Chapter 14. Iodine deficiency disorders

Iodine deficiency is responsible not only for very widespread endemic goitre and cretinism, but also for retarded physical growth and intellectual development and a variety of other conditions. These conditions together are now termed iodine deficiency disorders (IDD). They are particularly important because:

- perhaps one-quarter of the world's people consume inadequate amounts of iodine;
- the disorders have a major impact on the individual and on society;
- of the four major deficiency diseases, IDD is the easiest to control.

In fact, as H.R. Labouisse wrote in 1978 when he was Executive Director of the United Nations Children's Fund (UNICEF), "Iodine deficiency is so easy to prevent that it is a crime to let a single child be born mentally handicapped for this reason" (quoted in Hetzel, 1989). Nonetheless this crime persists.

Endemic goitre and severe cretinism are the exposed part of the IDD iceberg. These are abnormalities that are visible to the populations where they are prevalent, and they can be diagnosed relatively easily by health professionals without the use of laboratory or other tests. The submerged and larger part of the iceberg includes smaller, less visible enlargements of the thyroid gland and an array of other abnormalities. In many areas of Latin America, Asia and Africa iodine deficiency is a cause of mental retardation and of children's failure to develop psychologically to their full potential. It is also associated with higher rates of foetus loss (including spontaneous abortions and stillbirths), deaf-mutism, certain birth defects and neurological abnormalities.

For several decades the main measure used to control IDD has been the iodization of salt, and when properly conducted and monitored it has proved extremely effective in many countries. It is also relatively cheap. Several international meetings, including the International Conference on Nutrition held in Rome in 1992, called for the virtual elimination of IDD by the year 2000. This goal is achievable, provided the effort receives international support and real national commitment in each of the many countries where the disorders remain prevalent.

Causes

The most important cause of endemic goitre and cretinism is dietary deficiency of iodine. The amount of iodine present in the soil varies from place to place and this influences the quantity of iodine present in the foods grown in different places and in the water. Iodine is leached out of the soil and flows into streams and rivers which often end in the ocean. Many areas where endemic goitre is or has been highly prevalent are plateau or mountain areas or inland plains far from the sea. These areas include the Alps, the Himalayas and the Rocky Mountains; smaller mountain ranges or highland areas in countries such as China, the United Republic of Tanzania, New Zealand, Papua New Guinea and countries of Central Africa; and inland areas and plains in the United States, Central Asia and Australia (Figure 8).

A less important cause of IDD is the consumption of certain foods which are said to be goitrogenic or to contain goitrogens. Goitrogens are "antinutrients" which adversely influence proper absorption and utilization of iodine or exhibit antithyroid activity. Foods from the genus Brassica such as cabbage, kale and rape and mustard seeds contain goitrogens, as do certain root crops such as cassava and turnips. Unlike goitrogenic vegetables, cassava is a staple food in some areas, and in certain parts of Africa, for example Zaire, cassava consumption has been implicated as an important cause of goitre.

FIGURE 8. Areas of the world where iodine deficiency is prevalent
**Epidemiology**

Any enlargement of the thyroid gland is called a goitre. The thyroid is an endocrine gland centrally situated in the lower front part of the neck. It consists of two lobes joined by an isthmus. In an adult each lobe of the normal thyroid gland is about the size of a large kidney bean. In areas of the world or communities where only sporadic goitre occurs or where health workers see only an occasional patient with an enlarged thyroid gland, the cause is not likely to be related to the individual's diet. Sporadic goitre may for example be due to a thyroid tumour or thyroid cancer. However, if goitre is common or endemic in a community or district, then the cause is usually nutritional. Endemic goitre is almost certainly caused by iodine deficiency, and where goitre is endemic other iodine deficiency disorders can also be expected to be prevalent.

Where goitre is endemic, often large numbers of people have an enlargement of the thyroid gland, and some have enormous unsightly swellings of the neck. The condition is usually somewhat more prevalent in females,
especially at puberty and during pregnancy, than in males. The enlarged gland may be smooth (colloid goitre) or lumpy (adenomatous or nodular goitre).

The iodine content of foods varies widely, but the amount of iodine present in common staple foods such as cereals or root crops depends more on the iodine content of the soil where the crop is grown than on the food itself. Because the amount of iodine in foods such as rice, maize, wheat or legumes depends on where they are grown, food composition tables cannot provide good figures for their iodine content. Foods from the ocean, including shellfish, fish and plant products such as seaweed, are generally rich in iodine.

In many populations, particularly in the industrialized countries of the North and among affluent groups almost everywhere, diets do not depend mainly on locally grown foods. As a result many of the foods purchased and consumed may contribute substantially to iodine intakes. For example, persons living in the Rocky Mountains of North America, where goitre used to be endemic, now do not rely much on locally produced foods; they may consume bread made from wheat grown in the North American central plains, rice from Thailand, vegetables from Mexico or California, seafood from the Atlantic coast and so on. Similarly, affluent segments of society in La Paz, Bolivia consume many foods not grown in the altiplano, and these imported foods will have adequate quantities of iodine. In contrast, the poor in the Bolivian highlands eat mainly locally grown foods and do develop goitre.

Many countries of Asia, Africa and Latin America have major iodine deficiency problems, although some countries have made great progress in reducing the prevalence of IDD. China and India, with their vast populations, still have a high prevalence of IDD. Not all African countries have been surveyed, but it is known that IDD is prevalent in Ethiopia, Nigeria, Tanzania, Zaire, Zimbabwe and many smaller nations. In the Americas, endemic goitre has been largely controlled in the United States and Canada, but many Andean countries including Bolivia, Colombia, Ecuador and Peru still have relatively high endemic goitre and cretinism rates. IDD is also encountered in the Central American countries and in parts of Brazil.

During a survey conducted by the author in the 1960s in the Ukinga Highlands of Tanzania, 75 percent of the people examined had goitre. This was the highest prevalence yet reported in Africa. Prevalence rates of over 60 percent have been reported from communities in many African, Asian and Latin American countries.

Generally goitre prevalence rates of 5 to 19.9 percent are considered mild, 20 to 29.9 percent moderate and 30 percent and over severe. But even with rates of 10 to 15 percent the need for action is important. Where prevalence rates are moderate, urgent action is needed. Where rates are severe, early action is critical (see Table 25).

Clinical manifestations

Endemic goitre

Enlargement of the thyroid gland is the most frequently described and most obvious clinical manifestation of iodine deficiency. It is believed that when dietary intakes of iodine fall below about 50 µg per day in adults, the thyroid gland begins to compensate by enlarging slowly over time. Where there is a chronic dietary deficiency of iodine the thyroid often begins to enlarge during childhood, and it becomes more markedly enlarged around the time of puberty, particularly in girls. In many areas where goitre is endemic the majority of people have some evidence of thyroid enlargement.

TABLE 25

Severity and public health significance of IDD
<table>
<thead>
<tr>
<th>Severity</th>
<th>Clinical features(^a)</th>
<th>Typical goitre prevalence (%)</th>
<th>Median urinary iodine (µg/litre)</th>
<th>Need for correction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Goitre</td>
<td>Hypothyroidism</td>
<td>Cretinism</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Stage I)</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>5.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>++</td>
<td>+</td>
<td>0</td>
<td>20-29.9</td>
</tr>
<tr>
<td>Severe</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

\(^a\) 0 = absent; + = mild/least severe; ++ = moderate/more severe; +++ = most severe.

The thyroid gland secretes hormones vital to metabolism and growth. The gland is made mainly of follicles called acini, minute sacs filled with colloid. Each sac manufactures thyroid hormones, stores them and secretes them into the bloodstream as needed. The main thyroid hormone is thyroxine. The amount of thyroxine secreted is controlled by another endocrine gland, the anterior pituitary, and its hormone, called thyroid stimulating hormone (TSH) or thyrotrophic hormone. The function of the thyroid gland is somewhat similar to that of the thermostat of the heating system in a house. It controls the rate of metabolism and influences the Basal metabolic rate (BMR), to some extent the heart rate and also growth in children.

The normal adult thyroid gland contains about 8 mg of iodine. In simple goitres the total iodine content might be only 1 or 2 mg even though the gland is larger than normal. Thyroxine contains 64 percent iodine.

A lack of dietary iodine makes it increasingly difficult for the thyroid to manufacture enough thyroxine. The gland enlarges to try to compensate and make more thyroxine. This enlargement is described by pathologists as a hyperplasia of the gland. It is triggered by increased production of TSH by the pituitary gland. Microscopic examination of a gland undergoing hyperplasia shows ingrowths or invaginations of the lining epithelium into the normal architecture of the colloid-containing acini. There is an intense multiplication of cells, with an excess of colloid. This compensatory reaction is an attempt to trap more iodine, and it is partly successful. Many people with colloid goitres show no evidence of poor thyroid function.

Investigation of goitre prevalence is one of the most important means of assessing whether there is an IDD problem of public health importance. Examination of well-chosen samples of schoolchildren has often been recommended as the first step; this survey is relatively easy because schoolchildren are collected together in one place and are usually disciplined, so large numbers can be examined over a short time. To get a full picture of the prevalence in the area, however, it is important at some stage to examine a representative sample of community members of all ages and both sexes.

The thyroid gland of each person should be examined both visually and by palpation to judge its size. Visual examination informs the examiner whether a goitre is visible with the head in normal position or with the head tilted back. Palpation is usually done with the examiner sitting or standing facing the person being examined; the examiner's eyes should be level with the person's neck. By placing and rolling the thumbs on either side of the trachea below the Adam's apple or voice box, the examiner can feel the gland and judge its size. A normal thyroid gland is considerably smaller than the last joint (terminal phalanx) of the thumb. (In fact a normal thyroid lobe is perhaps one-fifth that size.) If each lobe is larger than this joint, then there is a goitre. Palpation
from behind is recommended by some because the fingertips are then used to determine gland size, and they are more sensitive than the tips of the thumbs.

It is useful to classify the goitre size using an accepted classification system. Such a system was recommended by the World Health Organization (WHO) over 30 years ago and, as modified by WHO, UNICEF and the International Council for Control of Iodine Deficiency Disorders (ICCIDD), is still used (Table 26). Use of the system assures reasonable comparisons by different observers and in different regions. The main use of grading goitres is for survey purposes and to allow comparisons of goitre prevalence rates between areas. It is not possible to be completely objective, and there will seldom be complete agreement between two examiners, but there will be a reasonable measure of agreement.

Persons with goitre are more likely than others to have manifestations of poor thyroid function, especially hypothyroidism. A large goitre, and especially one that enlarges behind the upper part of the sternum, may cause pressure on the trachea and oesophagus, which may interfere with breathing, cause an irritative cough or voice changes and occasionally affect swallowing.

### TABLE 26

**WHO/UNICEF/ICCIDD simplified classification of goitre**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Thyroid gland size</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No palpable or visible goitre</td>
</tr>
<tr>
<td>1</td>
<td>A mass in the neck that is consistent with an enlarged thyroid that is palpable but not visible when the neck is in normal position. It moves upwards in the neck as the subject swallows. Nodular alteration(s) can occur even when the thyroid is not visibly enlarged.</td>
</tr>
<tr>
<td>2</td>
<td>A swelling in the neck that is visible when the neck is in normal position and is consistent with an enlarged thyroid when the neck is palpated.</td>
</tr>
</tbody>
</table>


Moderate and large goitres also create an undesirable appearance and possibly difficulty with wearing certain clothes. It has been reported that in some areas where endemic goitre is highly prevalent, goitres may be accepted as the normal condition or as a sign of beauty and people without a goitre may be considered abnormal. However, in the Ukinga Highlands of Tanzania, where prevalence was over 70 percent, the author found that the people were not pleased to have large neck swellings. Many people had symmetrical small scars in the skin covering the goitre, which was clear evidence that they had sought local medical treatment; in East Africa treatment frequently consists of cuts and scarification of the offending area, sometimes with herbal medicines rubbed into the cuts. Clearly these people hoped their goitres would disappear.

**Hypothyroidism**

If for any reason too little thyroid hormone is produced, the BMR goes down and a condition called hypothyroidism develops, which may lead to the clinical condition called myxoedema. In the adult this condition is characterized by coarsened features, dry skin and sometimes puffiness of the face. The person is often somewhat overweight, has a slow pulse and feels sluggish. Testing would reveal a low BMR and low levels of thyroid hormones in the blood.

In contrast, an overactive thyroid gland producing more thyroid hormone than necessary produces a condition known as hyperthyroidism or Graves' disease. The adult with this condition tends to be thin and asthenic, to be
nervous and to have a rapid pulse rate, particularly during sleep. Tests reveal high thyroid hormone levels and high BMR.

As stated above, persons with endemic goitre often have good compensation and do not have evidence of either hypothyroidism or hyperthyroidism. They are said to be euthyroid, which means that they have normal thyroid function despite thyroid enlargement. However, in endemic areas rates of hypothyroidism are elevated. In many cases the hypothyroidism is mild and not as obvious as classical myxoedema, but thyroid hormone levels are low, and low BMR, lower productivity and slower mental functioning may be chronic.

It is hypothyroidism in children, however, that is of most concern for developing countries, because of the strong evidence that it causes both mental retardation and slowing of physical growth. Mental retardation ranges from very severe, which is easy to recognize, to mild, which may be difficult to diagnose. In areas with a high prevalence of IDD large numbers of children may fail to reach their intellectual potential because of impaired school performance and lower IQ than in matched groups from areas without iodine deficiency. These children may later, as adults, fail to make as great a contribution to society and to national development as they would have made if they and their mothers had always consumed adequate amounts of iodine.

**Endemic cretinism**

Endemic cretinism, including deaf-mutism and mental retardation, begins in infancy. Iodine deficiency in a woman during pregnancy can lead to the birth of a cretinous child. The infant may appear normal at birth but is slow to grow and to develop, small in size, mentally dull, slow to learn and retarded in reaching normal development milestones. Many of these children are deaf mutes. As the child gets older he or she may have the typical appearance of a cretin, which includes a thick skin, coarse features, a depressed nose, a large protruding tongue and frequently strabismus (the medical term for eyes that look in different directions, cross-eye or squint). At two years of age the child may still be unable to walk unassisted, and at three years he or she may not be able to talk or understand simple commands.

Cretinism may occur in two forms, namely the neurological form and the hypothyroid form. However, many cretins have some manifestations of both. Features of the neurological form include profound mental deficiency; the characteristic appearance; an inability to walk or a shuffling gait; difficulty in controlling exact movements of the hands and feet (spasticity); and sometimes, but not always, an enlarged thyroid gland. Signs of hypothyroidism may or may not be obvious.

In contrast, the hypothyroid cretin by definition has evidence of low levels of thyroid hormone. The child usually has a slow pulse, a puffy face and thick skin; is very retarded in physical growth, in bone age and in mental development; and has low BMR. In much of Asia and in South America (and formerly in Europe) neurological cretinism predominates, whereas in eastern Zaire the myxoedematous form is more widespread. It is not certain if this occurrence is associated with cassava consumption.

In both forms of cretinism the neurological damage, the mental retardation and the dwarfing are not reversible by treatment. Worsening of the condition may be halted, but permanent damage has been done during pregnancy. Therefore the importance of prevention must be emphasized; it is imperative to ensure that women of child-bearing age are not iodine deficient.

**Mental retardation**

A consequence of iodine deficiency in communities that is perhaps more important than endemic goitre or overt cretinism is the failure of a large number of persons to grow optimally, either physically or mentally, even though they do not have the classical feature of cretinism. In some, neurological functioning may also be abnormal. Increasing evidence suggests that iodine deficiency is a major cause of children's failure to reach
their intellectual potential, even for those who are not cretins or severely mentally retarded. School performance may be impaired.

Iodine deficiency in an area may have adverse effects on domestic animals as well as humans. Iodine-deficient cattle, goats and poultry may exhibit poor growth and reproduction.

Laboratory tests

The most widely used laboratory test of iodine nutritional status is determination of urinary iodine. Measurement of urinary iodine excretion should ideally be done on 24-hour urine samples. In the field it is difficult to collect all urine passed over a 24-hour period, so casual urine samples are collected and the amount of iodine in the urine is related to the amount of creatinine and expressed as micrograms of iodine per gram of creatinine (µg/g). If mean iodine excretion is below 50 µg/g creatinine then it is usually concluded that iodine deficiency is a problem in the population. Levels below 20 µg/g creatinine are considered very low. When 24-hour urine collection is done, or where creatinine determinations are not conducted, urinary iodine levels below 5 µg/dl suggest iodine deficiency. Relatively few laboratories in developing countries have the equipment or trained personnel to do urinary iodine determinations. This is not a test that ordinary district or even regional hospitals can perform.

Other laboratory tests that are used are not measures of iodine status, strictly speaking, but of thyroid function. Serum thyroxine (T4) is measured and if low is evidence of poor thyroid function, which may be related to goitre. An alternative determination which is increasingly recommended is measurement of blood levels of TSH. Radioimmunoassay (RIA) techniques are now preferred for both T4 and TSH determinations. In most industrialized countries blood is taken from the umbilical cord or heel of all infants born in hospital and sent on filter paper to a special laboratory for determination of thyroxine or TSH. This test is done because about one in 4 000 infants born is hypothyroid because the thyroid gland did not develop properly. If the condition is not diagnosed and treated soon after birth there will be serious consequences, including poor brain development. Congenital hypothyroidism, however, is not related to IDD. Generally T4 levels below 4 µg percent are considered low, requiring treatment. As with urinary iodine, few hospitals in most developing countries are equipped to do T4 and TSH determinations.

Another test of thyroid function is measurement of radioactive iodine uptake levels, usually using I131 to assess the avidity or "hunger" of the subject's thyroid gland for iodine. In persons with hypothyroidism caused by iodine deficiency, most of the dose of iodine is taken up by the thyroid gland, and less than 10 percent remains.

In the past, protein bound iodine (PBI) in blood plasma was a widely used test.

Some practitioners recommend the use of ultrasonography to produce an image of the thyroid gland, which allows more accurate judgement of the size of the gland than is possible by visual examination and palpation. Ultrasound is being used increasingly in medicine to examine different organs of the body. It is an attractive method because it is non-invasive and does not involve subjection to X-rays. However, in developing countries ultrasonography will seldom be practical for surveys or for assessing IDD problems. The equipment is expensive, and a well-trained technologist is required to operate it and to interpret the results.

It is important for those seriously concerned with IDD assessment and control in Asia, Africa and Latin America to make wise judgements about how best to determine the extent of the problem and to evaluate the effectiveness of control measures. Often it will not be feasible to opt for the use of the more difficult and expensive laboratory methods for assessment of the problem or for evaluation, and even if it is feasible, it may not be a good use of limited financial and personnel resources. These methods, if available in a national or teaching hospital in the capital city or in a national nutrition laboratory, should usually be used mainly for diagnostic purposes for certain patients with metabolic diseases, for well-designed research projects and for subsamples of populations being intensively studied for IDD. They are usually completely inappropriate for
mass use in goitre surveys conducted either to assess the extent of IDD or to judge effectiveness of control measures.

**Treatment**

The treatment of goitre caused by iodine deficiency is easy and satisfying in the case of a simple goitre or a colloid goitre that is not very large. Usually either potassium iodide (6 mg daily) or Lugol's iodine (one drop daily for ten days, then one drop weekly) will lead to a fairly rapid reduction in the size of the goitre. One drop of Lugol's iodine provides about 6 mg of iodine. Alternatively, Lugol's iodine can be diluted in any small hospital laboratory so that one teaspoonful of the dilute solution yields 1 mg of iodine. Lugol's solution is very cheap and is widely available. Of primary school children treated in Tanzania, over 60 percent with Grade 1 goitre had no goitre after 12 weeks of receiving Lugol's iodine, and most larger goitres had improved markedly. An alternative treatment which is also effective but which needs careful medical supervision is the use of thyroid extract or medicinal thyroxine.

Large nodular goitres and some other goitres that do not respond to treatment with either iodine or thyroxine can only be properly treated by surgical excision. Surgery is especially needed if the goitre is causing symptoms because it is retrosternal or pressing on the trachea. Thyroidectomy requires a good well-trained surgeon and good medical management afterwards. Patients who have had total thyroidectomy must receive thyroxine or thyroid hormones for the rest of their lives.

**Prevention of IDD**

Clearly, rather than treating each individual who has goitre caused by iodine deficiency, it is much preferable to take measures to control iodine deficiency in the community, the district or the nation. The most common, and often the best, measure is iodization of salt, which will reduce the prevalence and also the severity of goitre over a relatively short period among those who consume the salt. Control measures are discussed in detail in Chapter 39.