PREVENTING AND CONTROLLING
IRON DEFICIENCY ANAEMIA
THROUGH PRIMARY HEALTH CARE

A GUIDE FOR HEALTH ADMINISTRATORS
AND PROGRAMME MANAGERS

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with the collaboration of
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WORLD HEALTH ORGANIZATION
GENEVA
The World Health Organization is a specialized agency of the United Nations with primary responsibility for international health matters and public health. Through this organization, which was created in 1948, the health professions of some 165 countries exchange their knowledge and experience with the aim of making possible the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life.

By means of direct technical cooperation with its Member States, and by stimulating such cooperation among them, WHO promotes the development of comprehensive health services, the prevention and control of diseases, the improvement of environmental conditions, the development of health manpower, the coordination and development of biomedical and health services research, and the planning and implementation of health programmes.

These broad fields of endeavour encompass a wide variety of activities, such as developing systems of primary health care that reach the whole population of Member countries; promoting the health of mothers and children; combating malnutrition; controlling malaria and other communicable diseases, including tuberculosis and leprosy; having achieved the eradication of smallpox, promoting mass immunization against a number of other preventable diseases; improving mental health; providing safe water supplies; and training health personnel of all categories.

Progress towards better health throughout the world also demands international cooperation in such matters as establishing international standards for biological substances, pesticides, and pharmaceuticals; formulating environmental health criteria; recommending international nonproprietary names for drugs; administering the International Health Regulations; revising the International Classification of Diseases, Injuries, and Causes of Death; and collecting and disseminating health statistical information.

Further information on many aspects of WHO's work is presented in the Organization's publications.
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Preface

Both the understanding of the epidemiology of iron deficiency anaemia and the technical means for preventing and controlling it have expanded greatly in recent years. There are as yet relatively few examples of the application of this knowledge to the development and implementation of comprehensive control strategies. On the other hand, a considerable body of evidence is accumulating, based on national experience in a diversity of settings, indicating that primary health care may well offer the most practical means for translating this new knowledge and understanding into lower prevalence rates of anaemia.

The Joint WHO/UNICEF Nutrition Support Programme (JNSP) is active in 18 countries in improving the nutritional status of children and their mothers through primary health care. JNSP has generated a body of knowledge concerning the practical aspects of integrating primary care at various levels of organization to achieve nutritional goals. It is in this context that JNSP has sponsored this publication, written to help health administrators and programme managers develop suitable strategies for preventing and controlling iron deficiency anaemia through primary health care.

Grateful thanks are expressed, through its Government, to the people of Italy, who made possible the publication of this book and the Joint Nutrition Support Programme itself.

The collaborators of the author were all participants in the May 1987 meeting of the International Nutritional Anemia Consultative Group (INACG) in Quito, Ecuador. Their help is gratefully acknowledged, as is that of INACG. By providing an international framework within which scientists can communicate with each other and share the findings of their research on anaemia, INACG has contributed to the expansion of knowledge about this threat to the well-being and productivity of millions of people the world over.

The principal author, Dr Edouard M. DeMaeyer, served the World Health Organization for 18 years as Medical Officer in its Nutrition unit at WHO headquarters in Geneva. After his retirement in December 1981, he continued to make his expertise in nutrition available to the Organization. Convinced that recent public health trends and advances in the understanding of iron deficiency anaemia were improving the prospects for controlling this scourge, he wrote this book at the invitation of WHO. Sadly, he died shortly before it appeared in print.
1. Introduction

Iron deficiency anaemia is a problem of serious public health significance, given its impact on psychological and physical development, behaviour, and work performance. It is the most prevalent nutritional problem in the world today, affecting more than 700 million persons (1). Simply stated, an iron deficiency occurs when an insufficient amount of iron is absorbed to meet the body's requirements. This insufficiency may be due to inadequate iron intake, to reduced bioavailability of dietary iron, to increased needs for iron, or to chronic blood loss. When prolonged, iron deficiency leads to iron deficiency anaemia.

Iron deficiency is by far the commonest nutritional cause of anaemia; it may be associated with a folate deficiency, especially during pregnancy. Other nutrient deficiencies such as vitamin B12, pyridoxine and copper are of little public health significance because of their infrequency. Infants, preschool children, adolescents and women of childbearing age, particularly pregnant women, are at greatest risk of developing iron deficiency anaemia. However, adult males may also be at risk, especially where there is inadequate food intake or frequent parasitic infestation.

The treatment of iron deficiency anaemia is technically quite simple, requiring only the administration of medicinal iron, although for a variety of reasons millions of sufferers are currently left untreated. Prevention is somewhat more complex. Fortunately, there are a number of simple control measures available that can be applied through primary health care, and these are the main subject of this book.
2. Assessment, prevalence and consequences of iron deficiency anaemia

Anaemia may be diagnosed with confidence when the haemoglobin concentration is lower than the level considered normal for the person's age/sex group. When the anaemia is due to iron deficiency, increasing the person's intake of absorbable iron will raise the haemoglobin concentration (2). However, many individuals with seemingly normal haemoglobin levels likewise respond to iron administration with a rise in haemoglobin, which implies that they were actually deficient in iron (3,4). Assessing the frequency of iron deficiency anaemia in a population by means of haemoglobin measurements thus tends to underestimate the true prevalence.

The distribution of normal haemoglobin values is generally similar the world over, making allowance for factors such as age, sex, pregnancy and altitude (5).

On the basis of information from published and unpublished sources, and the haemoglobin cut-off points recommended by a WHO Scientific Group (5), it is estimated (7) that about 30% of the world's population of 5000 million people are anaemic.

Young children and pregnant women are the most affected, with an estimated global prevalence of 43% and 51% respectively. Anaemia prevalence among school-age children is 37%, non-pregnant women 35%, and adult males 18% (see Table 1). There are few data concerning anaemia in adolescents and in elderly people, which precludes any precise estimates for these two groups, but it is thought that the prevalence rate for adolescents is close to that for adult females and the rate for the elderly is slightly higher than that for adult males.

Iron deficiency anaemia is considerably more prevalent in the developing than in the industrialized world (36%—or about 1400 million persons—out of an estimated population of 3800 million in developing countries, versus 8%—or just under 100 million persons—out of an estimated population of 1200 million in developed countries). Africa and South Asia have the highest overall regional prevalence rates. Except for adult males, the estimated prevalence of anaemia in all groups is more than 40% in both regions and is as high as 65% in pregnant women in South Asia. In Latin America the prevalence of anaemia is lower, ranging from 13% in adult males to 30% in
pregnant women. In East Asia, prevalence ranges from an estimated 11% in adult males to 22% in children of school age.

<table>
<thead>
<tr>
<th>Region</th>
<th>Children 0-4 years</th>
<th>Children 5-12 years</th>
<th>Men</th>
<th>Women 15-49 years</th>
<th>pregnant</th>
<th>all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed regions</td>
<td>12</td>
<td>7</td>
<td>3</td>
<td>14</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Developing regions</td>
<td>51</td>
<td>46</td>
<td>26</td>
<td>59</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>World</td>
<td>43</td>
<td>37</td>
<td>18</td>
<td>51</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

Anaemia may be caused not only by a deficiency of iron (or, less often, of other nutrients) but by other conditions. Malaria, hookworm disease (whether ancylostomiasis or necatoriasis), schistosomiasis and other infections play an important role in tropical climates. Congenital haemolytic diseases such as sickle-cell anaemia and thalassaemia are also found in certain populations, particularly in Africa, Asia, and some Pacific islands, although they rarely constitute a significant public health problem. In some Asian countries, however, such as Burma, Lao People's Democratic Republic, Thailand and Viet Nam, the high prevalence of thalassaemia should be taken into account when iron supplementation programmes are envisaged.

If all these factors are taken into consideration, it is estimated that some 700–800 million people worldwide are affected by iron deficiency anaemia. This is a very conservative estimate, however; the real figure is probably higher. Likewise, since iron deficiency anaemia is the end-stage of a relatively long process of deterioration in haemoglobin levels, many more persons are suffering from iron deficiency, with its adverse effects on health and physical stamina, than are frankly anaemic.

The consequences of iron deficiency, and especially iron deficiency anaemia, are many. They include the following:

**In infants and children (6-9):**
- impaired motor development and coordination;
- impaired language development and scholastic achievement;
- psychological and behavioural effects (inattention, fatigue, insecurity, etc.);
- decreased physical activity.
**Iron deficiency anaemia**

*In adults of both sexes (10,11):*
- decreased physical work and earning capacity;
- decreased resistance to fatigue.

*In pregnant women (12-15):*
- increased maternal morbidity and mortality;
- increased fetal morbidity and mortality;
- increased risk of low birth weight.

The key role that haemoglobin plays in transporting oxygen to tissues accounts for the diminished work capacity and physical performance of persons with a diminished concentration of haemoglobin. The biochemical basis of the impaired development and altered behaviour is unclear, although it may be related to certain functional changes at cellular level, e.g., alterations in certain iron-containing enzymes.

As for the health risks, controversy surrounds their origin. There is a growing body of evidence, based on animal studies, that iron deficiency as such, even before the stage of frank anaemia is reached, adversely affects the immune system. Defects in cell-mediated immunity and in the killing of bacteria have been well demonstrated. However, the clinical implications of these findings are not clear (16). Early studies of the effects of iron deficiency anaemia on the frequency of infection in anaemic children (17,18) suggested that children who received iron as a medication or as a food fortificant had lower rates of respiratory and gastrointestinal disease than untreated children. In contrast, a more recent study showed little protective effect from the correction of anaemia (19), although associated protein-energy malnutrition and unfavourable environmental sanitation may have contributed to this finding.

In recent years, it has even been proposed that iron administration itself might predispose a person to infection. There is some experimental evidence to suggest that iron-binding proteins protect animals from infection by withholding iron from the invading organisms that require it for growth (20). This phenomenon would explain why the administration of large doses of iron by injection could be harmful. However, increased susceptibility to infection has been demonstrated primarily when serum transferrin is nearly saturated with iron (see page 27). Under ordinary circumstances, transferrin is less than 35% saturated and only minimal changes occur in this percentage with iron consumption. Although iron deficiency may in fact protect the host against certain specific organisms under laboratory conditions, there is no evidence that such protection outweighs the many more tangible and persistent handicaps imposed by iron deficiency itself.
3. Etiology and epidemiology of iron deficiency anaemia

A thorough understanding of iron requirements, intake and bioavailability is needed to explain why some individuals—for example, women in their reproductive years (particularly pregnant women), infants and young children—are at greater risk of developing iron deficiency anaemia than others.

Iron requirements

A dietary intake of iron is needed to replace iron lost in the stools and urine and through the skin. These basal losses represent approximately 14 μg per kg of body weight per day, or approximately 0.9 mg of iron for an adult male and 0.8 mg for an adult female (21). The iron lost in menstrual blood must be taken into consideration for women of reproductive age (see Table 2).

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>in μg/kg/day</th>
<th>in mg/day&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–12 months</td>
<td>120</td>
<td>0.96</td>
</tr>
<tr>
<td>13–24 months</td>
<td>56</td>
<td>0.61</td>
</tr>
<tr>
<td>2–5 years</td>
<td>44</td>
<td>0.70</td>
</tr>
<tr>
<td>6–11 years</td>
<td>40</td>
<td>1.17</td>
</tr>
<tr>
<td>12–16 years (girls)</td>
<td>40</td>
<td>2.02</td>
</tr>
<tr>
<td>12–16 years (boys)</td>
<td>34</td>
<td>1.82</td>
</tr>
<tr>
<td>Adult males</td>
<td>18</td>
<td>1.14</td>
</tr>
<tr>
<td>Pregnant women&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactating women</td>
<td>24</td>
<td>1.31</td>
</tr>
<tr>
<td>Menstruating women</td>
<td>43</td>
<td>2.38</td>
</tr>
<tr>
<td>Post-menopausal women</td>
<td>18</td>
<td>0.96</td>
</tr>
</tbody>
</table>

<sup>a</sup> Absorbed iron is the fraction that passes from the gastrointestinal tract into the body for further use.

<sup>b</sup> See reference 29.

<sup>c</sup> Calculated on the basis of median weight for age.

<sup>d</sup> Requirements during pregnancy depend on the woman's iron status prior to pregnancy. See text for further explanation.
While the volume of menstrual blood lost is relatively constant for a given woman from month to month, it varies greatly between women. Several studies have shown that the median blood loss during menstruation ranges between 25 and 30 ml per month. This represents an iron loss of 12.5–15 mg per month, or 0.4–0.5 mg per day over 28 days. When basal losses are added, the total iron loss for menstruating women is about 1.25 mg per day. This means that the iron requirements of 50% of all women are in excess of 1.25 mg per day. Taking into account the skew of the frequency distribution of menstrual blood loss, one can calculate that only 2.5% of women have iron requirements in excess of 2.4 mg per day.

Although menstruation-related iron losses are reduced to nil during pregnancy, additional iron is nevertheless required for the fetus, the placenta and the increased maternal blood volume. This amounts to approximately 1000 mg of iron over the entire pregnancy (22). Requirements during the first trimester are relatively small, 0.8 mg per day, but rise considerably during the second and third trimesters to a high of 6.3 mg per day (see Fig. 1). Part of this increased requirement can be met from iron stores and by an adaptive increase in the percentage of iron absorbed. However, when iron stores are low or non-existent and dietary iron is poorly absorbed, as is often the case in developing countries, iron supplementation is essential. During lactation

FIG. 1. DAILY REQUIREMENTS FOR ABSORBED IRON IN 97.5% OF WOMEN (MEAN ± 2 S.D.) BEFORE, DURING AND AFTER PREGNANCYα

* The horizontal axis is not a true scale. Lactation, for example, usually continues for at least nine months.
the absence of menstrual blood loss is partially offset by the secretion of about 0.3 mg of iron per day in breast milk, in addition to basal losses. A woman's mean requirement during the first 6 months of lactation is estimated to be about 1.3 mg of iron per day (see Table 2).

Infants, children and adolescents require iron for their expanding red cell mass and growing body tissue. A normal infant at birth has about 75 mg of iron per kg of body weight, two-thirds of which is present in red blood cells. During the first 2 months of life there is a marked decrease in haemoglobin concentration with a consequent increase in iron stores. These stores are subsequently mobilized to supply iron for growth needs and to replace losses; hence, during this period there is a minimal requirement for dietary iron. By 4–6 months, however, iron stores have decreased significantly and the infant needs a generous dietary intake of iron. During the first year of life, a child triples its body weight and doubles its iron stores. Changes in the concentration of serum ferritin with age parallel the changes in iron stores (see Fig. 2).

Overall, as shown in Table 2, iron requirements per kg of body weight are substantially higher in infants and children than in adults. Since they have lower total energy requirements than adults, they eat less and

---

**FIG. 2. CHANGES IN CONCENTRATION OF SERUM FERRITIN WITH AGE**

*Mean values (geometric means) in healthy populations are shown. At all ages, a serum ferritin concentration below 10 or 12 μg per litre is considered indicative of depleted iron stores (25-28).*
are thus at greater risk of developing iron deficiency, especially if the iron in their diets is of low bioavailability.

Iron requirements increase in cases of chronic bleeding caused by such parasites as hookworm (Ancylostoma and Necator), Schistosoma and possibly Trichuris trichiura; these cause frequent infections in countries with hot, humid climates and poor sanitation. In the case of hookworm disease, blood loss varies from 2 to 100 ml per day according to the severity of the infestation (23). Some of the iron in the blood shed by the worm in the intestine will be reabsorbed further down the gastrointestinal tract, but the remainder will be lost via the stools. It is estimated that iron loss per thousand eggs per gram of faeces is 0.8 mg per day in the case of Necator americanus and 1.2 mg per day with Ancylostoma duodenale (24).

Infections interfere with food intake and the absorption, storage and use of many nutrients, iron among them. In many rural communities and urban slums where environmental sanitation is poor, morbidity from viral and bacterial infections is high. It is in these same communities that diets are most often energy deficient. Where the iron balance is precarious, repeated episodes of infection may result in the development of anaemia, particularly in young children whose morbidity burden is much higher than that of adults. This explains in part the high prevalence of anaemia among infants and preschool children. By implication, the control of infection may be the intervention with the greatest impact on the problem of anaemia and iron deficiency in these age groups.

Types of dietary iron

There are two distinct types of dietary iron—haem and non-haem iron. Haem iron is a constituent of haemoglobin and myoglobin and therefore is present in meat, fish and poultry, as well as in blood products. Haem iron accounts for a relatively small fraction of total iron intake—usually less than 1–2 mg of iron per day, or approximately 10–15% of the dietary iron consumed in industrialized countries. In many developing countries, haem iron intake is lower or even negligible. The second type of dietary iron, non-haem iron, is a more important source; it is found to varying degrees in all foods of plant origin.

Besides the iron derived from food, the diet may also contain exogenous iron originating from the soil, dust, water or cooking vessels. This is more frequently the case in developing countries, where the amount of such contamination iron in a meal may be several times greater than the amount of food iron. The cooking of foods in iron pots may increase the iron content of a meal several fold. This is especially true for soups containing vegetables of low pH which are
Etiology and epidemiology

simmered for a long time. Frying in iron pans does not usually increase the food’s iron content. Any iron released during cooking is integrated into the non-haem iron pool and is available for absorption. Another form of exogenous iron is that present in foods such as flour, sugar and salt which are deliberately fortified with iron or iron salts.

Table 3. SOURCES OF DIETARY IRON

<table>
<thead>
<tr>
<th>Chemical form and type of iron</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haem iron</td>
<td>Meat, fish, poultry and blood products. Accounts for 10–15% of iron intake in industrialized countries. Usually represents less than 10% of total intake (often negligible amounts) in developing countries. Bioavailability high: absorption 20–30%.</td>
</tr>
<tr>
<td>Non-haem iron</td>
<td>Mainly found in cereals, tubers, vegetables and pulses. Bioavailability determined by the presence of enhancing and inhibiting factors consumed in the same meal (see text).</td>
</tr>
<tr>
<td>— food iron</td>
<td>Soil, dust, water, iron pots, etc. Potential bioavailability usually low. May be present in large quantities, in which case its contribution to total iron intake is not insignificant.</td>
</tr>
<tr>
<td>— contamination iron</td>
<td>Various iron compounds used, of varying potential bioavailability. Bioavailability of soluble fraction determined by composition of meal.</td>
</tr>
<tr>
<td>— fortification iron(^a)</td>
<td>For...</td>
</tr>
</tbody>
</table>

\(^a\) Fortification is the process whereby one or more nutrients are added to a food to maintain or improve the quality of the diet of a group, a community or a population (30).

Overall, in any given diet the quantity of iron habitually ingested is relatively constant and difficult to modify, but some types of diet are inherently denser in iron than others. Iron density (the amount of iron ingested per unit of energy consumed) is actually higher in the diets of the developing world than in those typical of industrialized countries. All too often, however, this advantage is offset by the inadequacy of developing country diets in terms of total energy consumed. Where this is the case, the most straightforward way of increasing the amount of iron ingested is to increase total energy intake.
Even where people generally have enough to eat, children and women are a special case. Because of their lower energy needs they tend to consume less food than other groups, which makes it more difficult for them to meet their iron needs. Like all individuals subsisting on a low-energy diet, children and women are at risk of developing iron deficiency.

A factor just as important as the total iron content of the diet is the bioavailability of the iron ingested, i.e., its absorbability. How much iron is effectively absorbed by the body varies considerably depending on a number of factors, as explained below. Increasing total energy intake and enhancing the bioavailability of the non-haem iron ingested are thus the main dietary strategies for helping people to meet their iron requirements.

**Absorption of dietary iron**

The absorption of dietary iron is influenced by the amount and chemical form of the iron, the consumption during the same meal of factors enhancing and/or inhibiting iron absorption, and the health and iron status of the individual (see Tables 3 and 4).

**Table 4. MAJOR DETERMINANTS OF IRON ABSORPTION**

<table>
<thead>
<tr>
<th>DIETARY FACTORS:</th>
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<tbody>
<tr>
<td>(1) factors that enhance non-haem iron absorption:</td>
</tr>
<tr>
<td>— ascorbic acid (vitamin C)</td>
</tr>
<tr>
<td>— meat, poultry, fish and other seafood</td>
</tr>
<tr>
<td>— low pH (e.g., lactic acid)</td>
</tr>
<tr>
<td>(2) factors that inhibit non-haem iron absorption:</td>
</tr>
<tr>
<td>— phytates</td>
</tr>
<tr>
<td>— polyphenols, including tannins</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOST FACTORS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) iron status</td>
</tr>
<tr>
<td>(2) health status (infections, malabsorption)</td>
</tr>
</tbody>
</table>

Contamination iron usually has a very low bioavailability. One exception is the iron derived from cooking pots.

Iron compounds that are used for food fortification vary considerably in bioavailability. Easily soluble compounds, for example, ferrous
sulfate, are readily available but often discolour the food or turn it rancid. Other compounds such as metallic iron powders are only partially available, but usually cause fewer such technical problems (33).

Non-haem iron from these sources and from food is absorbed in a fundamentally different way from haem iron. Haem iron is readily available (20–30% absorption) and may account for as much as one-quarter of the iron absorbed from a diet rich in meat. Its bioavailability is little affected by the nature and composition of a given meal. In contrast, the absorption of non-haem iron is highly variable and depends on what other foods are eaten with the meal, especially on the balance between foods that promote and those that inhibit iron availability.

As shown in Table 4, meat and fish are enhancers of iron absorption. This means that they are doubly valuable. Not only do they directly contribute rich amounts of haem iron, but they enhance the absorption of the non-haem iron contained in the rest of the meal. Ascorbic acid (vitamin C) is another enhancing factor. In developing countries, where meat intake is low, ascorbic acid is the single most important enhancer of iron absorption. Adding as little as 50 mg of ascorbic acid to a meal, whether in pure form or in vegetables or fruits (for example, an orange or a lemon, or 100 g of cabbage, or 200 g of amaranth), will double iron absorption (see Fig. 3).

**FIG. 3. EFFECT OF IRON ABSORPTION ENHANCERS ON THE ABSORPTION OF NON-HAEM IRON**

![Graph showing the effect of iron absorption enhancers on the absorption of non-haem iron](image)

*The percentage absorption of non-haem iron from three types of diet containing differing amounts of absorption enhancers. A low availability diet is one containing less than 30 g of meat, poultry or fish (lean, raw weight) or less than 25 mg of ascorbic acid daily. An intermediate availability diet contains 30–90 g of meat, poultry or fish or 25–75 mg of ascorbic acid daily. A high availability diet is one that contains more than 90 g of meat, poultry or fish or more than 75 mg of ascorbic acid. Alternatively, a high availability diet may contain 30–90 g of meat, poultry or fish plus 25–75 mg of ascorbic acid. Based on data from Monsen et al. (31).*
Iron deficiency anaemia

Many compounds are known to inhibit the absorption of iron, among them phytates, polyphenols (including tannins), and soy protein.

Soy protein can impair iron absorption under certain circumstances, especially when it is used as a meat substitute. However, because of the intrinsically high iron content of soy protein products, the net effect of their addition to a meal is to increase, rather than decrease, the total amount of iron absorbed.

Phytates are present in wheat and other cereals. Even very small amounts of phytate markedly reduce iron absorption. Fortunately, this inhibitory effect can be counteracted with ascorbic acid.

Tannins, which are present in tea and to a lesser extent in coffee, are also iron absorption inhibitors (Fig. 4). Other polyphenols are found in nuts and legumes. Once again, the inhibitory effect of all polyphenols can be counteracted by adding ascorbic acid to the meal, as shown in Fig. 4.

Iron absorption is thus strongly influenced by the combination of foods eaten in a given meal. A typical Thai meal composed of rice, vegetables and spices will yield 0.16 mg of absorbed iron, but this

FIG. 4. EFFECT OF DIFFERENT BEVERAGES ON IRON ABSORPTION FROM A CONTINENTAL BREAKFAST

<table>
<thead>
<tr>
<th>Beverages</th>
<th>Iron absorption (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continental breakfast</td>
<td>0.00</td>
</tr>
<tr>
<td>+ tea</td>
<td>0.12</td>
</tr>
<tr>
<td>+ coffee</td>
<td>0.23</td>
</tr>
<tr>
<td>+ coffee and orange juice</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Based on data from Rossander et al. (32).

* Two rolls, margarine, orange marmalade and cheese.
* One cup (150 ml) of tea made by steeping 2.5g of dried tea leaves in 150 ml of freshly boiled water for five minutes.
* One glass (150 ml) of orange juice prepared from frozen concentrate and water.
figure more than doubles, to 0.40 mg, with the addition of some fish. To take an example from Latin America, 0.17 mg of iron is available from a meal consisting of maize, rice and black beans, but if vitamin C is added in the form of pure ascorbic acid (50 mg) or cauliflower (125 g), the amount of iron absorbed increases respectively to 0.41 mg or to 0.58 mg. Conversely, the drinking of tea, especially strong tea, with or shortly after the meal has a marked inhibitory effect on iron absorption. These few examples show the dramatic impact of adding small amounts of absorption inhibitors or enhancers to a meal. More research is urgently needed on similar modifications of other typical diets. In the meantime, based on what is already known, health education has a vital role to play in making people aware of the effects of various food combinations. For example, the inhibitory effect of tannins could be avoided by encouraging people to wait until after the meal before drinking tea or coffee. In general, however, it may be culturally more acceptable to encourage the addition of an absorption enhancer to the meal than to discourage consumption of an inhibitor.

Finally, iron absorption is related to the individual’s iron status. More iron is absorbed by iron-deficient persons and less by those who are iron-replete, although the regulatory mechanism involved is not understood. Unfortunately, this adaptive increase in iron absorption is not great enough to prevent deficiency in people consuming diets typical of the developing world.

Recommended iron intakes

Recommended intakes are influenced by two factors: the physiological requirements of the individual and the bioavailability of the dietary iron consumed. Recommended intakes by age, sex, and type of diet are presented in Table 5. Recommended intakes for women of reproductive age are relatively high in order to cover the requirements of women with large menstrual losses. At the same time, it is clear that some women may not need such a high intake. In pregnancy, requirements during the second and third trimesters cannot be satisfied by dietary iron alone, even if it is of high bioavailability. Iron supplementation is indicated unless a store of about 500 mg of iron is present at the beginning of pregnancy.

Bioavailability has a marked effect on recommended iron intakes: while intake should be 11 mg per day for menstruating women enjoying diets with high bioavailability, this amount needs to be increased to 32 mg per day or even more for those whose diets have low bioavailability, as shown in Table 5.
Table 5. RECOMMENDED IRON INTAKES (MG/DAY) DESIGNED TO COVER REQUIREMENTS OF 97.5% OF INDIVIDUALS IN EACH AGE/SEX GROUP FOR DIETS WITH DIFFERENT BIOAVAILABILITIES

<table>
<thead>
<tr>
<th>Age/sex group</th>
<th>Type of diet (% of iron absorbed)</th>
<th>very low bioavailability (&lt;5%)</th>
<th>low bioavailability (5-10%)</th>
<th>intermediate bioavailability (11-18%)</th>
<th>high bioavailability (&gt;19%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 months (both sexes)</td>
<td>b</td>
<td>b</td>
<td>b</td>
<td>b</td>
<td>b</td>
</tr>
<tr>
<td>4–12 months (both sexes)</td>
<td>24</td>
<td>13</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>13–24 months (both sexes)</td>
<td>15</td>
<td>8</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2–5 years (both sexes)</td>
<td>17</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>6–11 years (both sexes)</td>
<td>29</td>
<td>16</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12–16 years (girls)</td>
<td>50</td>
<td>27</td>
<td>13</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>12–16 years (boys)</td>
<td>45</td>
<td>24</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Adult males</td>
<td>28</td>
<td>15</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Adult females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• pregnant</td>
<td>59</td>
<td>32</td>
<td>16</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>• menstruating</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• lactating</td>
<td>33</td>
<td>17</td>
<td>9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>• menopausal</td>
<td>24</td>
<td>13</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

* Source: reference 29.

b For exclusively breast-fed infants 0–4 months old, see text.

c Basis for calculation of intake: 4%.

d Basis for calculation of intake: 7.5%.

e Basis for calculation of intake: 15%.

f Basis for calculation of intake: 22.5%.

g See Table 2 (page 11) and text.

The broad categories of iron bioavailability may be characterized as follows.

Low bioavailability diet. This is a simple, monotonous diet based on cereals, roots and tubers with negligible quantities of meat, fish or ascorbic acid. It contains a preponderance of foods that inhibit iron absorption.
absorption such as maize, rice, beans, wholewheat flour and sorghum, and is typical of many developing countries, particularly among poorer people. There are some diets from which iron absorption is even lower. In very low bioavailability diets composed almost entirely of cereals, as reported in India (34), iron absorption may be as low as 3–4%.

**Intermediate bioavailability diet.** Diets in this category consist mainly of cereals, roots or tubers, but include some foods of animal origin and/or ascorbic acid. A low bioavailability diet can be brought up to intermediate bioavailability by increasing the intake of foods that enhance iron absorption such as meat, fish or foods rich in ascorbic acid. Similarly, a high bioavailability diet can be reduced to an intermediate level by the regular consumption with meals of absorption inhibitors such as tea or coffee.

**High bioavailability diet.** This is a diversified diet containing generous quantities of meat, poultry, fish, or foods rich in ascorbic acid. Such a diet would be typical of most population groups in industrialized countries.

It is obvious that, with a low bioavailability diet, individuals in some age groups will not be able to meet their iron requirements at a food consumption level that is adequate for their energy needs. This is especially true for young children, adolescent girls, menstruating adult females, and pregnant women.

Special considerations apply to iron needs during the first years of life. The iron content of human breast milk is low—about 0.5 mg per litre—but so is the term infant’s iron requirement for the first 4–6 months of life. An infant taking in 600–650 ml of breast milk daily is ingesting approximately 0.3 mg of iron per day. The bioavailability of this iron is quite high, however; as much as 0.15 mg of iron per day may be absorbed. From about 6 months of age, the iron requirements increase markedly and the supply from breast milk alone is no longer sufficient. Low-birth-weight infants exhaust their iron stores at an earlier age and require additional exogenous iron before 6 months of age.

Cow’s milk has about the same iron content as human milk, although iron is better absorbed from breast milk. The bioavailability of iron from infant cereal products depends on the type of cereal used and, especially, on its iron and phytate content. Commercial products are often fortified with an iron compound as well as with ascorbic acid to enhance iron absorption. Fruits and vegetables should be carefully chosen to ensure that the infant’s ascorbic acid intake is high. While iron requirements during the first years of life are not very different from those of an adult male, energy requirements—and thus food intake—are much lower in infants and children. This means that the density and bioavailability of dietary iron must be particularly high for this group.
4. Screening for anaemia and assessing iron status

When and how to screen

The signs and symptoms of anaemia—pallor of the skin and of the conjunctiva, fatigue, shortness of breath, lack of appetite—are nonspecific and difficult to detect. Indeed, the clinical detection of anaemia is influenced by so many variables, such as skin thickness and pigmentation, that it is unreliable unless the anaemia is very severe. Laboratory tests should therefore be used to diagnose anaemia and determine its severity. Such tests are useful in individuals in whom anaemia is suspected, especially those from known high-risk groups; they can be repeated over time to monitor the effectiveness of treatment. Laboratory tests can also be used to determine the prevalence and severity of anaemia in a population as well as to single out the groups that are most affected.

It will be recalled that individuals begin to suffer from the adverse effects of iron deficiency well before they become frankly anaemic and hence detectable by the tests described above. Special laboratory tests have therefore been developed for the detection of iron deficiency. Such tests can also serve to show whether the anaemia present in a given population is due to iron deficiency or to another cause, such as parasitic infection, which would require completely different therapeutic or preventive measures. Tests of iron deficiency are thus suitable for monitoring the iron status of population groups. They should not be used routinely for diagnostic purposes in primary health care.

In the case of pregnant women, it is important to note that routine laboratory confirmation of iron deficiency anaemia is neither medically necessary nor justified from a cost-benefit point of view. Because most pregnant women eventually become anaemic, it makes sense as a preventive measure to give all women supplementation with medicinal iron during the second half of pregnancy. This can be done through primary health care. Supplementation will do no harm to the few women not requiring it; for the vast majority who are iron-deficient, it will be of great benefit.
Anaemia screening tests

The best laboratory tests for the diagnosis of anaemia involve measuring the packed volume of red cells (haematocrit) or the concentration of haemoglobin in circulating blood. Both determinations can be made on either capillary blood obtained by skin puncture or venous blood obtained by venepuncture. Skin puncture is easier to perform under field conditions, especially in developing countries, but the use of capillary blood substantially decreases diagnostic reliability. In the case of venous blood, sequential values in the same individual usually remain within 0.6 g of haemoglobin per dl. The discrepancy between capillary and venous values ranges between 0.5 and 1.0 g of haemoglobin per dl (35). In routine primary health care, an error of 0.5 g per dl is of little or no consequence. It may be a more serious drawback when the primary health worker is attempting to follow the effect of iron therapy in an anaemic individual. In general, however, carefully collected capillary samples provide acceptable results.

Capillary blood. A specimen of capillary blood is obtained from the finger tip (or the heel, for an infant). To obtain the best possible sample, warm the finger tip (or heel) first to promote blood flow. After sterilizing the area, make a clean puncture with a sterile lancet to obtain a free flow of blood. Avoid squeezing the extremity so as to minimize the contamination of blood with tissue fluid. Depending on the procedure to be followed, the blood is taken into a pipette, heparinized tube or glass cell, or else dropped on to filter paper.

Venous blood. Venous blood is generally taken from the antecubital vein with a sterile 20 or 21 SWG needle and a dry sterile syringe. Smaller gauge needles are not suitable for obtaining free blood flow. Alternatively, a vacuum tube (for example, a Vacutainer) may be used. In persons whose veins are not easily seen or felt, the skin area may be warmed and a tourniquet or sphygmomanometer cuff applied. Clean the area of venepuncture with 70% alcohol and allow it to dry before inserting the sterile needle into the vein. Draw blood into the syringe, remove the tourniquet or sphygmomanometer cuff and withdraw the needle, keeping the swab in place for a few minutes to ensure that any leaking is staunched.

Safety precautions. It is very important in both laboratory and field to avoid the transmission through blood of infection with hepatitis B virus or the human immunodeficiency virus (HIV) which causes acquired immunodeficiency syndrome (AIDS). Blood lancets, needles and syringes should ideally be disposed of after a single use. However, this is not always practicable. Sterilizing in a hot air oven or in a pressure cooker (autoclave), or disinfecting by thorough boiling (20 minutes), is sufficient. It is not adequate to leave such equipment in an alcohol bath. Procedures should always be established to prevent any risk of transmission from subject to subject or from subject to technician.
Haemoglobin concentration

There are several laboratory techniques for measuring haemoglobin concentration. Most of those that have been and are still used in primary health care are inaccurate in routine practice and should be discarded (36-39).

The accurate and reliable procedures are those which convert haemoglobin to one of its compounds, the concentration of which is determined by matching the colour with a known standard in a photoelectric colorimeter or by measuring absorption in a spectrophotometer. Three such techniques in common use are the cyanmethaemoglobin (HbCN), the oxyhaemoglobin (HbO₂) and the alkaline haematin methods (40).

The cyanmethaemoglobin method (41) has become the most popular of the three because it measures practically all haemoglobins except sulphaemoglobin. Another major advantage of this method is that the standards used remain stable for a long time. In this method blood is mixed with Drabkin's solution in order to convert haemoglobin into cyanmethaemoglobin, the absorbance of which is then measured at 540 nm in a photoelectric colorimeter or in a spectrophotometer.

An absolute prerequisite for using cyanmethaemoglobin to determine haemoglobin concentration is to dilute the blood in 250 times its volume of Drabkin's solution. Adding an exact amount of blood to a measured amount of diluent is simple to do in an established laboratory where the blood can be drawn and measurements made the very same day. However, if blood is collected in the field, it will have to be transported to a laboratory for the determination.

The transport of blood samples presents serious problems in developing countries. In warm, humid climates, unrefrigerated blood quickly becomes unsuitable for haemoglobin determination because of evaporation or contamination. A possible alternative is to carry a quantity of stoppered test tubes each containing an accurately measured 5-ml volume of diluent (Drabkin's solution). The blood is collected and 20 μl is immediately added to the diluent, the tube is once again stoppered, and the blood-reagent mixture is transported to a laboratory where measurements can be made. Leakage of diluent from the stoppered tubes is not infrequent, however, and this seriously compromises the accuracy of the results obtained. There are two ways to overcome this problem:

1. Drabkin's solution (5 ml) is pipetted into the test tube at the time of blood collection; automatic pipettes or seripettors may be used for this purpose. Once an accurate dilution has been made, a small spillage of the sample will do no harm since it will not
change the concentration. However, evaporation from open vials will affect the concentration and hence the results.

2. An accurate volume of blood is delivered on to No. 1 Whatman filter paper (cut into 1.5 x 1.5 cm squares). The blood is allowed to dry and the squares of paper are labelled with a pencil. The squares are placed in small envelopes and sent to a laboratory. There, they are dropped into accurately measured amounts of diluent (Drabkin's solution), and the blood is allowed to diffuse out of the filter paper and into the diluent for two hours. The solution is then mixed by shaking and read in a photoelectric colorimeter or a spectrophotometer. This method is relatively easy to reproduce and reasonably suitable for those situations where a laboratory is located at some distance from blood collection points. Small battery-operated colorimeters are now available that allow determinations to be made in the field.

**Packed cell volume (haematocrit)**

Microhaematocrit can be measured instead of haemoglobin concentration (41). This is done by centrifuging a minute quantity of blood that has been collected in a heparinized capillary tube. One of the advantages of this method is its technical simplicity, particularly when applied to the small blood samples obtained by skin puncture. Another advantage is that it can be performed in the field with battery-operated microcentrifuges. On average, haematocrit values are roughly equivalent to three times the haemoglobin concentration.

**Diagnosing anaemia on the basis of haemoglobin values**

With both methods of determination, it is essential to interpret results in relation to age-specific and sex-specific reference standards (5). Table 6 shows reference values for haemoglobin concentration after six months of age, laboratory testing rarely being done before this age.

Data from population surveys indicate a slight, gradual decrease in haemoglobin concentration in elderly men (42). It remains to be confirmed whether this is a normal concomitant of aging (possibly related to decreased androgen levels) or, alternatively, whether it represents a true increase in the prevalence of anaemia. Because of this uncertainty, haemoglobin levels for this group have not been tabulated. The haemoglobin concentration over time remains much more stable in women, in whom the lower limit of normal is considered to be 12 g of haemoglobin per dl from six years of age onwards. An exception occurs during
Iron deficiency anaemia

pregnancy, when haemoglobin concentration decreases concurrently with a large expansion in blood volume.

Table 6. HAEMOGLOBIN LEVELS INDICATIVE OF ANAEMIA IN POPULATIONS LIVING AT SEA LEVEL

<table>
<thead>
<tr>
<th>Age/sex group</th>
<th>Haemoglobin level (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 6 months–5 years</td>
<td>&lt;11</td>
</tr>
<tr>
<td>Children 6–14 years</td>
<td>&lt;12</td>
</tr>
<tr>
<td>Adult males</td>
<td>&lt;13</td>
</tr>
<tr>
<td>Adult females (non-pregnant)</td>
<td>&lt;12</td>
</tr>
<tr>
<td>Adult females (pregnant)</td>
<td>&lt;11</td>
</tr>
</tbody>
</table>

* Source: see reference 5.

Although anaemia is often graded as “mild”, “moderate”, and “severe”, the haemoglobin values at which the division into these three categories is made vary and are arbitrary. For the purposes of this book, anaemia is considered to be mild, moderate or severe when haemoglobin concentrations are above 80%, between 80% and 60%, or less than 60% of the cut-off levels, respectively. Practically speaking, given the relatively small differences between age/sex groups, one can diagnose mild anaemia when the haemoglobin concentration is above 10 g/dl but below the cut-off level, moderate anaemia when the concentration is between 7 and 10 g/dl, and severe anaemia when it is below 7 g/dl.

Iron deficiency tests

Several laboratory tests can confirm the presence of iron deficiency. The most commonly used are those that measure serum ferritin, transferrin saturation, and erythrocyte protoporphyrin.

Serum ferritin

Ferritin is normally present in serum, but in such small quantities that until recently it remained undetected. It is measured by radioimmuno-
assay or by enzyme-linked immunoassay (41). An advantage of measuring the serum ferritin level is that it permits an evaluation of iron status not only in persons with iron deficiency but also in those with an excess. At all ages a serum ferritin value of less than 10–12 μg/l (or ng/ml) indicates a depletion of iron stores. The assay, which until recently was expensive and time-consuming, has been simplified and can now be used as a routine laboratory procedure (43).

Transferrin saturation

Almost all of the iron in the serum is bound to the iron-binding protein, transferrin. Transferrin saturation is calculated by measuring both serum iron and total iron-binding capacity using spectrophotometric techniques (41), dividing the iron concentration by the iron-binding capacity, and multiplying by 100 to express the result as a percentage. Values below 16% in adults are considered indicative of iron deficiency. The corresponding cut-off values for infants and children are 12% and 14%, respectively.

Erythrocyte protoporphyrin

Protoporphyrin accumulates in red blood cells when it has insufficient iron to combine with to form haem. Erythrocyte protoporphyrin can be measured rapidly by a simple fluorescence assay (41) performed directly on a thin film of blood. The instrument specifically designed for the assay requires little operator time or training, although it needs frequent recalibration by the manufacturer. Erythrocyte protoporphyrin is elevated (i.e., higher than 80 μg per dl of red blood cells below the age of four years and 70 μg per dl above that age) in cases of iron deficiency; values are also high when there is lead poisoning (44). This test is therefore useful for screening infants and young children in low-income urban areas where both conditions are common.

Combined nutritional deficiencies

Iron deficiency is often found in association with a deficiency of folic acid. Combined folate and iron deficiency may occur in preterm infants who are fed unfortified formula based on evaporated milk. Infants fed on goat’s milk are also at risk, as are those suffering from diarrhoea, malnutrition, infection and haemolytic anaemia. Combined folate and iron deficiency is especially common in women in the second half of pregnancy.
Anaemia is common in children suffering from severe protein-energy malnutrition, even where there is no evidence of a concurrent deficiency of iron. However, it should be borne in mind that malnourished children who receive nutritional rehabilitation will have a growth spurt that may provoke iron deficiency unless iron is included in the diet from about two weeks after the initiation of treatment. Laboratory evaluation of iron status is thus more reliable after the general malnutrition has been treated for about two weeks than initially.

Vitamin $B_{12}$ deficiency in strict vegetarians (those taking no milk, eggs, or other food of animal origin) and in patients suffering from ileal malabsorption or specific disorders of vitamin $B_{12}$ absorption (pernicious anaemia) may result in megaloblastic anaemia.

If iron and vitamin $B_{12}$ deficiencies coexist, the latter will become apparent only after the former has been treated. Iron deficiency will mask a folate deficiency in the same manner.
5. Treatment of iron
deficiency anaemia

In clinical practice, any patient suspected of being anaemic is tested
and, if the anaemia is confirmed, treated with medicinal iron sup-
plements. The situation is very different in large-scale public health
programmes, particularly in developing countries, where systematic
laboratory testing is organizationally and financially impossible. In
these settings, the approach that is most cost-effective is to give iron
supplements to entire high-risk groups, particularly pregnant women.
With this approach the distinction between treatment and prevention is
blurred, as supplementation will act to reverse anaemia in some indi-
viduals and prevent it from developing in others. For the purposes of
this book, routine supplementation of high-risk groups is considered as
prevention and will be discussed in Chapter 6 along with other
preventive approaches, such as manipulation of the diet.

Therapy as such must rely on medicinal iron, since dietary changes
alone cannot correct iron deficiency anaemia, especially when severe.
The treatment of choice is the oral administration of ferrous fumarate,
gluconate or sulfate, parenteral administration being reserved for
patients who are completely intolerant of oral iron. Only the most
severe cases (haemoglobin concentration less than 3 g/dl) call for a
blood transfusion.

Oral iron therapy

Iron tablets

In 1832 Blaud introduced iron therapy in the form of what came to be
called “Blaud’s pill”: a tablet containing ferric carbonate as its main
constituent (45). Effective in correcting iron deficiency anaemia, it
remained the mainstay of treatment until other iron preparations were
introduced and it became obvious that ferrous iron was better absorbed
than ferric iron. To this day practically all medicinal iron preparations
contain ferrous compounds. Ferrous fumarate, gluconate and sulfate are
commonly used. Other ferrous compounds previously or still in use
include ferrous succinate, lactate, glycine sulfate, glutamate, citrate,
tartrate and pyrophosphate. Although ferrous succinate is probably more
completely absorbed, these compounds, in addition to being more
expensive, offer no advantages over ferrous fumarate, gluconate or
sulfate.
Iron tablets contain a percentage of elemental iron that varies with the molecular weight of the iron compounds. Some examples are given in Table 7.

**Table 7. PERCENTAGE AND AMOUNT OF IRON IN SOME COMMONLY USED IRON TABLETS**

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Iron compound (mg) per tablet</th>
<th>Elemental iron (mg) per tablet</th>
<th>% of iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous fumarate</td>
<td>200</td>
<td>66</td>
<td>33</td>
</tr>
<tr>
<td>Ferrous gluconate</td>
<td>300</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Ferrous sulfate (7H₂O)</td>
<td>300</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>Ferrous sulfate, anhydrous</td>
<td>200</td>
<td>74</td>
<td>37</td>
</tr>
<tr>
<td>Ferrous sulfate, exsiccated (1H₂O)</td>
<td>200</td>
<td>60</td>
<td>30</td>
</tr>
</tbody>
</table>

Uncoated (compressed) tablets and sugar-coated tablets are the least expensive formulations and disintegrate well in the stomach. However, they become oxidized over time and hence less effective, especially in humid climates.

Enteric-coated tablets are somewhat more expensive. They have the added drawback that they disintegrate only partially when exposed to gastric juices. All coated preparations and batches therefore need to be subjected to an *in vitro* hydrochloric acid disintegration test; those that do not disintegrate in 0.1 mol/litre HCl within two hours should be rejected (46).

The rationale for slow-release preparations is that iron absorption is inversely related to the amount of iron present in the duodenum-jejenum, while the frequency of gastrointestinal side-effects is directly proportional to that amount. Slow-release preparations allow only a small amount of iron at any given moment to come into contact with the duodenal mucosa, thus improving both absorption and gastrointestinal tolerance. As a consequence, the same therapeutic effect can be obtained with a smaller dose of iron (as compared with plain tablets) while compliance with treatment is improved because there are fewer side-effects.
Liquid preparations

There are many iron-containing syrups and liquid preparations (drops) available. Usually they are expensive, deteriorate in storage, and contain minerals and vitamins that are unnecessary for most patients. However, liquid preparations are useful for administration to infants and children, who often reject solid preparations or are unable to swallow them.

Combinations with other nutrients

During pregnancy, women tend to become deficient in both iron and folate. It is therefore desirable to combine both haematinics in one tablet. The addition of folate (250 μg) to ferrous sulfate (60 mg of iron) increases the tablet’s cost by an insignificant amount if at all.

Because ascorbic acid is a known enhancer of iron absorption, it has been incorporated into many iron preparations. When enough is added (at least 200 mg) ascorbic acid increases medicinal iron absorption by about 30% (47). Unfortunately, however, not only is ascorbic acid relatively expensive, but it increases the frequency of side-effects and thus the risk of poor compliance (48,49).

Dosage

Erythropoietic activity following iron administration is directly related to the severity of anaemia; the increase in haemoglobin concentration is inversely proportional to the initial concentration. The best absorption of therapeutic iron therefore occurs during the first few weeks of treatment. For example, adults taking 100 mg of iron (in the form of iron sulfate) twice a day with meals absorbed an average of 14% during the first week of therapy as compared with 7% after three weeks and 2% after four months (48). The first month of therapy would thus appear to be the most important time for ensuring the success of treatment. A positive response to treatment can be defined as a daily increase in haemoglobin concentration of 0.1 g/dl from the fourth day onwards. Although the response in terms of haemoglobin concentration is virtually complete after two months, iron therapy should continue for another two to three months to build up iron stores to about 250–300 mg, or the serum ferritin level to 30 μg/l.

For adolescents and adults the recommended dose is 60 mg of elemental iron per day in cases of mild anaemia, and 120 mg per day (2 x 60 mg) in cases of moderate to severe anaemia.
Iron deficiency anaemia

For infants and children the recommended dose is 3 mg of iron per kg of body weight per day. Higher doses have been used, e.g., twice this amount, but they are probably unnecessary. They also increase the risk of accidental overdose, especially in children between one and five years of age.

For pregnant women the daily administration of folate (500 μg) with iron (120 mg) is beneficial since anaemia during pregnancy is usually caused by a deficiency of both nutrients. A suitable combination tablet, to be taken twice a day, would contain 250 μg of folate and 60 mg of iron.

Side-effects

The oral administration of iron can cause gastrointestinal side-effects in some individuals such as epigastric discomfort, nausea, vomiting, constipation, and diarrhoea. The frequency of these side-effects is directly related to the dose of iron. It is independent of the specific iron compound used; no one compound is better tolerated than any of the others. However, as explained above, certain formulations are better tolerated, particularly the slow-release preparations. In addition, iron consumed with a meal is better tolerated than when it is taken on an empty stomach (50), although the amount of iron absorbed is reduced.

The major reason for the failure of iron therapy is non-compliance due to the side-effects caused by an excessively high initial dose of iron. The patient typically takes the pills for a few days and bears with the discomfort, but stops taking the medication as soon as he or she experiences an increased sense of well-being from the rise in haemoglobin; unfortunately, this occurs long before the haemoglobin has reached a normal level.

In cases of gastrointestinal intolerance, it is vital not to discontinue therapy and risk treatment failure. Rather, the dose of iron should be reduced and then gradually increased again until the full dose is reached and is well tolerated. If slow-release preparations are available and affordable, they should be used. With plain tablets, the frequency of side-effects can be reduced if the patient takes them with meals.

Parenteral iron therapy

There is little justification for giving parenteral iron when oral therapy is possible. The parenteral route is indicated only when oral adminis-
Treatment

Treatment causes severe vomiting that cannot be stopped by lowering the dose of iron, or in cases of persistent non-compliance. The most commonly used preparation for intramuscular or intravenous administration is Imferon R (iron dextran). The advantage of the intravenous method is that the complete iron requirement can be supplied in a single dose. This technique, known as total dose infusion, has been used especially in obstetric practice (51), where it solves the problem of non-compliance and permits the increased requirement during pregnancy to be met in full. The recommended intravenous dose for adults (including pregnant women) is 500 mg of iron in 10 ml of saline solution given over a period of 10 minutes following a test dose of 1-2 drops. Intravenous infusion must be done only in a hospital. The recommended intramuscular dose is 100 mg of iron in 2 ml of saline solution. Intramuscular administration should be used only when there are no adequate facilities available for intravenous administration.

Cost of treatment

According to the most recent information available, UNICEF supplies sugar-coated tablets containing ferrous sulfate (60 mg of elemental iron) plus folate (250 μg) for US$ 1 per 1000 tablets (FOB, UNIPAC, Copenhagen). On the open market, the price of uncoated or sugar-coated tablets containing 60-100 mg of elemental iron ranges from $4 to $10 per 1000 tablets. The cost of slow-release preparations is currently about two times higher, although bulk purchases by governmental and international agencies could lower the price significantly. Such preparations are, however, considerably more effective, a fact that needs to be borne in mind when comparative costs are assessed.

A total of 250 tablets containing 60-100 mg of iron will prevent or correct iron deficiency in most people, including pregnant women.
6. Prevention of iron deficiency anaemia

The four basic approaches to the prevention of iron deficiency anaemia are supplementation with medicinal iron, education and associated measures to increase dietary iron intake, the control of infection, and the fortification of a staple food with iron.

Supplementation with medicinal iron

Supplementation with medicinal iron has the advantage of producing rapid improvements in iron status. As a strategy, it also has a desirable specificity: it can be targeted at the population groups in greatest need of iron or at greatest risk of becoming iron-deficient. Indeed, iron supplementation programmes have a greater chance of success when directed at specific groups. Coverage of the entire population is virtually impossible except where there is an exceptionally effective health delivery system, and in any case it is unnecessary. Supplementation programmes do best to concentrate on high-risk groups such as pregnant women, infants and preschool children, and on “captive audiences”, for example, schoolchildren or plantation workers who can receive their supplements at school or work.

The effectiveness of iron supplementation is constrained by two important factors: the gastrointestinal side-effects of oral iron (see page 32) and the difficulty of sustaining motivation for two to three months in “patients” who do not perceive themselves to be ill. Both factors result in poor compliance with treatment, which poses a great challenge to health educators and social marketing strategists.

Pregnant women

Pregnant women are a priority group for iron supplementation. Identifying this group and distributing iron tablets to each pregnant woman is a task within the competence of primary health workers and should become their formal responsibility. The recommended daily dose is two tablets, each containing 60 mg of elemental iron plus 250 μg of folate, taken throughout the second half of pregnancy, i.e., approximately 250 tablets in all. Such supplementation taken under supervision has been demonstrated to prevent the development of anaemia. The recommended dose can be reduced initially to ensure
compliance. Supplementation should occur primarily during the second half of pregnancy, when the iron requirement is greatest. During early pregnancy, morning sickness will in any case reduce the effectiveness of supplementation.

As already discussed, the major obstacle to iron supplementation is poor compliance with treatment. This is often due to side-effects, but it may also stem from women's lack of awareness that they have a real need for iron during pregnancy. Mere delivery of the message and the tablets is not enough to ensure success. Women must be convinced of the importance of iron for their health and the health of their unborn child. To be persuasive, primary health workers and paramedical personnel need skill in the techniques of communication and motivation, all too often a neglected area of training (51a).

Preschool children

Iron supplementation of preschool children is also important and requires special planning. It may be accomplished relatively easily wherever such children congregate, such as the child-care centres that exist in many developing countries. To ensure the proper supervision, supplements can be administered by those responsible for the centres, thus freeing the primary health worker for other tasks. In addition, of course, every opportunity must be taken to supervise supplement intake at child health clinics and during other contacts with the health service.

Many supplementation programmes call for a 2–3 month course of one or more iron tablets daily. Although such a regimen is necessary to correct severe anaemia, it is doubtful whether such a long course is required for the mild-to-moderate anaemia usually found in this age group. To ensure more uniform iron coverage and higher compliance rates, it may be more practical to give the children a 2–3 week course based on a lower dose (30 mg of elemental iron daily in tablet or liquid form) several times a year.

Schoolchildren

Children of school age usually do not have the same high prevalence of anaemia as preschool children. They can be reached at their school if the primary health worker can establish the necessary links with it and ensure the regular intake of tablets under the teacher's supervision. Short courses are best, as for preschool children; the daily dose should be between 30 mg and 60 mg of elemental iron, depending on the child's age and weight.
Iron deficiency anaemia

Infants

Preventing anaemia in late infancy and early childhood through primary health care includes protecting and promoting breast-feeding for as long as possible, given the high absorbability of breast-milk iron, and encouraging the timely introduction of weaning foods that either enhance iron absorption or have been fortified with iron. Among rural populations in most developing countries, successful and prolonged breast-feeding is the rule; the contrary is more typical of urban areas, which is where efforts to promote breast-feeding should be concentrated. Breast milk appears to be adequate to cover the dietary iron requirements of normal-birth-weight infants up to the age of 6 months. Low-birth-weight infants may, however, require iron supplementation as from the age of 2 months.

The control of anaemia with commercially prepared iron-rich weaning foods is likely to have only limited success in rural communities, since these preparations are often expensive and thus beyond the reach of most families. Weaning foods rich in iron and/or vitamin C, such as purées of cooked vegetables and raw fruits, are not difficult to prepare in the home. However, parents need to be motivated and taught how to do so.

Dietary modification

Dietary iron intake can be increased in poor communities in two ways. The first is to ensure that people consume larger amounts of their habitual foods so that their energy needs are fully met. How much additional iron is thereby ingested will depend on how fully the existing energy gap is bridged. Since no qualitative changes in the diet are needed, this approach may appear to be simple but it involves increasing the purchasing power of households—which is beyond the capabilities of the health sector alone. Nevertheless, the practical importance of this strategy should not be underestimated, particularly in situations where it may be difficult to improve the bioavailability of the iron ingested. In parts of rural India, for example, total iron consumption increased by about 25–30% when the energy shortage was corrected (52,53). The result has some impact on iron status despite the fact that bioavailability remains unchanged.

Enhancing the bioavailability of the iron ingested, rather than its total amount, is the second basic approach to dietary manipulation. There are a number of strategies available, each with its advantages and drawbacks, but all are based either on promoting the intake of iron absorption enhancers, including haem iron, or on reducing the ingestion
of absorption inhibitors such as tannin and phytic acid (see Table 3, page 15, and Table 4, page 16).

It will be recalled that haem iron, in addition to serving as an iron source in its own right, effectively enhances the absorption of non-haem iron eaten during the same meal. Any campaign to promote the inclusion of meat in predominantly starch-based diets will, however, run into the obstacle of its high cost and, in many developing countries, the scarcity of animal foods. Even where efforts are being made to increase the production and availability of meat, it would be unrealistic to assume that meat consumption by poor rural people, among whom anaemia is most prevalent, will increase significantly in the near future. Religious and philosophical objections to the consumption of meat may also pose a problem. In short, a recommendation to include meat in the diet in order to combat iron deficiency anaemia should be made with caution, and only where people are likely to act on it.

In contrast, efforts to increase the ascorbic acid content of the diet have a greater chance of success. Vitamin C, whether naturally present in food or added in the form of crystalline ascorbic acid, has an enormous effect on the absorption of non-haem iron. The effect is dose-dependent; as shown in Fig. 5, the presence of 25, 50, 100, 250, and 500 mg of vitamin C in a given meal is associated with an approximate 2-, 3-, 4-, 5-, and 6-fold enhancement of iron absorption,

**FIG. 5. EFFECTS OF INCREASING QUANTITIES OF ASCORBIC ACID ON THE ABSORPTION OF NON-HAEM IRON IN A MEAL**
Iron deficiency anaemia

respectively (54,55). Table 8 gives the ascorbic acid content of some vitamin C-rich foods.

Table 8. APPROXIMATE ASCORBIC ACID CONTENT OF SELECTED FRUITS AND VEGETABLES

<table>
<thead>
<tr>
<th></th>
<th>Approximate amount of vitamin C (mg) per 100 g of food</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fruits:</strong></td>
<td></td>
</tr>
<tr>
<td>Guava, fresh</td>
<td>326</td>
</tr>
<tr>
<td>Lemon, fresh (juice)</td>
<td>37–50</td>
</tr>
<tr>
<td>Orange, fresh</td>
<td>46</td>
</tr>
<tr>
<td>Pineapple, fresh</td>
<td>37</td>
</tr>
<tr>
<td>Mango, fresh</td>
<td>42</td>
</tr>
<tr>
<td><strong>Vegetables:</strong></td>
<td></td>
</tr>
<tr>
<td>Cabbage, raw</td>
<td>54–60</td>
</tr>
<tr>
<td>Cabbage, boiled</td>
<td>15</td>
</tr>
<tr>
<td>Cauliflower, raw</td>
<td>60–96</td>
</tr>
<tr>
<td>Cauliflower, boiled</td>
<td>20</td>
</tr>
<tr>
<td>Potato, raw</td>
<td>21</td>
</tr>
<tr>
<td>Potato, boiled</td>
<td>12–18</td>
</tr>
<tr>
<td>Sweet potato, raw</td>
<td>25–37</td>
</tr>
<tr>
<td>Sweet potato, boiled</td>
<td>15</td>
</tr>
<tr>
<td>Spinach, boiled</td>
<td>7–25</td>
</tr>
<tr>
<td>Tomato, raw</td>
<td>20–26</td>
</tr>
<tr>
<td>Turnip, boiled</td>
<td>17</td>
</tr>
</tbody>
</table>

*Source: references 56 and 57.

In many rural homes, vegetables and fruits are eaten only infrequently and in small amounts. Persuading families to add these foods to their basically starchy diet can have a considerable impact. However, the difficulties involved in translating these ideas into action are by no means trivial and must not be underestimated. Past efforts have yielded mixed results, for example in India, where families were encouraged to start kitchen gardens and grow suitable vegetables through the Applied Nutrition Programme. Experience shows that success depends on such factors as the availability of water, appropriate fencing to protect what is grown, and an appreciation of the value of the produce (58).

Approximately 50–80% of the vitamin C originally present in food can be lost during cooking. Moreover, the vitamin C content of food that is cooked and left standing decreases considerably; reheating reduces it still further. In many rural households, food for the day is all cooked at the same time, providing two meals that may be eaten as much as
12 hours apart. Under such circumstances, it is difficult to ensure that enough vitamin C is retained in the food unless a good source of ascorbic acid is added or the food has a high vitamin C content to begin with. The consumption of fruits and vegetables in raw form will overcome this problem, although the risk of gastrointestinal infection from raw vegetables should not be ignored. Nutrition education provided by primary health workers needs to stress these points.

A further strategy is to encourage the use of a number of common household processing methods—germination, malting, and fermentation—which can enhance iron absorption by increasing the vitamin C content, by lowering the tannin and phytic acid content, or both (59-61). For example, the germination of some cereals and legumes for 24-48 hours is associated with the appearance of 10-70 mg of ascorbic acid per 100 g, an 8-25% reduction in tannin concentration, and a 25-35% decrease in phytic acid concentration. The bioavailability of iron from such germinated grains, as determined in vitro, increases almost 2-fold. The malting of minor millets results in a 5-10-fold improvement in bioavailability.

**Control of viral, bacterial and parasitic infections**

Effective, timely curative care could diminish the adverse nutritional consequences of viral and bacterial disease. Although the number of infective episodes is unlikely to be reduced, proper curative services can at least contribute to a reduction in the duration and severity of infections. This alone would help improve iron status even if there is no increase in dietary iron consumption. For the reasons discussed earlier, preschool children, in particular, would benefit from such improvements in health care.

It is vital to educate the family about proper feeding practices during and after periods of infective illness. This is especially important where young children are concerned, since they are often placed on a semi-starvation diet when ill. Primary health workers need to convince families to give sick children as much liquid as possible and to continue feeding them as much as they will tolerate with gentle persuasion. Breast-feeding should not be interrupted. Continued breast-feeding does much to prevent infectious diseases, quite apart from its direct effect on iron status.

Immunization continues to gain in acceptance, and primary health care can strengthen this activity considerably. However, there are as yet no vaccines available against the most frequent gastrointestinal and respiratory infections. The control of these infections requires preventive public health measures—the provision of safe water and
Iron deficiency anaemia

improvements in environmental sanitation and in personal hygiene. These are among the essential elements of primary health care.

When it comes to parasitic infestation, it has been established beyond dispute that hookworm (*Ancylostoma* and *Necator*) and *Schistosoma* play a role in the etiology of anaemia by causing chronic blood loss. The role of other common intestinal parasites is less certain. There is some evidence that a number of parasites can interfere with the absorption of some nutrients, particularly if the worm load is heavy; this has been shown for *Giardia*, which reduces iron absorption (62). From both a health and a nutritional standpoint it is undesirable to harbour parasites, and recommendations are frequently made that deworming should be done routinely as part of primary health care. It is open to question, however, whether this is the best way of dealing with the problem.

Deworming in the absence of simultaneous efforts to eradicate the reservoir of infection is quickly followed by reinfestation and a renewed need to deworm. The high cost of anthelminthic drugs and the logistic problems associated with large-scale deworming militate against the cost-effectiveness of such repeated operations. Deworming *per se* can be temporarily effective in decreasing the parasitic load but may be of only minor benefit in terms of haemoglobin level. The provision of additional iron, either through supplementation with medicinal iron or by food fortification, results in a much greater increase in haemoglobin concentration, even when deworming is not done.

The decision to include deworming as a routine primary health care activity in communities where hookworm anaemia is endemic should therefore be taken carefully, particularly when no parallel effort is made to reduce or eliminate reinfestation through, for instance, the provision of cheap footwear. In individual cases of severe anaemia resulting from a heavy hookworm load, treatment should obviously include deworming.

**Food fortification**

The fortification of a widely consumed and centrally processed staple food with iron is the backbone of anaemia control in many countries. Fortification involves centralized decision-making, legislation, and action by flour mills and other food processing plants. Since it leaves little or no room for community involvement, fortification cannot be considered to be within the scope of primary health care and will be discussed only briefly here. The reader is referred to other sources (30,63) for a fuller description of this approach as used under various circumstances.

Food fortification is one of the most effective ways of preventing iron
deficiency. It can be targeted to reach some or all population groups, and it does not necessarily require the cooperation of the individual. The initial cost is modest, and recurring expenses are less than those of supplementation. The major difficulty is identifying a suitable food to be fortified and, of equal importance, a form of iron that is adequately absorbed without altering the taste or appearance of the food. The target population needs, of course, to be accustomed to the fortified food and must be able to afford it.

Fortification with iron is more difficult technically than fortification with other nutrients because the bioavailable forms of iron are chemically reactive and tend to produce undesirable changes in the food. For example, soluble ferrous salts often produce colour changes by forming complexes with sulfur compounds, tannins, polyphenols, and other substances. Discoloration is particularly undesirable when the food to be fortified is light in colour. In addition, reactive iron compounds catalyse oxidative reactions, resulting in undesirable odours and flavours.

Since people are unlikely to accept a fortified food in which the added iron can be detected, fortification programmes have tended to rely on inert iron compounds that are poorly absorbed and therefore more or less ineffective. Nowadays, however, big efforts are being made to find more suitable forms of fortification iron.

Ferrous sulfate has been used extensively for the fortification of bread and other bakery products that are stored for only short periods. When such fortified foods are stored for a few months, they develop a rancid flavour. Ferrous fumarate, which is somewhat more expensive, is successfully used to fortify a corn-soya-milk preparation (CSM) that is distributed as a weaning or supplementary food by the United States Agency for International Development in its food assistance programmes. The use of ferrous lactate and ferrous gluconate is limited, for economic reasons, to the fortification of such products as milk and soy-based infant formulas. Elemental iron is also slightly more expensive than ferrous sulfate. Of good bioavailability and stability, it is commonly used to fortify wheat flour and bread in North America and Western Europe.

In industrialized countries, the most commonly fortified food products are wheat flour and bread, corn-meal and grits, milk products including infant formulas, and weaning foods (infant cereals). Breast-feeding promotion is an important concern of primary health care programmes, as unsupplemented breast-feeding helps to prevent iron deficiency anaemia. Nevertheless, after 6 months of age, all breast-fed infants should be provided with an additional source of iron. Infant formula can be effectively fortified with ferrous sulfate, ferrous gluconate, or ferrous lactate. In addition, given the limited quantities of formula that need to be fortified, ascorbic acid can be included at reasonable cost to enhance the bioavailability of the iron.
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In Chile, the use of milk formula fortified with iron and ascorbic acid has been found to reduce the prevalence of anaemia at 15 months of age to less than 2%, as compared with 28% among infants who received non-fortified formula. Powdered milk is thus a good vehicle for iron fortification in that country since it is distributed free by the Government to more than 80% of infants and lactating mothers. Infants aged 6–12 months are given 2 kg of milk powder a month (64).

In other developing countries, consideration has been given to the fortification of salt, sugar, rice, fish sauce, and fish paste. The combined use of ferric orthophosphate and sodium acid sulfate in the fortification of table salt has recently been reported to produce acceptable long-term iron bioavailability with only slight discoloration.

In recent field trials in India, salt was fortified in this way in order to provide an additional iron intake for adults of 10–15 mg per day (65). The product was tested for 12–18 months in various settings and was generally well accepted. A new, less expensive formulation containing ferrous sulfate, orthophosphoric acid, and sodium acid sulfate, has been found to be equally effective. A decrease in the prevalence of anaemia was observed in the areas where it had previously been high. The cost of salt fortification, which raises the price of the salt by 20%, is estimated to be about US$ 0.07 per person per year. The problem with salt as a vehicle for iron fortification is the difficulty in foreseeing all of its interactive possibilities with food because it is used in so many culinary preparations.

EDTA (ethylene diamine tetraacetate), widely used in the food processing industry as a chelating agent, has been found to be an effective enhancer of iron bioavailability. The iron salt of EDTA has been successfully used to fortify sugar in Guatemala (13 mg iron/100 g sugar) (66). Field trials have shown that its consumption (40 g per day per person) improves the population’s iron status. Fortified sugar costs approximately 2% more than non-fortified sugar. Recent work with unrefined Egyptian wheat flour indicates that the disodium salt of EDTA enhances the bioavailability of ferrous sulfate supplement by reducing the inhibitory effects of both wheat phytate and high bread-baking temperatures. These properties of sodium iron EDTA make it an attractive substance for future fortification programmes.

It should be recognized that while food fortification with iron poses few or no problems in the developed world, it requires an industrial infrastructure that does not exist in some developing countries, particularly in Africa.
7. **Costs and benefits of prevention**

Levin has prepared a cost-benefit analysis of iron deficiency anaemia prevention through fortification and supplementation (67).

The costs involved in fortification programmes include the fortificants, stabilizers, mixing, possibly special packaging, and distribution. In India, the cost of fortification increases the price of salt by about 20%, while adding iron to sugar in Guatemala raises its cost by only about 2%. It should be noted, however, that the price of salt is low and the amount consumed every day is small, so that a 20% increase is still acceptable. Levin estimates that the cost per person per year in a large-scale programme of fortification with iron is about US$ 0.20–0.30. The cost would probably be double if ascorbic acid were added as well.

Levin's calculation of costs related to supplementation with medicinal iron is based on delivery systems built around community- or village-based health care. These costs include salaries, medicinal iron (possibly combined with folate), transport, and distribution. On this basis, intervention costs range between $2 and $3 per person per year for the delivery of ferrous sulfate tablets, depending on population density and the other services provided by the same health workers.

When it comes to benefits, anaemia control produces an immediate increase in physical work output and leads over the longer term to lower morbidity and mortality, higher productivity outside the workplace, improved quality of leisure time, increased learning capacity, and a greater sense of well-being, among other things.

Because the value of many of these benefits is difficult or impossible to measure in material terms, Levin's study looks solely at the benefits accruing from increased labour productivity. Using 1980 figures, he calculates that the annual per capita benefits range from $7 in Indonesia to $43 in Kenya and $57 in Mexico following a 10% increase in haemoglobin concentration resulting from iron fortification. With a 25% increase in haemoglobin concentration after medicinal iron supplementation, the annual per capita benefits are about $18 in Indonesia, $107 in Kenya, and $142 in Mexico. These figures are impressive, given the annual earnings of agricultural workers in these societies.

In the three countries surveyed, each United States dollar of cost for anaemia prevention programmes is estimated to have yielded from
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US$6 to $58 in benefit. Levin concludes, based on a variety of mainly conservative assumptions, that the cost-benefit ratio of both iron fortification and iron supplementation programmes exceeds unity by a considerable margin, and that they therefore represent highly productive investments for developing countries.
8. The planning and execution of anaemia control programmes

Many countries have long-standing activities aimed at the prevention and control of iron deficiency anaemia, but few have a coordinated strategy for combating this condition. Activities tend to be carried out piecemeal and are rarely evaluated, although problems of supply and compliance are known to be very serious. Population coverage is poor because the iron tablets are distributed mainly through hospitals and clinics.

The development of primary health care in many countries now affords a precious opportunity to control iron deficiency anaemia through a strategy that is direct, inexpensive and more effective. Depending on the local epidemiological characteristics of anaemia and the form that primary health care is taking, each country can fashion an overall strategy from the basic control approaches described in Chapter 6: medicinal iron supplementation, dietary modification, and infection control. Food fortification is highly effective but is feasible only where the necessary industrial infrastructure exists. It is generally unwise for an anaemia control strategy to rely on only one of these four approaches; in isolation, it is unlikely to have a sufficient effect.

Components of the anaemia control strategy

Supplementation with medicinal iron is a highly specific and cost-effective control measure (see pages 34–36). Iron or iron-folate tablets and solutions can be delivered formally through the health system or informally through the sale of over-the-counter preparations. The success of supplementation depends on a well organized primary health care system, adequate population coverage in relation to the target group or groups, a regular supply of appropriately selected supplements, a low prevalence of side-effects, and effective education and motivation of recipients to ensure compliance with the treatment regimen. The problem of access to those in need of supplementation is not inconsiderable but it should diminish as the primary care system expands. If the anaemia control strategy is properly integrated into general health care such as maternal and child health programmes, iron-folate tablets can be given at antenatal examinations, at postnatal and family planning visits, and at child health clinics. The aim should be to prevent anaemia in those at special risk, such as pregnant women.
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and preschool children, and to treat it when suspected and diagnosed in others.

For supplementation to be successful, programme managers must develop very clear criteria on dosage, follow-up, referral, and management of side-effects and non-compliance, among other things, and incorporate these into the training of health personnel and into standard supervisory procedures. A special consideration is the risk of iron overload when supplements are planned for populations with common genetic abnormalities of haemoglobin synthesis or iron metabolism. While programme managers must bear this risk in mind, they should be aware that the beneficial effects of treatment and prevention of iron deficiency anaemia far outweigh the dangers of possible iron overload.

Since iron intake and bioavailability and the organization of health care differ so much from one place to another, it may be useful to proceed stepwise in the implementation of a supplementation programme. A preliminary small-scale field trial may help to determine the optimum iron dosage for the various target groups and to find solutions to any logistic and other problems.

A final consideration when supplementation is envisaged is its cost. While supplementation is undeniably cost-effective and medicinal iron is relatively inexpensive, the total outlay can be considerable in countries where the target groups are very large. According to recent estimates (I), about 40% of the population in Africa and south-east Asia is anaemic. On the assumption that the anaemia is due to iron deficiency in two-thirds of these cases, it can be estimated that iron supplements would be needed by approximately one-quarter of the total population. Even with the inexpensive iron-folate tablets supplied by UNICEF, supplementation would cost approximately US$65 per 1000 population, not counting the cost of distribution. In many countries such a heavy investment would be considered excessive when weighed against other public health priorities. In these countries it may be more justifiable for the anaemia control strategy to rely mainly on the other control approaches—dietary manipulation, infection control and, where feasible, food fortification—and to reserve routine supplementation for special groups such as pregnant women.

Dietary modification (see pages 36–39) makes use of a number of “messages”, some of which are similar to the general nutrition advice that is likely to be given through primary health care. These are: eat more haem and non-haem iron, ensure that infants and young children consume enough energy for their needs (in older age groups, raising energy consumption will probably depend more on improved food supply than on improved nutritional know-how), and give infants unsupplemented breast-feeding for the first 4–6 months and supplement it thereafter with a proper complementary diet.
Other messages, while more specific to anaemia control, in no way contradict general nutrition advice. These are the messages designed to discourage the consumption of iron absorption inhibitors with meals (e.g., avoid drinking tea at mealtime) and to encourage the concurrent consumption of foods rich in vitamin C, such as citrus fruits, pawpaw, mango, and many vegetables (see Table 8, page 38). A food composition table will list many more sources of vitamin C that are appropriate for each country and season.

It will be apparent that certain dietary aspects of the anaemia control strategy can be linked with other nutrition activities, ongoing or planned, and can even be incorporated into the national food and nutrition policy or strategy, where such exists. The strategy can also include links with other sectors. For example, it can call for the development of a fruit-tree distribution programme in collaboration with the agricultural extension services or the forestry department.

**Infection control** is the third basic approach that can be woven into an anaemia control strategy. Its objective should be to lower the prevalence of infective morbidity and heavy parasitic infestation to a level below public health significance in populations who are at risk of iron deficiency anaemia. Like supplementation and dietary manipulation, infection control can be successful only if the proper links are established with relevant elements of primary health care. The specific aims (pages 39–40) are to secure prompt and effective health care for infections, to feed children properly when ill, to improve the disposal of faeces and other solid wastes, to encourage better personal hygiene, and to improve access to clean water.

**Situation analysis**

The first step in developing a control strategy is to carry out a situation analysis. The purpose is twofold: to establish a minimal data base for initial decision-making, and to identify information gaps that will have to be filled in time. At the very least, information is needed initially on the following:

- the epidemiology of anaemia, including age and sex distribution, geographical distribution, and main causes (iron deficiency, combined iron and folate deficiency, infections, etc.);

- the administrative infrastructure, i.e., the distribution of health staff and facilities, community organization, transport and storage facilities, the management structure of primary health care including supplies and budgeting, etc.;

- the geographical, nutritional, and socioeconomic setting, for example, access of the population to health and social services,
main dietary sources (actual and potential) of iron and ascorbic acid, major inhibitors of iron absorption, and local customs with an influence on anaemia prevalence, including positive practices (unsupplemented breast-feeding up to 4 or 6 months) and negative (semi-starvation of sick children, drinking of tea with meals);

- current and past experience showing what has been tried and found to be successful or unsuccessful for anaemia control in the country and in similar situations elsewhere.

Those carrying out the situation analysis will have to gather their information from a variety of sources, in particular from any investigations and surveys that are specially undertaken, but also from government reports, nongovernmental organizations, unpublished research, and personal experience.

Characteristics and goals of the strategy

Even before the situation analysis has been completed, an outline can be drawn up of the general characteristics, objectives and goals of the strategy. Based on the results of the situation analysis and together with the people who carried it out, the outline can then be improved and made more specific. In most situations, the strategy will have the following general features.

1. It will be integrated so far as possible into the national primary health care system so as to keep costs low through the sharing of facilities, training and supervision, and so as to maximize health benefits through the strategy's support to maternal and child health, general nutrition and other allied health care.

2. It will be based on general scientific, epidemiological and therapeutic principles, but will use technologies and approaches that are specifically adapted to the country and the problem.

3. Operational responsibility for coordinating the strategy will be vested in the ministry or analogous body responsible for health, but the strategy itself will involve other sectors, such as agriculture and education (particularly extension services), and other branches of government, for example, that responsible for the drafting and adoption of legislation.

4. Monitoring and evaluation, including screening for iron deficiency anaemia where possible, will be incorporated into the strategy as a management tool to encourage flexibility and the improvement of programme operations over time.
The objectives of the anaemia strategy are unlikely to include the complete elimination of iron deficiency anaemia, since this cannot be achieved in most countries in the foreseeable future. The strategy must, however, set target levels of achievement (goals) for the most vulnerable groups and concentrate in the first instance on severe anaemia. In many countries the prime target groups will be women in the second half of pregnancy and preschool children.

Supplies

Supplies are a basic consideration wherever the anaemia control strategy relies on supplementation. Periodic estimates are needed of the quantities of the various supplements required over time, and a logistics system has to be developed to ensure regular delivery. In most countries, this will require joint programming by those responsible for the anaemia strategy, the ministry of health’s medical stores, and the essential drugs programme. It is vital to establish budget lines for the necessary purchases.

An appropriate packaging system must also be developed. One approach is to use packets similar to those developed for oral contraceptives, which can help patients remember to take their tablets regularly. Supplements need to be clearly labelled to remind both health workers and patients of the correct dosage. In many countries it is not easy to find suitable containers, especially for liquid preparations. All these problems must be solved if the anaemia strategy is to be successful.

Public education

With the possible exception of food fortification, the success of all four technical approaches to anaemia control depends on the active participation of the population. Hence the need for a public education support strategy based on careful analysis of the behavioural changes required.

The major changes in behaviour that are needed centre on compliance with supplementation regiments, changes in cooking and eating habits, and measures for infection control, including better personal hygiene and more rational feeding of sick children—responsibilities that in many societies are assigned primarily to women (68). It is important to recognize that each of these behavioural changes implies an expenditure of extra time and effort. The question of how this extra workload can be spread fairly and effectively will need to be examined in every
Iron deficiency anaemia

Community before any educational messages are designed and targeted at given groups.

Educational messages are unlikely to succeed unless they take account of the real motivations of the target group. In devising effective messages, educational planners should bear in mind the older lessons learnt from community development and borrow freely from the newer methods of social marketing adapted from advertising (69,70). Many past efforts at anaemia control failed in part because their educational strategies ignored these insights and techniques. There is also a growing body of educational experience relating to nutrition and health in general that needs to be tapped (71,72). Among other things, this experience points to the wisdom of involving people beforehand rather than simply bombarding them with ready-made messages. Community development groups, where they exist, can help draw up the anaemia control strategy, including the health and nutrition promotion that they themselves can carry out with support from service providers.

Monitoring and evaluation

A continuing monitoring and evaluation strategy is best incorporated into the country’s existing health information system, so that it becomes part of the established routine.

Measuring the prevalence and severity of iron deficiency anaemia is essential, although there are still many technical obstacles to screening for anaemia in the community. Studies are under way to develop a reasonably accurate, rapid and inexpensive method which can be carried out with apparatus that does not break easily and is not dependent on electricity (see Chapter 4).

Monitoring and evaluation should also look at how the anaemia control strategy is progressing technically and managerially. The supply of haematinics, for example, needs to be watched carefully. This is often best done through the monitoring and evaluation system developed for the country's essential drugs programme. Potential problems such as noncompliance need to be monitored so that serious failures can be anticipated and preventive or remedial measures taken in good time. All monitoring and evaluation data should be used to improve and adjust programme operations.
Distribution of responsibilities within the health care system

In areas where moderate or severe iron deficiency anaemia exists, the anaemia control strategy is likely to include all of the basic approaches—supplementation, dietary modification, and infection control. In such settings the distribution of responsibilities among the different levels of the health system can be summarized as follows.

<table>
<thead>
<tr>
<th>Level of health system</th>
<th>Duties/responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community level:</td>
<td></td>
</tr>
<tr>
<td>Community/primary</td>
<td>Ensure that all women routinely take iron-folate supplements during the second half of pregnancy. When possible, screen other high-risk groups (especially preschool children) and treat all cases of anaemia. If screening is not possible, give iron-folate supplements to these groups at least. Establish links with child-care centres and schools where the taking of supplements can be supervised. In liaison with community development groups, carry out health and nutrition education for dietary modification and infection control. In cases of infectious or parasitic disease, provide or refer for timely curative care. Improve levels of personal and community hygiene.</td>
</tr>
<tr>
<td>health worker</td>
<td></td>
</tr>
<tr>
<td>First-level health facility:</td>
<td>Supplement all women with iron-folate during the second half of pregnancy. Screen other high-risk groups and treat all cases of anaemia. Refer patients with severe anaemia (haemoglobin concentration less than 7 g/l) to the district hospital for treatment. Treat patients with hookworm, <em>Schistosoma</em> and <em>Giardia</em> infestations. Carry out health and nutrition education.</td>
</tr>
</tbody>
</table>
Iron deficiency anaemia

First referral level: rural or district hospital

Screen individuals in high-risk groups. Test others when anaemia is suspected clinically. Treat all cases of anaemia. Diagnose and treat all cases of parasitic infestation.

District health officer

Determine the epidemiology of iron deficiency anaemia, if possible by determining the iron status of the population. Organize and integrate the treatment and prevention of iron deficiency anaemia into the primary health care system at all levels. Maintain supplies at all levels in district. Organize training for health personnel, including community/primary health workers, in the treatment and prevention of iron deficiency anaemia, related nutrition education, and the control of relevant infectious and parasitic diseases. Mobilize district resources such as community and political groups and coordinate with other sectors (education, water and sanitation, forestry, agriculture).

Provincial or national health administrator

Monitor and evaluate the technical and logistic aspects of the programme. Ensure an efficient flow of suitable supplies. Mobilize resources to overcome problems.

* The control measures described in this book and summarized above hold out great hope for reducing the burden of iron deficiency anaemia. However, it would be a mistake to think that they will be easy to apply. Changes in cooking practices, for example, are far more difficult to achieve than to propose. The effective delivery of messages intended to motivate healthy women to keep taking their iron tablets, regardless of unpleasant side-effects, requires skills of a level and type not often found in primary health workers. Health care systems, especially at their periphery, need considerable upgrading before they can ensure timely curative care for infectious and parasitic diseases. All
these inadequacies must be corrected if primary health care is to make a significant contribution to the control of iron deficiency anaemia.

At the same time, it must be borne in mind that most of the control measures used against anaemia will reinforce the action taken against numerous other health and nutrition problems, and vice-versa. Anaemia control through primary health care should therefore be seen not as an isolated activity but as an integral part of total health care and socioeconomic development.
REFERENCES


15. Yusufji, D. et al. Iron, folate and vitamin B₁₂ nutrition in


* This report is also available in French and Spanish. Single copies of all INACG reports are available without charge to individuals in developing countries. Multiple copies and copies for individuals in developed countries are available at a nominal charge depending on the printing and mailing costs. Please address requests to: The Nutrition Foundation, Inc., 1126 Sixteenth Street NW, Washington, DC 20036, USA.


* For information on how to obtain copies of INACG reports, see footnote to page 55.
References


45. Blaud, P. Sur les maladies chlorotiques, et sur un mode de traitement spécifique dans ces affections. [Concerning the chloroses and a specific method of treating these conditions.] *Revue médicale française et étrangère, 45*:341-367 (1832).


Iron deficiency anaemia


* For information on how to obtain copies of INACG reports, see footnote to page 55.
Iron deficiency anaemia afflicts millions of people the world over, primarily women of childbearing age and their young children in developing countries.

Cost-benefit studies have shown that it makes economic good sense to prevent this debilitating, and sometimes fatal, condition by supplementing the diet with medicinal iron. This and other control approaches that lend themselves to implementation through primary health care are the main subject of this guide.

The information included in this book will allow programme managers to build up a coherent strategy for the control of iron deficiency anaemia. First, the factors that govern the body’s absorption of iron are explained and the daily iron requirements of various population groups summarized. Building on this information, the book shows how relatively simple dietary changes could prevent anaemia. It also outlines other useful interventions, such as better feeding of ill children and the distribution of iron tablets. Up-to-date laboratory methods for detecting anaemia and iron deficiency are described, although the guide stresses that routine laboratory confirmation is unnecessary in the case of pregnant women, who almost invariably require medicinal iron. The final section of the book provides guidance on fashioning an appropriate control strategy and assigning responsibility for the various tasks involved.