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IRON DEFICIENCY ANAEMIA

Report of a Study Group

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GENEVA

1959

STUDY GROUP ON IRON DEFICIENCY ANAEMIA

Geneva, 29 September-4 October 1958

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IRON DEFICIENCY ANAEMIA

Report of a Study Group

The WHO Study Group on Iron Deficiency Anaemia met in Geneva from 29 September to 4 October 1958 to discuss the present status of the problem from the point of view of etiology, evaluation and prevention.

Professor Richard V. Vilter was unanimously elected Chairman.

1. Introduction

General considerations

Haemoglobin surveys carried out in various regions show that anaemia constitutes a public health problem of considerable importance in the under-developed and tropical areas of the world. In some countries, for example, India and Mauritius, it seems probable that the high rates of maternal mortality are influenced by the prevalence of anaemia. Although common in the adult male, these anaemias affect particularly certain vulnerable groups, namely, expectant and nursing mothers, infants and young children. Malnutrition and chronic blood loss are usually underlying factors. There is reason to believe that anaemia impairs health and working capacity and leads to economic loss, but there is no precise information as to the extent to which it contributes to morbidity in a community.

In the majority of cases, supplementation of diet with iron alone gives a prompt response, but in some, other factors, such as protein, seem to be necessary in order to bring about a complete recovery.

Recent work carried out in India, Africa and Central and South America shows that iron deficiency anaemia is the most common type in these countries, and that marked improvement is readily induced by the oral administration of iron alone. In India, dietary analyses of food consumed by anaemic persons indicate that the intake of iron is within or above the recommended allowance, and that the widespread anaemia may be associated with other factors such as excessive losses and/or poor absorption of iron.

In Mauritius also it has been shown that anaemia, because of its extent and severity, constitutes a major public health problem. Investigations indicate that 50% or more of certain groups of the population may be affected, and in 95% of these patients the anaemia is the iron-deficient type and responds readily, and in most cases fully, to orally-administered ferrous sulfate.

A limited number of studies designed to determine the relative prevalence of anaemias of different types in the general population have been made. These suggest that the great majority are of the iron-deficient type and confirm the results of therapeutic trials with iron. However, there is need for more work along these lines in different countries.

Definition of iron deficiency anaemia

The terms "iron deficiency anaemia" or "iron-deficient type of anaemia" used in this report refer to an anaemia brought about primarily by deficiency of iron in the body, characterized by progression from a normocytic normochromic blood picture to one that is microcytic, hypochromic, and responds to treatment with iron.

2. Haematological Values for Detection of Anaemias

To detect and evaluate the anaemia problem of a community, it is necessary to have standards of reference, even if they be somewhat arbitrary, so that not only the severe cases, but also the less obvious ones, may be discovered. Such standards are also of considerable importance for the comparison of surveys done in different parts of the world. The Group reviewed the large body of haematological data derived from studies of apparently normal persons throughout the world, and from these data and the personal observations of the Group members, haemoglobin values, which can be considered as the lower limits of normal for the purpose of determining the presence or absence of anaemia in nutritional surveys, have been selected (see Table I). They are intended to act as general standards of reference for the investigator and to indicate that lower values than these are suggestive of anaemia. In individuals, however, higher

TABLE I. HAEMOGLOBIN VALUES BELOW WHICH ANAEMIA CAN BE CONSIDERED TO EXIST, AND ASSOCIATED HAEMATOLOGICAL VALUES

Years	Sex	Hb g/100 ml	RBC M/mm ³	PCV %	MCH mm ³	MCHC %
0.6- 4		10.8	4.1	32	79	33
5- 9		11.5	4.1	33	80	34
10-14		12.5	4.5	37	82	34
Adults	Male	14	4.7	42	87	34
	Female	12	4.0	35	87	34
	Pregnant female	10	3.3	29	87	34

values of one or more of these may be compatible with anaemia. This is so particularly in the case of the megaloblastic anaemias which may, at times, be characterized by relatively high haemoglobin levels.

The Group considers that optimum haematological values in tropical and temperate zones are the same. Proper upward correction for high altitudes must be made. The Group recognizes also that, in the field, it is often impracticable to determine packed-cell volume and red-blood-cell counts. However, these are included in the table in the hope that as time passes more studies can encompass such parameters and that volume indices will be computed, even in field surveys.

The cyanmethaemoglobin method, the oxyhaemoglobin method as measured by the Gray-Wedge photometer, and the acid haematin method as measured by the Sahli technique, are acceptable procedures for haemoglobin determination and will give comparable results when standardized.

3. Determination of Prevalence of Iron Deficiency Anaemia

The value of statistics on the extent of anaemia in any area will depend upon the accuracy of the procedures used. Those described below will give dependable results.

For field work where limited personnel, space and equipment are available, four simple procedures can be used—haemoglobin estimation, haematocrit determination, erythrocyte count, and stained blood-smear examination. Of these four procedures, the Group considers that determination of haemoglobin and haematocrit are the most objective and acceptable; erythrocyte count is subject to considerable error and is of limited value; and examination of a stained blood-smear provides much useful information, but requires considerable skill and equipment.

Measurement of haemoglobin

Methods for measuring haemoglobin vary widely and those employing photoelectric colorimetry, as in the cyanmethaemoglobin method, are objective and reliable, but the expense involved may make such procedures impracticable. Simple methods for haemoglobin surveys, where trained personnel and equipment are not available, resolve themselves into the oxyhaemoglobin method using the Gray-Wedge photometer, the specific gravity method, and the Tallquist method. The Gray-Wedge photometer is suitable for field observations involving a large number of estimations, but must be standardized against solutions of known haemoglobin content. When this is not practicable, the Group considers that the specific gravity method offers certain advantages as it is inexpensive, easy to operate and of a high degree of accuracy. In surveys in which the primary aim is to

make a rapid assessment of the number of anaemic individuals below a selected haemoglobin level using the specific gravity method, it is only necessary to use one bottle of copper sulfate solution of suitable density. Where more than one range of values is required, two or three bottles may be used, thus facilitating grouping of the values into, for example, less than 6 g, less than 8 g, or less than 10 g of haemoglobin per 100 ml of blood. When even the specific gravity method cannot be employed, it may be necessary to resort to the Tallquist method, but it must be remembered that this is subject to considerable errors which render the results of highly questionable value.

Haematocrit

Haematocrit estimations carry a high degree of accuracy and are recommended by the Group for use when feasible. Where it is difficult to collect 1 ml or more of blood for estimating the haematocrit by the Wintrobe method, the Group considers the microhaematocrit method, using capillary blood, to be eminently suitable and almost as accurate as the Wintrobe method. If a standard centrifuge is not available, centrifuging of the microhaematocrit tubes can be carried out on a simple car-ventilator fan—run from the car battery—with a holder that will take eight micro-tubes. The diameter of the head should be 22.5 cm from the centre of the shaft to the bottom of the haematocrit tube; a speed of 3000 revolutions per minute is essential, and the tubes should be spun for 35 minutes.

In places where better facilities exist, procedures such as determination of the amount of haemosiderin in bone marrow, cytological evaluation of the bone marrow, determination of serum iron, electrophoretic behaviour of haemoglobin, and radioactive iron studies can be employed with benefit in elucidating the nature of the anaemia.

Sampling of population for anaemia survey

It is essential that proper sampling methods along modern concepts be employed, and that wherever possible those competent in such methods be consulted in the planning of surveys.

The size and manner of drawing the sample will depend upon the facilities available. In view of the fact that pregnant or lactating women, and infants and young children, are particularly vulnerable, a survey of the haematological picture in these groups provides a ready but weighted indication of the magnitude of the anaemia problem. These groups are readily accessible in areas where maternal and child welfare centres are already in existence. Additional information, obtained from a survey of a random sample of the adult male and female population, can be of great value in assessing the anaemia problem in the general population.

4. Iron Absorption

Dietary intake of iron varies from one area to another. In most tropical countries dietary iron is equal to or greater than that accepted for adequate diets in North America or Europe.

Iron absorption has been studied intensively for many years and there is extensive literature on most aspects of the subject.

Various techniques have been used to investigate iron absorption, among which are: (a) chemical balance experiments; (b) increase in serum iron observed during the six to eight hours after the oral ingestion of a large dose of iron; (c) radioiron measurements either by balance studies or by measurement of the amounts of radioiron incorporated in haemoglobin; and (d) the rise in haemoglobin after iron administration to anaemic subjects. Each of these methods has its limitations.

Probably the greatest amount of dietary iron is absorbed in the duodenum, and there is progressively less absorption in the distal portions of the gastro-intestinal tract. The amount of dietary iron absorbed depends on many factors, some of which are:

- (1) the reduction of ferric to ferrous iron;
- (2) intestinal dysfunction such as chronic diarrhoea and steatorrhoea;
- (3) quality and quantity of diet;
- (4) amount of iron in the diet;
- (5) infections;
- (6) state of the iron stores;
- (7) state of protein nutrition.

(1) The actual mechanisms by which reduction of the ferric to the ferrous balance state occurs are not completely understood; however, reduction may be facilitated by the simultaneous presence of large amounts of ascorbic acid and by -SH groups such as are contained in many proteins.

(2) Chronic diarrhoeal conditions frequently noted in tropical countries may decrease iron absorption because of the rapid passage of food through the intestinal tract, and change in the intestinal mucosa.

In steatorrhoea, such as may follow surgical procedures (e.g., subtotal gastrectomy, and short-circuiting operations), iron absorption may also be decreased.

(3) About 2%-10% of the iron present in most European and North American diets is absorbed by normal people, while patients with iron-deficiency anaemia in these areas absorb from 20% to 70%. Tropical diets, although not deficient in iron, are generally rich in bulky carbohydrate foods and have high phosphate and phytate with low calcium levels.

On such a diet, iron absorption may be impaired because of factors such as the combination of iron with phytates and phosphates to form insoluble salts. Results of recent work are conflicting, and knowledge of this aspect of iron absorption is inadequate.

(4) In normal people the percentage of iron absorption is higher at low levels than at high levels of intake, although the total amount absorbed may be greater in the latter case.

(5) Infection may interfere with the absorption of iron from the gastrointestinal tract. Of even greater importance is the diversion of iron from haemoglobin synthesis into areas of iron storage.

(6) The relation of the iron stores to absorption of dietary iron is complex. The mucosal-block theory, the validity of which has been questioned, suggests that high iron stores and high serum iron levels reduce the absorption of iron from the gastro-intestinal tract, while iron depletion has the opposite effect. However, in conditions characterized by high iron stores such as cytosiderosis, haemochromatosis, pernicious anaemia, various haemolytic states, and pyridoxine deficiency, there may be normal or increased absorption of iron. In iron deficiency anaemia, where the iron stores are depleted, as shown by diminution or absence of haemosiderin in the marrow, iron absorption is high. There is some indication that aberrant iron metabolism in patients with cytosiderosis may in part explain these conflicting situations.

(7) The part that protein nutrition plays in absorption of iron needs further investigation to determine its exact role.

5. Iron Loss

Technical difficulties involved in the determination of iron excretion are so great that only approximate values can be adjudged. Some of these difficulties have been overcome by the use of isotopes of iron. Current data, however, indicate that in temperate climates the total loss is 0.5-1.0 mg/day in faeces, urine and sweat. It is probable that significant amounts are lost in desquamated intestinal cells, though true excretion of iron by intestinal cells has not been found.

Pregnancy, and particularly repeated pregnancy, menorrhagia and lactation, constitute an important drain on iron reserves. When these occur before completion of growth and expansion of blood volume, the drain on iron stores may be more severe.

Of excessive losses of iron from the body in the tropics, those caused by hookworm infection are generally agreed to be the most important. Faecal iron losses in infected persons have been found to be as great as 10 mg per day, which undoubtedly can produce gross tissue iron-

depletion. However, recent work using erythrocytes labelled with Cr^{51} and Fe^{59} indicates that an average of 30% of the iron from haemoglobin eliminated into the intestine is reabsorbed. Blood losses per worm in *Necator americanus* infections appear to be much less than in those with *Ancylostoma duodenale*. Patients with severe hookworm infections may also have other nutritional deficiencies.

Evidence indicates that some iron is present in the sweat and particularly in cell-rich sweat, though there is controversy regarding the amounts which may be lost from the body by sweating. A wide divergence of results is apparent between those workers using chemical and those using radioactive techniques, the chemical methods indicating the larger losses. These iron losses may well be important in the causation of anaemia, more particularly among persons whose dietary iron content is low. Further work in this field is needed.

Since most tropical diets appear to be adequate in iron, the widespread anaemia in the tropics is probably associated with excessive losses or poor absorption.

Many co-existing factors may, it is clear, be present in tropical countries where iron deficiency anaemia is common, and it is impossible to assess with certainty the importance of each one of these.

6. Evaluation of Iron Requirements

The Study Group is in accord with the recommendations (see Table II) for dietary allowances of the Food and Nutrition Board of the National Research Council of the USA, for persons in a temperate climate who are

TABLE II. RECOMMENDED DAILY DIETARY IRON INTAKE FOR NORMALLY ACTIVE PERSONS IN A TEMPERATE CLIMATE *

	Iron (mg)		Iron (mg)
Men	10	Children 1- 3 years	7
Women :	12	4- 6 years	8
in pregnancy (second half)	15	7- 9 years	10
in lactation (850 ml daily)	15	10-12 years	12
Infants 0- 1 month	—	Boys 13-15 years	15
2- 6 months	5	16-19 years	15
7-12 months	7	Girls 13-15 years	15
		16-19 years	15

* After: United States of America, National Research Council, Food and Nutrition Board (1958) *Recommended dietary allowances*; Rev. 1958, Washington, D.C. (Publication No. 589)

normally active and healthy. These recommendations are not applicable to many tropical areas, where food habits are different from those of the USA and Europe, and where widespread intestinal parasitism results in varying degrees of blood loss. Analyses of some diets in the tropics indicate intakes of iron well in excess of the recommended allowances of the USA National Research Council, sometimes as high as 20-30 mg daily, and yet iron deficiency anaemia is endemic in these areas. Possible reasons for this will be found in the sections on iron absorption and iron loss (see pages 7-9). It is difficult to estimate the amount of iron required: (1) to provide from a tropical diet absorption of 1-2 mg of iron for normal daily needs; (2) to compensate for iron losses, particularly from the skin, in tropical climates; and (3) to make good the losses associated with intestinal parasitism. One can say only that the iron content of diets probably must be much higher than the allowances recommended for temperate zones.

It must be realized that there are two problems in evaluating iron requirements. One involves the determination of what is sufficient to meet the usual physiological stresses; the other, to provide additional iron to meet non-physiological losses. Where parasitism associated with blood loss is not endemic, increasing the food iron intake above existing levels may be sufficient to prevent iron deficiency anaemia. In areas where such parasitic infection is a major problem, it is probable that enrichment of food and inorganic iron will be necessary (see below).

7. Prevention and Treatment

Prevention

In the prevention of iron deficiency anaemia several approaches are possible: (1) the improvement in dietary habits; (2) the control of parasitism associated with blood loss; (3) the fortification of foods; and (4) the use of prophylactic iron, especially for vulnerable groups.

The Study Group recognizes that the etiology must be established. It has been pointed out that in *temperate* areas, adult men and non-menstruating women will rarely be found to have iron deficiency anaemia without a source of blood loss. In such cases, the eradication of the primary cause is mandatory.

In areas where iron deficiency anaemia is common, an increase of iron intake through unfortified natural foodstuffs is desirable. This alone will not overcome the anaemia, but it will help to maintain normal haemoglobin levels once other measures have brought about an elevation. It is no doubt difficult to change the dietary habits of peoples, but an educational programme carried out over many years in maternal and child health centres, schools and with other groups will produce results. Increasing the availability of iron-rich foods either by reducing their price and/or

increasing their production will also help to induce the people to eat them. Foods such as vegetables and pulses will be helpful because of their high content of iron and because they are good sources of other important nutrients.

Attention is drawn to the fact that in certain parts of the world cooking practices such as the use of iron containers or utensils contributes significantly to the iron content of the diet. On the other hand other practices, for instance, discarding the water in which food has been cooked, may result in large losses of iron.

Control or elimination of an underlying disease process such as hookworm infection is highly desirable. In this respect, emphasis should be put on the interruption of transmission of hookworm by sanitation of the environment and by prevention of contact with infective larvae, as well as by radical treatment of infected persons. These measures will require long periods of time to be effective.

The Study Group recommends the enrichment of foodstuffs with iron where iron deficiency anaemia is prevalent. Before such a programme is undertaken, however, it is essential that the anaemia problem be investigated by the methods previously recommended; that the level of existing dietary iron intake be assessed; and that a suitable vehicle be selected for enrichment. The food to be selected must be determined at the local level, and the choice will depend on the customs of the people. Rice and other cereals, milk powder, vegetable protein concentrates, fish meal, salt and occasionally sugar may be considered for fortification. Perhaps in certain areas where one universally-eaten foodstuff suitable for fortification does not exist, consideration must be given to fortification of several common foodstuffs. The choice of level of enrichment of iron will depend on the quantity of the foodstuff ordinarily consumed. The level should be so adjusted to afford at least partial protection of vulnerable groups without exposing others to the risk of excessive iron stores.

In Mauritius, an island in which there is a considerable amount of iron deficiency anaemia, the addition of 6.6 mg of elemental iron per day, administered in the form of ferrous sulfate ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$) on five days per week, resulted in significant increases in haemoglobin levels. In the Philippine Islands, rice enriched with iron to provide 12 mg of extra-elemental iron per day brought about a significant elevation of the haemoglobin levels. These experiences are given for the guidance of those who must decide on the amounts of iron to be used in enrichment programmes. It may be necessary to raise or lower these amounts, depending upon the circumstances extant in the area. At least, these amounts have not rendered the fortified foodstuffs unacceptable, nor is there any evidence that they are dangerous. While an enrichment programme is in progress, the haematological survey must be continued, in order to check on the success of the programme and to indicate when normal haemoglobin levels have

been attained. When this is achieved the amount of iron added may be reduced so that an essentially normal haemoglobin level can be maintained without excessive iron intake.

Each region will have to determine the proper amount of additional iron necessary for such maintenance. As long as blood loss due to continued parasitic infection persists, some degree of enrichment will be necessary to maintain the initial gains in health and productivity.

Pregnant women will derive great benefit from additional iron in the form of a three-grain (180-mg) tablet of ferrous sulfate containing 63 mg of elemental iron, or the equivalent of another iron compound, once daily throughout pregnancy and the first six months of lactation. Should the woman's haemoglobin be below 10 g per 100 ml of blood, additional iron should be prescribed. Such treatment will supply iron for both mother and infant, thus providing for the needs of those two groups in any community who have the highest requirements for iron.

It is unwise and uneconomical to give as a routine folic acid and vitamin B₁₂ to pregnant women, since the great majority of anaemias of pregnancy are of the iron-deficiency type in which these substances are not required. A great deal of money and time can be saved which can be better used improving the diagnostic facilities. Should an anaemic patient fail to respond to iron, a thorough investigation of the reasons should be made and appropriate measures should be instituted.

The Group recommends that a combination of the above approaches will help to prevent iron deficiency anaemia.

In conclusion, the Group wishes to reiterate that, in many countries in which iron deficiency is common, the diets are also deficient in other nutrients and that programmes should be directed to an over-all improvement of the quality of these diets, particularly with respect to protein.

Treatment

Ordinarily it is unwise to give iron by injection. Except under very special circumstances, ferrous sulfate (or equivalent iron compounds) given orally in doses of 1-2 g per day will effectively relieve iron deficiency anaemia without the addition of other haemopoietic substances.

8. Recommendations

(1) Only a limited number of observations have been made so far to determine the incidence of various types of anaemia in the general population. There is an urgent need for such studies to be made in several parts of the world where anaemia is common.

(2) Although there is ample circumstantial evidence indicating the close association of anaemia with high maternal and infant mortality, there is scanty information as to the precise extent to which anaemia contributes to mortality, morbidity, and impairment of working capacity. The Study Group recommends that a pilot project be undertaken designed to throw light on these important problems. For this purpose, an area where anaemia is prevalent may be selected, and the population may be divided into two comparable groups, to one of which an iron supplement is given while the other is used as a control. The manner of supplementation and the dose of iron supplement may be determined according to local conditions. A longitudinal study of the population in the two areas should provide valuable information on the effect of improvement of the anaemia on mortality, general health and working efficiency.

(3) So far as is known, there appears to be no appreciable deficiency of iron in most tropical diets. However, the type of diet consumed in most tropical countries, being rich in phosphates, phytates and bulk, and deficient in calcium, might reduce the absorption of available iron. The evidence on this subject is conflicting, and further critical work is necessary.

In tropical countries, where iron losses may be greater than in temperate areas, dermal losses in sweat and its contained cells may reach proportions which would upset the iron balance. Here again, further work is desirable.

(4) The Study Group reviewed the existing state of knowledge on the part played by hookworm infection in the etiology of iron deficiency anaemia. The Group is convinced that considerable losses of blood occur as a result of such infection; there is evidence to indicate, however, that a significant proportion of the iron contained in the blood lost is reabsorbed, although sufficient is being lost to upset the iron balance. It should also be pointed out that cases of severe iron deficiency anaemia are encountered in tropical areas of which the population shows no evidence of heavy infection with hookworms and no appreciable intestinal bleeding. Further, it has been demonstrated that in some cases of heavy hookworm infection with considerable blood losses, these are reduced as the haemoglobin level rises.

With these considerations in view, the Group recommends that further studies be made to elucidate the precise relationship between hookworm infection and anaemia. In such studies special attention may be focused on the following:

- (a) The net iron losses suffered by the body as a result of infection with hookworms, in relation to the levels of haemoglobin in the blood and the severity of the hookworm loads.
- (b) Iron reabsorption from blood liberated into the intestine.

(c) The effect of hookworm infection on the absorption, metabolism and utilization of other nutrients such as protein, fats, folic acid, B₁₂ and other vitamins.

(d) The effect of hookworm infection on clotting mechanisms and bleeding tendencies.

(e) The relative importance of *Necator americanus* as compared with *Ancylostoma duodenale* in causing blood losses.

(5) In view of the widespread occurrence of protein-deficiency and iron-deficiency types of anaemia in the tropics, and the several suggestions made in the literature that protein deficiency plays a part in the etiology of iron deficiency anaemia, the Group recommends that this subject be investigated in greater detail, the several possible mechanisms by which protein deficiency may adversely influence haemopoiesis being borne in mind. Additional studies should be undertaken on :

(a) the effect of protein deficiency on haemopoiesis under carefully controlled experimental conditions in animals ;

(b) the effect of protein on iron metabolism ;

(c) the effect of feeding trials of various amino acids and proteins on blood formation in patients with an iron deficiency type of anaemia.

(6) The part played by metabolic disturbances as compared with high iron intake in the etiology and pathogenesis of abnormal tissue iron deposits (cytosiderosis) needs further investigation. This subject may throw some light on iron metabolism that will be helpful in understanding iron deficiency anaemia.

(7) The Study Group considers that there is inadequate knowledge of the incidence of iron deficiency anaemia in infants and children in tropical areas.

Investigations are necessary into the relation between anaemia in the mother and the new-born child ; the iron content of milk from anaemic and normal mothers ; the possible relation between early marriage and multiple pregnancies before the age of 18 while blood volume is expanding and growth proceeding ; and the assessment of variations in menstrual iron losses in the same woman at different times, and in different women.

In making the studies on the relationship between anaemia in mothers and haematological levels in babies, it should be emphasized that the babies should be studied over a period of at least one year in order that signs of iron deficiency developing during the later months of infancy may be detected.

In assessing the haematological levels of new-born infants, due attention should be paid to such factors as the time at which the cord is clamped, the level at which the child is held in relation to the placenta, and whether or not the cord is milked.

(8) Although there are numerous accepted methods of haemoglobinometry, most of these are not easily adapted to field surveys. Attention should be given to the development of an inexpensive method of haemoglobinometry which will give quick, reliable results requiring minimum equipment and technical skill for use in field surveys and busy clinics.

(9) In view of the great importance of some of the parasitic infections in the etiology of iron deficiency anaemia by blood loss (in particular, hookworm), the Group recommends that effective control programmes be instituted wherever possible. Attention should be directed specifically to the prevention of transmission by improved environmental sanitation and the effective therapy of infected persons.

(10) In view of the discrepancy observed between levels of iron intake and incidence of iron deficiency anaemia, the Study Group considers that the iron content of foodstuffs in these areas be re-evaluated, using methods that will ensure that the foods analysed are in the form in which they are consumed, and that the analyses are accurate. Investigations are required into losses and gains that occur in the preparation of food.

(11) Although significant elevation of haemoglobin levels have been attained by supplementation of diets with as little elemental iron as 6 mg, the Study Group considers that further investigations may be made in order to determine the optimal level of fortification with iron which will protect the population from the development of anaemia. In this connexion it is also desirable to undertake further studies to determine maximal levels of iron supplementation that will be acceptable and free from health hazards. Such studies would have to be made on both human subjects and experimental animals.

Additional studies are warranted to determine whether certain natural foods of high iron content will serve the same purpose as fortification with elemental iron.

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