Nutritional anaemias are extremely prevalent worldwide. Unlike protein-energy malnutrition (PEM), vitamin A deficiency and iodine deficiency disorders (IDD), these anaemias occur frequently in both developing and industrialized countries. The most common cause of anaemia is a deficiency of iron, although not necessarily a dietary deficiency of total iron intake. Deficiencies of folates (or folic acid), vitamin B₁₂ and protein may also cause anaemia. Ascorbic acid, vitamin E, copper and pyridoxine are also needed for production of red blood cells (erythrocytes). Vitamin A deficiency is also associated with anaemia.

Anaemias can be classified in numerous ways, some based on the cause of the disease and others based on the appearance of the red blood cells. These classifications are fully discussed in medical textbooks.

Some anaemias do not have causes related to nutrition but are caused, for example, by congenital abnormalities or inherited characteristics; such anaemias, which include sickle cell disease, aplastic anaemias, thalassaemias and severe haemorrhage, are not covered here.

Based on the characteristics of the blood cells or other features, anaemias may be classified as microcytic (having small red blood cells), macrocytic (having large red blood cells), haemolytic (having many ruptured red blood cells) or hypochromic (having pale-coloured cells with less haemoglobin). Macrocytic anaemias are often caused by folate or vitamin B₁₂ deficiencies.

In anaemia the blood has less haemoglobin than normal. Haemoglobin is the pigment in red cells that gives blood its red colour. It is made of protein with iron linked to it. Haemoglobin carries oxygen in the blood to all parts of the body. In anaemia either the amount of haemoglobin in each red cell is low (hypochromic anaemia) or there is a reduction in the total number of red cells in the body. The life of each red blood cell is about four months, and the red bone marrow is constantly manufacturing new cells for replacement. This process requires adequate amounts of nutrients, especially iron, other minerals, protein and vitamins, all of which originate in the food consumed.

Iron deficiency is the most prevalent important nutritional problem of humans. It threatens over 60 percent of women and children in most non-industrialized countries, and more than half of these have overt anaemia. In most industrialized countries in North America, Europe and Asia, 12 to 18 percent of women are anaemic.

Although deficiency diseases are usually considered mainly as consequences of a lack of the nutrient in the diet, iron deficiency anaemia occurs frequently in people whose diets contain quantities of iron close to the recommended allowances. However, some forms of iron are absorbed better than others; certain items in the diet enhance or detract from iron absorption; and iron can be lost because of many conditions, an important one in many tropical countries being hookworm infection, which is very common.

Nutritional anaemias have until recently been relatively neglected and not infrequently remain undiagnosed. There are many reasons for the lack of attention, but the most important are probably that the symptoms and signs are much less obvious than in severe PEM, IDD or xerophthalmia, and that although anaemias do contribute to mortality rates they do not often do so in a dramatic way, and death is usually ascribed to another more conspicuous cause such as childbirth. However, research now indicates that iron deficiency has very important implications, including poorer learning ability and behavioural abnormalities in children, lower ability to work hard and poor appetite and growth.

Causes and epidemiology
To maintain good iron nutritional status each individual needs to have an adequate quantity of iron in the diet. The iron has to be in a form that permits a sufficient amount of it to be absorbed from the intestines. The absorption of iron may be enhanced or inhibited by other dietary substances.

Human beings have the ability both to store and to conserve iron, and it must also be transported properly within the body. The average male adult has 4 to 5 g of iron in his body, most of it in haemoglobin, a little in myoglobin and in enzymes and around 1 g in storage iron, mainly ferritin in the cells, especially in the liver and bone marrow. Losses of iron from the body must not deplete the supply to less than that needed for manufacture of new red blood cells.

To produce new cells the body needs adequate quantities and quality of protein, minerals and vitamins in the diet. Protein is needed both for the framework of the red blood cells and for the manufacture of the haemoglobin to go with it. Iron is essential for the manufacture of haemoglobin, and if a sufficient amount is not available, the cells produced will be smaller and each cell will contain less haemoglobin than normal. Copper and cobalt are other minerals necessary in small amounts. Fолates and vitamin B_{12} are also necessary for the normal manufacture of red blood cells. If either is deficient, large abnormal red blood cells without adequate haemoglobin are produced. Ascorbic acid (vitamin C) also has a role in blood formation. Providing vitamin A during pregnancy has been shown to improve haemoglobin levels.

Of the dietary deficiency causes of nutritional anaemias, iron deficiency is clearly by far the most important. Good dietary sources of iron include foods of animal origin such as liver, red meat and blood products, all containing haem iron, and vegetable sources such as some pulses, dark green leafy vegetables and millet, all containing non-haem iron. However, the total quantity of iron in the diet is not the only factor that influences the likelihood of developing anaemia. The type of iron in the diet, the individual's requirements for iron, iron losses and other factors often are the determining factors.

Iron absorption is influenced by many factors. In general, humans absorb only about 10 percent of the iron in the food they consume. The adult male loses only about 0.5 to 1 mg of iron daily; his daily requirement for iron is therefore about 10 mg per day. On an average monthly basis, the adult pre-menopausal woman loses about twice as much iron as a man. Similarly, iron is lost during childbirth and lactation. Additional dietary iron is needed by pregnant women and growing children.

The availability of iron in foods varies greatly. In general, haem iron from foods of animal origin (meat, poultry and fish) is well absorbed, but the non-haem iron in vegetable products, including cereals such as wheat, maize and rice, is poorly absorbed. These differences may be modified when a mixture of foods is consumed. It is well known that phytates and phosphates, which are present in cereal grains, inhibit iron absorption. On the other hand, protein and ascorbic acid (vitamin C) enhance iron absorption. Recent research has shown that ascorbic acid mixed with table salt and added to cereals increases the absorption of intrinsic iron in the cereals two- to fourfold. The consumption of vitamin C-rich foods such as fresh fruits and vegetables with a meal may therefore promote iron absorption. Egg yolk impairs the absorption of iron, even though eggs are one of the better sources of dietary iron. Tea consumed with a meal may reduce the iron absorbed from the meal.

The normal child at birth has a high haemoglobin level (usually at least 18 g per 100 ml), but during the first few weeks many cells are haemolysed. The iron liberated is not lost but is stored in the body, especially in the liver and spleen. As milk is a poor source of iron, this reserve store is used during the early months of life to help increase the volume of blood, which is necessary as the baby grows. Premature infants have fewer red blood cells at birth than full-term infants, so they are much more prone to anaemia. In addition, iron deficiency in the mother may affect the infant's vital iron store and render the infant more vulnerable to anaemia. A baby's store of iron plus the small quantity of iron supplied in breastmilk suffice for perhaps six months, but then other iron-containing foods are needed in the diet. Although it is desirable that breastfeeding should continue well beyond six months, it is also necessary that other foods containing iron be introduced into the diet at this time.
Although most solid diets, both for children and adults, provide the recommended allowances for iron, the iron may be poorly absorbed. Many people have increased needs because of blood loss from hookworm or bilharzia infections, menstruation, childbirth or wounds. Women have increased needs during pregnancy, when iron is needed for the foetus, and during lactation, for the iron in breastmilk. It is stressed that iron from vegetable products, including cereal grains, is less well absorbed than that from most animal products.

Anaemia is common in premature infants; in young children over six months of age on a purely milk diet; in persons infected with certain parasites; and in those who get only marginal quantities of iron, mainly from vegetable foods. It is more common in women, especially pregnant and lactating women, than in men.

In most of the world, both North and South, the greatest attention to iron deficiency anaemia is directed at women during pregnancy, when they have increased needs for iron and often become anaemic. Pregnant women form the one group of the healthy population who are advised to take a medicinal dietary supplement, usually iron and folic acid. Pregnant and lactating women are a group at especially high risk of developing anaemia.

It is only in recent years that the prevalence and importance of iron deficiency apart from anaemia has been widely discussed. Clearly, however, if the causes of iron deficiency are not removed, corrected or alleviated then the deficiency will lead to anaemia, and gradually the anaemia will become more serious. Increasing evidence suggests that iron deficiency as manifested by low body iron stores, even in the absence of overt anaemia, is associated with poorer learning and decreased cognitive development.

International agencies now claim that iron deficiency anaemia is the most common nutritional disorder in the world, affecting over 1,000 million people. In females of child-bearing age in poor countries prevalence rates range from 64 percent in South Asia to 23 percent in South America, with an overall mean of 42 percent (Table 23). Prevalence rates are usually considerably higher in pregnant women, with an overall mean of 51 percent. Thus half the pregnant women in these regions, whose inhabitants represent 75 percent of the world's population, have anaemia. Unlike reported figures for PEM and vitamin A deficiency, which are declining, estimates suggest that anaemia prevalence rates are increasing.

In most of the developing regions, and particularly among persons with anaemia or at risk of iron deficiency, much of the iron consumed is non-haem iron from staple foods (rice, wheat, maize, root crops or tubers). In many countries the proportion of dietary iron coming from legumes and vegetables has declined, and rather small quantities of meat, fish and other good sources of haem iron are consumed. In some of the regions with the highest prevalence of anaemia the poor are not improving their dietary intake of iron, and in some areas the per caput supply of dietary iron may even be decreasing year by year.

In many parts of the world where iron deficiency anaemia is prevalent it is due as much to iron losses as to poor iron intakes. Whenever blood is lost from the body, iron is also lost. Thus iron is lost in menstruation and childbirth and also when pathological conditions are present such as bleeding peptic ulcers, wounds and a variety of abnormalities involving blood loss from the intestinal or urinary tract, the skin or various mucous membrane surfaces. Undoubtedly one of the most prevalent and important causes of blood loss is hookworms, which can be present in very large numbers. The worms suck blood and also damage the intestinal wall, causing blood leakage. Some 800 million people in the world are infested with hookworms. Other intestinal parasites such as *Trichuris trichiura* may also contribute to anaemia. Schistosomes or bilharzias, which are of several kinds, also cause blood loss either into the genito-urinary tract (in the case of *Schistosoma haematobium*) or into the gut. Malaria, another very important parasitic infection, causes destruction of red blood cells that are parasitized, which can lead to what is termed haemolytic anaemia rather than to iron deficiency anaemia. In programmes to reduce anaemia actions may be needed to control parasitic infections and to reduce blood loss resulting from disease as well as to improve dietary intakes of iron.

**TABLE 23**
Prevalence of iron deficiency anaemia among females of child-bearing age

<table>
<thead>
<tr>
<th>Region (%)</th>
<th>Prevalence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Asia</td>
<td>64</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>48</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>42</td>
</tr>
<tr>
<td>Near East and North Africa</td>
<td>33</td>
</tr>
<tr>
<td>Central America and the Caribbean</td>
<td>28</td>
</tr>
<tr>
<td>China</td>
<td>26</td>
</tr>
<tr>
<td>South America</td>
<td>23</td>
</tr>
<tr>
<td><strong>Overall mean</strong></td>
<td><strong>42</strong></td>
</tr>
</tbody>
</table>

*Source:* UN ACC/SCN, 1992a.

Anaemia resulting from folate deficiency is less prevalent than that from iron deficiency or iron loss. It occurs when folate intakes are low and when red cells are haemolysed or destroyed in conditions like malaria. The anaemia of both folate and vitamin B₁₂ is macrocytic, with larger than normal red blood cells. Folic acid or folates are present in many foods including foods of animal origin (e.g. liver and fish) and of vegetable origin (e.g. leafy vegetables). Vitamin B₁₂ is present only in foods of animal origin. In most countries vitamin B₁₂ deficiency is uncommon.

**Clinical manifestations**

Haemoglobin in the red blood cells is necessary to carry oxygen, and many of the symptoms and signs of anaemia result from the reduced capacity of the blood to transport oxygen. The symptoms and signs are:

- tiredness, fatigue and lassitude;
- breathlessness following even moderate exertion;
- dizziness and/or headaches;
- palpitations, with the person complaining of being aware of his or her heartbeat;
- pallor of the mucous membranes and beneath the nails;
- oedema (in chronic, severe cases).

These symptoms and signs are not confined to iron deficiency anaemia but are similar in most forms of anaemia. Most occur also in some other illnesses and thus are not specific to anaemia. Because none of the symptoms seem severe, dramatic or life threatening, at least in the early stages of anaemia, the disorder tends to be neglected.

An experienced health worker can sometimes make a preliminary diagnosis by examining the tongue, the conjunctiva of the lower eyelid and the nailbed, which may all appear paler than normal in anaemia. The examiner can compare the redness or pinkness below the nail of the patient with the colour beneath his or her own nails. Enlargement of the heart may result and can be detected in advanced severe anaemia. Oedema usually occurs first in the feet and at the ankles. There may also be an increased pulse rate or tachycardia.
Occasionally the nails become relatively concave rather than convex and become brittle. This condition is termed koilonychia. Anaemia is also reported to lead both to abnormalities of the mouth such as glossitis and to pica (abnormal consumption of earth, clay or other substances).

What is surprising is that many persons with very low haemoglobin levels, especially women in developing countries, appear to function normally. With chronic anaemia they have adapted to low haemoglobin levels. They may indeed do reduced work, have fatigue and walk more slowly, but they still give the appearance of performing their normal duties even though severely anaemic. Severe anaemia can progress to heart failure and death.

Anaemia, as well as producing the symptoms and signs discussed above, also leads to a reduced ability to do heavy work for long periods; to slower learning and more difficulty in concentration by children in school or elsewhere; and to poorer psychological development.

A very important aspect of anaemia in women is that it markedly increases the risk of death of the mother during or after childbirth. The woman may bleed severely, and she has low haemoglobin reserves. There is also an increased risk for her infant.

**Laboratory tests**

The diagnosis of anaemia requires a laboratory test. In this respect it differs from the serious manifestations of PEM, vitamin A deficiency and IDD; kwashiorkor, nutritional marasmus, advanced xerophthalmia, goitre and cretinism can all be diagnosed with some degree of certainty by skilled clinical observation. Consequently, whereas few district hospitals and practically no health centres have laboratories set up to test, for example, levels of serum vitamin A or urinary iodine, most are able to do haemoglobin or haematocrit determinations. These tests require quite cheap apparatus and can be performed by a trained technician, nurse or other health worker.

Determinations of haemoglobin or haematocrit levels are the most widely used in the diagnosis of anaemia. It is now realized that although these tests provide information on the absence, presence or severity of anaemia, they do not provide information on the iron stores of the individual. In terms of nutritional assessment to guide nutrition planning and interventions, or for research, it may be important to know more about the iron status of an individual than can be gained from haemoglobin and haematocrit determinations.

Many methods are used to measure haemoglobin levels. These range from simple colorimetric tests to more advanced tests which require a proper laboratory. Some new portable colorimeters can be used in the field; they are simple to use and provide reasonably accurate measurements. In the laboratory of even a moderate-sized hospital the so-called cyanmethaemoglobin method is frequently used; it is accurate and can be used to test blood collected by finger prick in the field. The different methods and their advantages are discussed in various books, of which some are included in the Bibliography.

Haematocrit level or packed cell volume (PCV), i.e. the percentage of the blood that is packed cells rather than straw-coloured serum, can also be determined by a simple test. Blood (also obtained from a finger pricked) is placed in a capillary tube and centrifuged, usually at 3 000 rpm. The centrifuge can be electric (run if necessary from a vehicle battery) or hand operated.

A thin blood film examined under the microscope can be used to judge if the red blood cells are smaller (microcytic) or larger (macrocytic) than normal (normocytic). In iron deficiency they are microcytic and in folate or vitamin B12 deficiency they are macrocytic. Pale cells are termed hypochromic.

Cut-off points taken from the World Health Organization (WHO) suggestions for the diagnosis of anaemia based on haemoglobin and haematocrit determinations are given in Table 24.
Certain other laboratory tests are useful in judging iron nutritional status rather than for diagnosing anaemia or its severity. In recent years it has been increasingly recognized that iron status is important because mild or moderate iron deficiency, prior to the development of anaemia, may adversely influence human behaviour, psychological development and temperature control. A person whose diet is low in iron or who is losing iron goes through a period when body iron stores (which are mainly in the liver) are gradually depleted before he or she develops anaemia as judged by low haemoglobin or haematocrit levels (see Figure 7). Anaemia is the end stage after iron stores have been depleted. To monitor iron stores it is useful to determine serum ferritin levels, because they are the first to decline. This is not a simple or cheap test to do, and few small or medium-sized hospitals in developing countries have the ability to do it, but teaching hospitals and nutrition research laboratories sometimes can. Unfortunately serum ferritin levels are influenced by infections, which are common in developing countries. Other determinations that may be done to evaluate iron status and which are described in textbooks include free erythrocyte protoporphyrin (FEP) and transferrin saturation (TS) (Figure 7).

**TABLE 24**

**Suggested criteria for diagnosis of anaemia using haemoglobin (Hb) and haematocrit (PCV) determinations**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Hb below (g/dl)</th>
<th>PCV below (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult male</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>Adult female (non-pregnant)</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td>Pregnant female</td>
<td>11</td>
<td>30</td>
</tr>
<tr>
<td>Child 6 months to 6 years</td>
<td>11</td>
<td>32</td>
</tr>
<tr>
<td>Child 6 to 14 years</td>
<td>12</td>
<td>32</td>
</tr>
</tbody>
</table>

*Source: WHO, 1975a.*

**FIGURE 7. Changes in body iron compartments and laboratory parameters of iron status during development of iron deficiency due to a continuous negative iron balance**
Increasing depletion of body iron

Iron stores

Haemoglobin (red cell) iron

Serum ferritin

Transferrin saturation (TS)

Free erythrocyte protoporphyrin (FEP)

Haemoglobin concentration

Lowest haemoglobin level in normals
Treatment

The treatment of anaemia depends on the cause. Iron deficiency anaemia is relatively easy and very cheap to treat. There are many different iron preparations on the market; ferrous sulphate is among the cheapest and most effective. The recommended dose of ferrous sulphate is usually 300 mg (providing 60 mg of elemental iron) twice daily between meals for adults. Iron tends to make the stools black. Because side-effects can occur, particularly involving the intestinal tract, sometimes people do not take their iron tablets regularly. Slow-release iron capsules have become available and seem to be associated with fewer side-effects. Most capsules contain ferrous sulphate in small pellets, so the iron is slowly released. Only one capsule or dose needs to be taken each day, but the capsules cost much more than ferrous sulphate tablets. Therefore it is unlikely that slow-release preparations will replace standard ferrous sulphate tablets for use in clinics in developing countries.

New research conducted in China suggests that ferrous sulphate is as effective when given once every week as when given once a day. If further trials confirm this observation, the finding will alter both the treatment of anaemia and the efforts to prevent it using medicinal iron supplements in prenatal clinics. In Indonesia, where vitamin A deficiency is a problem, it has been shown recently that giving vitamin A as well as iron improves the haemoglobin levels of pregnant women more than iron tablets alone.

Severely anaemic patients who are very ill, vomiting, unable to tolerate oral iron, uncooperative or unlikely to be seen by the doctor again can be given injectable iron preparations and/or treated with packed cell transfusion if facilities are available. In all cases the underlying cause of the anaemia should be sought and treated if possible.

Iron dextran is the injectable preparation most commonly used. Intravenous injection is preferable. The standing rule is to give a very small test dose initially and to wait for five minutes for any sign of an anaphylactic reaction. If there is no reaction, then 500 mg can be given from a syringe over a period of five to ten minutes. These injections may be given at intervals over a few days.

Alternatively, a total dose infusion can be provided at one time. This procedure must be employed only by doctors experienced in the technique and in calculating dosage levels.

It is common during pregnancy to provide folate as well as iron, or combined with iron, as part of the treatment of or prophylaxis against anaemia. For prevention, where anaemia is prevalent, doses of 120 mg of iron and 5 mg of folate daily are recommended. For treatment of established anaemia, doses of 180 mg of iron and 10 mg of folate are suggested.

In vitamin B$_{12}$ deficiency an oral dose of 1 µg vitamin B$_{12}$ daily is needed.

Successful treatment usually leads to a response in haemoglobin levels within four weeks.

Persons with iron deficiency anaemia on very poor diets should be advised to consume more fresh fruits and vegetables at mealtimes. These foods contain vitamin C, which enhances the absorption of non-haem iron in cereals, root crops and legumes. They also contain folic acid and an array of other vitamins and minerals. If it is feasible and in line with the anaemic patient's budget and culinary habits, he or she could also be advised to consume, even in small quantities, more foods rich in haem iron such as meat, especially liver or kidney. Creating awareness of the nutritional needs of different family members and helping household decision-makers to understand how these needs can best be met from available resources are important steps in preventing iron deficiency.