred to the gynaecology department because of menorrhagia have been found to lose as little as 25 ml. of blood during a ‘heavy’ period while some patients with severe iron deficiency anaemia have lost up to 200 ml. of blood during a ‘normal’ period. Direct measurement of menstrual blood loss in 100 normal women by Barer and Fowler (1936) gave a range of 6.5-179 ml. per period (mean loss 50 ml.).

Twenty one subjects who were members of a hospital staff gave a range of 10-55 ml. (mean 25 ml.) (Baldwin, Whalley and Pritchard, 1961). Our own measurements on 17 healthy members of the hospital staff aged 21 to 40 years gave a range of 4-87 ml. per period (mean 35 ml.).

We have studied a number of women with iron deficiency anaemia and excessive menstrual losses of as much as 600 ml. per period have been found in some of them. We have found no case where menorrhagia has been materially improved by treatment with iron, contrary to the findings of Taymor, Sturgis and Yahia, (1964) who suggest that menorrhagia may be due specifically to iron deficiency. When menorrhagia with no obvious gynaecological cause persists long-term treatment with iron may be necessary to maintain iron balance and in extreme cases hysterectomy may be unavoidable.

Figure 1 shows the amount of blood lost during menstruation by 151 normal women. The data have been derived from Barer and Fowler, (1936); Millis, (1951); Baldwin and others, (1961); and Jacobs (unpublished). The figures for daily iron requirements assume a loss of iron from the body of 1 mg. per day, apart from menstruation, and 10% iron absorption from the diet. Thirty-eight per cent of these women have a menstrual loss of 40 ml. or more which is equivalent to 0.6 mg. iron per day. Most of them will develop iron deficiency with or without anaemia because only a small number will have the required dietary iron intake of over 16 mg. per day. Some auto-
matic compensation will occur because an increasing proportion of the dietary iron will be absorbed from the gut as iron deficiency develops. Nevertheless, iron balance in these women will be precarious and they will tend to be in a state of latent or overt iron deficiency.

The intermittent removal of iron from the body through the process of pregnancy tends to reduce body stores. This is illustrated in Table 2. The iron conserved through amenorrhoea does not usually compensate for the amount lost to the foetus while placental blood together with bleeding during labour also take their toll. The effect of this is cumulative with repeated pregnancies.

In an individual case of iron deficiency anaemia it may not be clear, even after detailed investigations, why a patient is in negative iron balance but it seems likely that both inadequate intake and excessive loss are important factors. Unless a specific bleeding lesion is found there is little that can be done to prevent the marginal negative balance found so commonly in women. The rational measure would be to increase iron intake by an appropriate amount, but this would not, of course, be the same for each individual and could only be determined by a tedious process of trial and error in each case. A more practicable approach to the treatment of "idiopathic" iron deficiency in women is to provide all such women with a regular supplement of iron the size of which should enable most of them to maintain a positive iron balance. A total daily iron intake of 24 mg. would bring this about in all women whose menstrual loss is less than 100 ml. per month (Fig. 1) and this could be achieved by a supplement of 10-15 mg. iron daily.

**Treatment**

In men, iron deficiency anaemia is commonly associated with serious organic disease and treatment with iron should not be started until a diagnosis has been made.

It is probably impracticable to submit all anemic women to detailed investigations; to do so would be to overload existing pathology laboratories and radiology departments. Specific enquiries should be made regarding such things as weight loss, dyspepsia, colour of stools, aspirin consumption and blood loss other than menstruation. Information about menstrual blood loss should be critically assessed with a view to detecting gynaecological abnormality rather than evaluating the amount of blood lost. If the amount of blood lost seems grossly excessive then further investigation of this will be necessary. In the great majority of cases there will be no clue to abnormal blood loss and the anaemia should be treated with an oral iron preparation. The effectiveness of the treatment should be judged by periodic haemoglobin estimations and a final haemoglobin estimation should be carried out four months after the cessation of treatment so that a relapse can be detected.

Those women who have an inadequate response to oral iron or a relapse after four months should be investigated more thoroughly. Occult intestinal bleeding, in particular, should be looked for (Bedford and Wollner, 1958). The patient should not be discharged from medical care until a satisfactory reason for the iron deficiency has been discovered and, if possible, treated.

**Prevention**

The occurrence of low haemoglobin levels in the community presumably indicates a form of preventable ill-health. The form of this ill health is, however, difficult to define. The symptoms of anaemia are vague and do not correlate well with haemoglobin levels. There is evidence that women with normal haemoglobin levels may benefit from an increased iron intake (Beutler and others, 1960). If this is so general prophylactic measures would benefit a greater part of the population than merely those with overt anaemia. In Cardiff an attempt is being made to measure the physical disability caused by iron deficiency anaemia and to discover whether a similar disability occurs in non-anæmic women.

There are a number of possible ways in which the incidence of iron deficiency could be reduced. Probably none is fully utilised at the present time. The administration of medicinal iron to especially vulnerable groups is one such measure. Most authorities agree that because iron-deficiency anaemia is so common in pregnancy iron should be given to pregnant women as a routine procedure. This should be carried out with the same enthusiasm as urine examinations, or blood pressure measure-

**TABLE 2**

<table>
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<tr>
<th>Iron Balance of Normal Pregnancy</th>
<th>Debit (mg.)</th>
<th>Credit (mg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>To Foetus</td>
<td>300—500</td>
<td></td>
</tr>
<tr>
<td>Placenta + cord</td>
<td>34—170</td>
<td></td>
</tr>
<tr>
<td>Blood loss at delivery</td>
<td>100—250</td>
<td></td>
</tr>
<tr>
<td>6 months lactation</td>
<td>100—180</td>
<td></td>
</tr>
<tr>
<td>15 months amenorrhoea</td>
<td></td>
<td>135—585</td>
</tr>
<tr>
<td>Net Loss</td>
<td>0—965 mg.</td>
<td></td>
</tr>
</tbody>
</table>
ments, and continued throughout pregnancy. Iron should be given to all pregnant women, whether they appear anaemic or not. The satisfactory results of this have been well demonstrated by Kerr and Davidson (1958). Other special subjects likely to develop iron-deficiency anaemia should also be given regular supplements of iron; patients who have undergone partial gastrectomy for example form a particularly vulnerable group.

The highest incidence of anaemia is found in women during the reproductive period of life. Studies of 14-year-old schoolgirls in Cardiff have shown that there is very little anaemia at this age (Elwood and others, 1964) but subsequent work indicates that anaemia becomes a problem during adolescence. A prospective study is being carried out to find the value of regular iron supplements in preventing the anaemia of adolescence. A cohort of 14-year-old schoolgirls are all receiving a daily tablet and will be followed up for 5 years. They have been randomly allocated to three groups. The first group receive 30 mg. iron daily, the second 10 mg. iron daily and the third a placebo. Co-operation in actually taking the tablets is checked by administration of the correct number of tablets, by random home visiting and urine testing for a riboflavin tracer present in all tablets. The incidence of anaemia in the three groups will be measured during the investigation and at the end of five years.

A more satisfactory way of administering prophylactic iron to a large population is by adding it, in adequate amounts, to a universally consumed food stuff. The most suitable food for this purpose is bread and existing legislation does in fact specify that white flour must contain 1.65 mg. iron per 100 g. Flour is normally fortified with ferrum redactum to meet this legal requirement. An investigation carried out by Elwood (1963) indicates that not only does ferrum redactum appear to be poorly absorbed from bread but increasing the normal amount nearly forty-fold has little effect on its efficiency. Present methods of fortification of bread with iron seem to be of doubtful value and further studies of iron-enriched bread are being carried out to determine what compounds are most satisfactorily absorbed from the intestine after being subjected to the baking process.

If prevention of anaemia is not always possible the early recognition of cases is necessary to prevent chronic ill-health. Clinical examination of patients is not enough to exclude the diagnosis of anaemia. There is a poor correlation between the doctors assessment of pallor and the actual haemoglobin level (McAlpine, Douglas and Robb, 1957). Many patients with chronic iron deficiency are called neurotic and treated as such. The only satisfactory screening test for anaemia is the haemoglobin estimation and the prevalence of anaemia at present is so high that as large a population as possible should be screened. There are several means of arranging this. Haemoglobin estimations could be carried out by the general practitioner when patients are seen in the surgery. In the past this has meant either the possession of expensive equipment requiring calibration and constant checking or the use of cheaper but inaccurate devices for haemoglobinometry. The present availability of a simple battery-operated apparatus for accurate haemoglobin estimations using a drop of whole blood means that accurate results can be obtained in any surroundings and without a laboratory. Failing this many pathology departments have an "open door" policy with regard to blood tests requested by general practitioners. This should be fully utilised wherever it is available.

There is evidence that mass screening for anaemia reveals a substantial amount of unsuspected disease. Clinics for this purpose, or combined with other screening procedures such as urine testing, cervical cytology or audiometry, could well be established by local authorities. It is almost certain that a higher proportion of positive findings would emerge from such a clinic than in mass miniature radiography units at present. Multi-screening clinics including haemoglobin estimations have been employed recently in Middlesex, (Maddison, 1962), and Rotherham, (Donaldson, 1965). In the former the clinic remained open all the time but in the latter a concentrated publicity campaign resulted in a large number of people being tested during one week.

It is important that case finding by haemoglobin estimation does not lead to the indiscriminate therapeutic use of iron without the proper diagnosis and follow-up that has already been mentioned. The minimum evidence on which to base the diagnosis of iron deficiency anaemia includes either a typical blood film or a low MCHC. Other forms of anaemia requiring urgent treatment, such as pernicious anaemia, will be missed if the preliminary screening test is also used, by itself, for diagnosis.
Summary
Iron deficiency anaemia is common in Great Britain. It is especially common in young women and in most cases is due to an imbalance between iron intake and iron loss rather than to any specific pathological lesion. The prevalence of anaemia could be reduced by prophylactic measures and active case finding.

We are indebted to Professor H. Scarborough for his valuable criticism.

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