Iodine deficiency disorders

Summary

- Iodine deficiency disorders (IDD) are most prevalent in mountainous, alluvial plains and areas far away from oceans due to low iodine intake
- About 2 billion people in the world have low iodine intake
- Cretinism is only the tip of the iceberg of IDD manifestations
- Iodine deficiency is the most frequent cause of avoidable mental retardation
- Goitrogenous factors like thiocyanate and selenium deficiency contribute to goiter formation
- Neurological cretinisme is irreversible
- Myxoedematous cretinisme can be reversed when treated early
- Prevalence of endemic goiter, urinary iodine concentrations, TSH dosage and prevalence of cretinism determine endemicity of IDD
- Salt, water or oil are used for iodine fortification

Introduction

Iodine is an oligo-element that is present in the human body in a very small quantity (15 to 20 mg for adults). Its only known function is as essential element in the production/composition of the thyroid hormones T3 and T4. These hormones have a specific role in the metabolism of all cells of the organism and in the growth process of most organs, in particular the brain. In a situation of iodine shortage, thyroid hormone synthesis and availability is reduced, with numerous health consequences. In the past the deficiency was called “endemic goitre”, related to the most prominent sign of the deficiency “the goitre”, but the health problems due to iodine deficiency are far more important than goitre alone. It is now replaced by “iodine deficiency disorders” or “IDD”.

Epidemiology

At present there are no exact figures on the prevalence iodine deficiency disorders available: in 1990 it has been estimated that among the 1572 million people in the world exposed to

iodine deficiency (28.9 % of the world population), 11.2 million were affected by overt cretinism, the most extreme form of mental retardation due to the deficiency and that another 43 million people were affected by some degree of mental impairment. It therefore appeared that iodine deficiency was the leading cause of preventable mental retardation. A WHO report of 2007 concludes that global progress in controlling iodine deficiency has been made, but still 2 billion people (of which 266 million school-aged children) have insufficient iodine intake. This report warns that more than adequate or even excessive iodine intake in 34 countries.

Although present in 95 countries, the problems due to iodine deficiency occur most in mountainous regions: the mountain chains of the Himalayas, the Andes (where the neurological form is dominant), the mountainous regions of Vietnam, etc. Regions that are situated at a low level, far away from the oceans, like the central part of the African continent (where the myxoedematous form is dominant) and to a lesser degree the European continent, are also affected as well as the high plains of China and Australia. The groups with the highest risk for iodine deficiency are in order of importance the fetus, the newborn, the pregnant and nursing woman, the young child. The prevalence increases with age until puberty, and is higher among women than among men.

The real problem of the iodine deficiency, from a public health point of view, is not goitre itself, but the mental retardation secondary to the thyroid deficiency that is present in fetal life and in the beginning of postnatal life. The socio-economic consequences (high number of disabled, learning difficulties in children, infant death in children with cretinism) are quite important and they are a real obstacle to the development.

Aetiology

1. Low iodine intake

Several arguments confirm that iodine deficiency is the main cause of the observed problems: there is an inverse relation between the prevalence of goitre and the urinary excretion of iodine over 24 hours, used as an indicator of iodine intake. The correction of the iodine deficiency decreases the prevalence of endemic goitre, cretinism and of hypothyroidism. Low iodine intake can be explained by 2 phenomena:

Geography

A soil that is poor in iodine produces water and foods, poor in iodine. The ocean is the essential reservoir for iodine. The iodized ions are oxidized in elementary iodine on the surface of the water by the sunlight. The iodine is volatile and diffuses in the atmosphere and returns to the soil by rain. So it's brought along by rivers, running water and melting ice. The poorest soils in iodine are found in mountainous regions: these were covered by the glaciers of the Quaternary and because these melted the underlying iodine was swept away with the erosion. Most mountainous districts in the world have been or are still endemic goitre regions. The disease may be seen throughout the Andes, in the whole sweep of the Himalayas, in the Alps where iodide prophylaxis has not yet reached the entire population, in Greece and the Middle Eastern countries, in many foci in the People's Republic of China, and in the highlands of New Guinea. The iodine content of the drinking water is low, as is the quantity of iodide excreted each day by residents of these districts.

Non-mountainous regions, far away from the oceans can have poor iodine concentrations in their soils. Plants absorb iodine from the ground, plants are eaten by animals and plants and animals are eaten by humans, so the iodine concentration in food is often a good reflection of the distance from the sea.

Examples of iodine deficient low-land regions are the belt extending from the Cameroon grasslands across northern DRC and the Central African Republic to the borders of Uganda and Rwanda, Holland, Central Europe and the interior of Brazil.
Last, a wash-away effect in soils that are regularly flooded can be seen, like the alluvial plains in deltas of big rivers.

Isolation

Food diversity and the mobility of the populations bring along a spontaneous reduction of the prevalence of the endemic goitre. Isolation leads to poor food exchanges and diversification. The phenomenon of opening isolated regions, observed in the last decades, explains as much of the decrease in the prevalence of IDD as the iodination campaigns. It is also the reason for the observed spontaneous historical reduction of the prevalence of IDD in most countries.

2. Goitrogenous factors

The role of additional factors playing a role the aetiology of IDD has been suspected because goitre exists in regions where the iodine intake is adequate. The additional role of goitrogens from food origin or in the environment has been looked into and has been proved in a number of regions in the world.

Thiocyanates inhibit the iodine pump and increase the renal clearance of iodide. They are derived from manioc, in a variable quantity that depend on the nature of the soil, the type of cassava that is cultivated, the way of preparation and consummation of cassava. DRC, Mozambique and Indonesia are countries where thiocyanate can be found. Thiocyanate is derived from intestinal breakdown linamarin – a cyanogenic glycoside – from cassava and its conversion to thiocyanate by the liver. Thiocyanate is a competitive inhibitor of the Na/I symporter in thyroid follicular cells. A reciprocal relationship exists between iodide and thiocyanate in that increasing amounts of iodide protect increasingly against the thiocyanate derived from the cassava. It now seems well established that cassava may contribute to the severity of endemic goitre and probably the incidence of endemic cretinism, but there are many severe endemics where cassava is not eaten. In these regions, it is possible that other goitrogens in the local food may contribute to the effects of a prevailing iodine deficiency. Thiocyanate may cross the human placenta and affect the thyroid of the fetus.

Thioureas act on the level of the oxidation and metabolism of iodine in the thyroid.

3. Selenium deficiency

It has been shown that selenium deficiency may have profound effects on thyroid hormone metabolism and possibly also on the thyroid gland itself. In this situation the function of type I deiodinase (a selenoprotein) is impaired. Type I deiodinase plays a major role in T4 deiodination in peripheral tissues like kidney, liver and gut. It has been shown that when in an area of combined iodine and selenium deficiency, only selenium is supplemented, serum T4 decreases. This effect is explained by restoration of type I deiodinase activity leading to normalization of T4 deiodination and conversion to T3, while T4 synthesis remains impaired because of continued iodine deficiency.

Selenium deficiency also leads to a reduction of the selenium containing enzyme glutathione peroxidase. Glutathione peroxidase detoxifies H_2O_2 which is abundantly present in the thyroid gland as a substrate for the thyroperoxidase that catalyzes iodide oxidation and binding to thyroglobulin, and the oxidative coupling of iodotyrosines into iodothyronines. Reduced detoxification of H_2O_2 may lead to thyroid cell death. Elevated H_2O_2 levels in thyrocytes may be more toxic under situations of increased TSH stimulation such as is present in areas with severe iodine deficiency. Finally decreased availability of glutathione peroxidase impairs thyroid hormone synthesis in the thyroid gland, a fact that could also contribute to decreased T4 synthesis. Selenium deficiency certainly plays a role in the aetiology of the type of myxedematous endemic cretinism seen in Central Africa but does not by itself constitute a cause of endemic goitre. Extensive epidemiological data collected in China indicated that all selenium-deficient areas were IDD-endemic areas. However, the reverse is not true: IDD can be very severe in many selenium-rich areas.

Iodine needs

The physiologic needs are equal to the hormonal quantity of iodine that is produced every day. This means 50 to 100 ug/day for an adult. The quantity starts increasing in puberty certainly among women. Among the girls of 11 to 12 years a slight increase in the volume of the thyroid body is not rare (transitory hypertrophy).

RECOMMENDED INTAKE	ug/day	
0 - 6 months	35	8 ug/kg 5 ug/100ml of milk 7 ug/100 kcal
6 - 12 months	45	
1 - 10 years	60 – 100	
>= 11 years	100 - 115	
pregnancy – lactation	125 - 150	

Table: Recommended daily intake of iodine (µg/day)

Pathophysiology

Goitre

Because of a deficiency of iodine, the synthesis of the thyroid hormones is reduced. A low level of thyroxin in the blood stimulates the hypophysis to free TSH. This results in a hyperplasia of the cells of the thyroid gland with increase in thyroid volume (goitre). This in turn makes a higher captivation of circulating iodine possible. If the normal production of thyroid hormones cannot be maintained, hypothyroidism appears.

However, efficient adaptation to iodine deficiency is possible in the absence of goitre as demonstrated in nongoitrous patients in endemic goitre areas such as New Guinea and the Congo. Moreover, adequate adaptation to iodine deficiency has been demonstrated in areas of severe iodine deficiency in the absence of endemic goitre. This clearly indicates that goitre is not required for achieving efficient adaptation to iodine deficiency. Rather in these conditions, efficient adaptation to iodine deficiency is possible thanks to a high iodide trapping capacity but with only a slight enlargement of the thyroid. At this stage, the characteristic hyperplastic picture includes abundant parenchyma, high follicular epithelium and rare colloid.

On the contrary in large goitres, the major part of the gland is occupied by extremely distended vesicles filled with colloid with a flattened epithelium. The mechanism responsible for the development of colloid goitre is not fully understood but it does not appear to be TSH hyperstimulation. It must be the consequence of an imbalance between thyroglobulin synthesis and hydrolysis, i.e. secretion. In these conditions, iodide is diluted while thyroglobulin is in excess, resulting in a lesser degree of iodization of thyroglobulin and consequently a decrease in iodothyronine synthesis and secretion. Hydrolysis of large amounts of poorly iodinated thyroglobulin will result in an important leak of iodide by the thyroid and enhanced urinary loss of iodide, further aggravating the state of iodine deficiency. Therefore, large colloid goitres in endemic iodine deficiency represent maladaptation instead of adaptation to iodine deficiency because they may produce a vicious cycle of iodine loss and defective thyroid hormones synthesis.

Iodine deficiency in the fetus

The fetus and the new born are more sensitive than the adult to the effects of low levels of circulation thyroid hormone seen in iodine deficiency or goitrogenous substances. There is an immaturity of the adaptation mechanisms and iodine reserves are small. The period of growth, pregnancy and lactation increases the needs and make the individual more vulnerable.

The human brain develops during its fetal life until the end of the third life-year. Consequently an iodine and/or thyroid hormone deficiency during this critical period of life causes irreversible changes in the development of the brain. Iodine deficiency in the fetus is the result of iodine deficiency in the mother. The consequence of iodine deficiency during pregnancy is impaired synthesis of thyroid hormones by the mother and the fetus. An insufficient supply of thyroid hormones to the developing brain may result in mental retardation.

The physiologic role of thyroid hormones can be defined as to insure the timed coordination of different developmental events through specific effects on the rate of cell differentiation and gene expression. Thyroid hormone action is exerted through the binding of T3 to nuclear receptors which regulate the expression of specific genes in different brain regions following a precise developing schedule during fetal and early postnatal life. The T3 which is bound to the nuclear receptors is primary dependent on its local intracellular production from T4 via type II deiodinase and not from circulating T3.

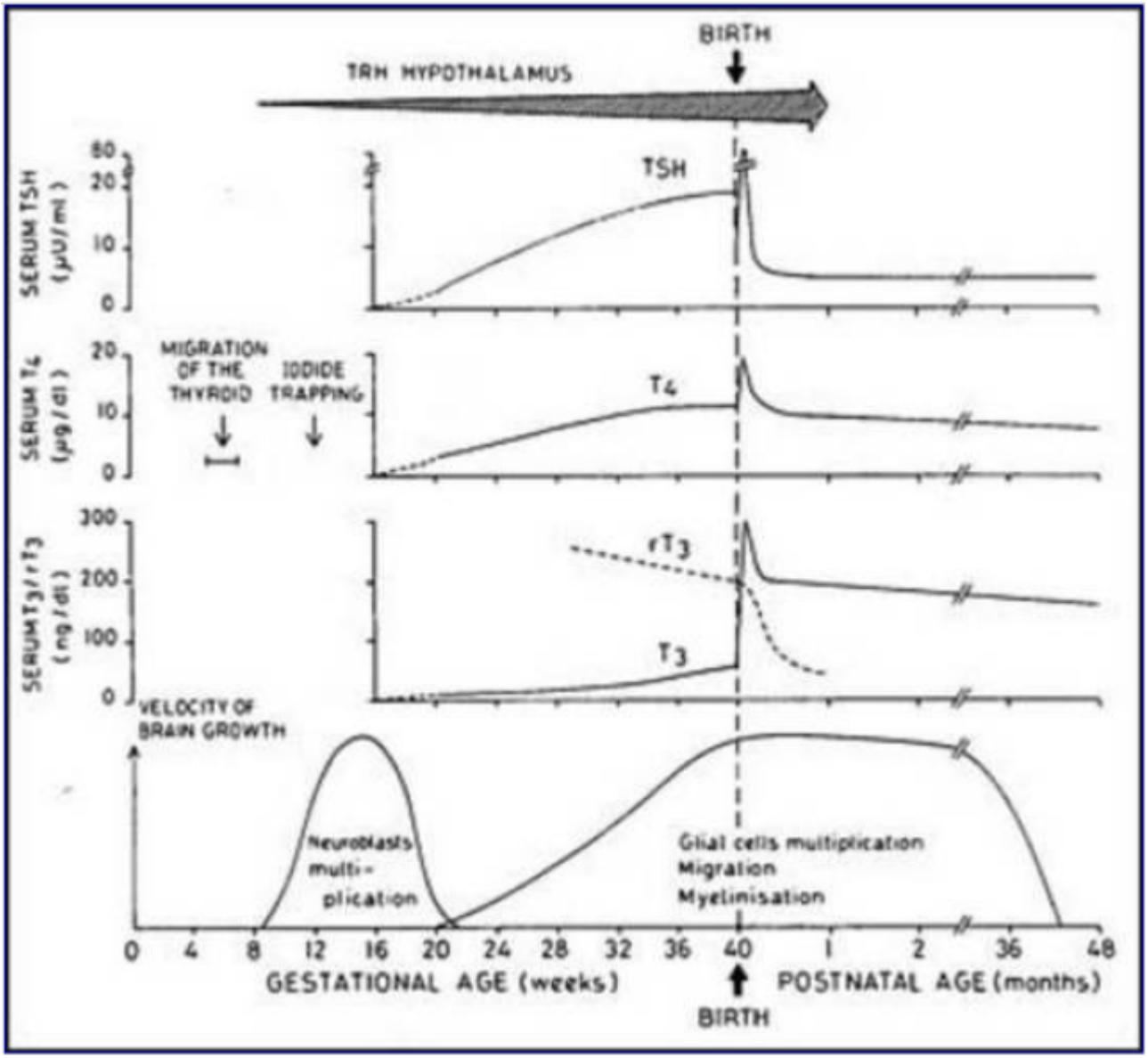

Figure: Ontogenesis of thyroid function and regulation in humans during fetal and early postnatal life

Brain growth is characterized by two periods of maximal growth velocity. The first one occurs during the first and second trimesters between the third and the fifth months of gestation. This phase corresponds to neuronal multiplication, migration and organization. The second phase takes place from the third trimester onwards up to the second and third years postnatally. It corresponds to glial cell multiplication, migration and myelinization. The first

phase occurs before fetal thyroid has reached its functional capacity. It is now largely agreed that during this phase, the supply of thyroid hormones to the growing fetus is almost exclusively of maternal origin while during the second phase, the supply of thyroid hormones to the fetus is essentially of fetal origin. Thyroid hormones are transferred from mother to fetus both before and probably after the onset of fetal thyroid function, contrasting with the previous dogma that this transfer is minimal or does not exist. Nuclear T3 receptors and the amount of T3 bound to these receptors increase about six to tenfold between 10 and 16 weeks, also before the secretion of hormones by the fetal thyroid. This transfer is decreasing but persists during later gestation. Up to 30 % of serum T4 in cord blood at birth could be of maternal origin.

Clinical aspects

The term Iodine Deficiency Disorders (IDD) refers to all the ill-effects of iodine deficiency in a population that can be prevented by insuring that the population has an adequate intake of iodine. These effects are listed in in the table below.

Fetus Abortions	Stillbirths Congenital anomalies Increased perinatal mortality Endemic cretinism
Neonate Neonatal goitre	Neonatal hypothyroidism Endemic mental retardation Increased susceptibility of the thyroid gland to nuclear radiation
Child and goitre	Adolescent (subclinical) hypothyroidism Impaired mental function Retarded physical development Increased susceptibility of the thyroid gland to nuclear radiation

Adult goitre with its complications	Hypothyroidism Impaired mental function Spontaneous hyperthyroidism in the elderly Iodine-induced hyperthyroidism Increased susceptibility of the thyroid gland to nuclear radiation

The Spectrum of Iodine Deficiency Disorders, IDD, Adapted from Hetzel, Laurberg et al.; Stanbury et al.

Goitre

Goitre is an increase in thyroid volume of four to five times that can cause aesthetic problems or compression of the oesophagus and trachea. Goitre can be associated with hypothyroidism, but also Iod-Basedow (not to be confused with Basedow's disease which is the same as Graves' disease) hyperthyroidism can occur in a patient with an endemic goitre due to iodine deficiency relocates to an iodine-abundant geographical area. Cancer is a rare complication of goitre.

Cretinism

Cretinism exists in two extreme forms, but most presentations are intermediate forms. **Neurological** cretinism is be secondary to a state of maternal and fetal hypothyroidism supervening in the beginning of fetal life. The child is euthyroid but presents with spastic diplegia (symmetrical paralysis), deaf-muteness, strabismus and serious mental retardation. This condition is irreversible. **Myxedematous** cretinism is the long-term consequence of a permanent, earlier unknown hypothyroidism; it begins during the fetal or neonatal period if mothers are deprived of iodine during the later process of pregnancy. Myxedematous cretinism has a picture of hypothyroidism with important stature and variable mental retardation. This condition can still respond to thyroid hormone replacement therapy and early detection and treatment is crucial to safeguard the baby's prognosis.

The mental deficiency is the iceberg of which cretinism is only the top. Retardation of

intellectual development was noted in up to 5% of the total population in an endemic zone. This makes iodine deficiency the most frequent cause of avoidable mental retardation. These people often have a clinically and biologically euthyroid aspect since the retardation is a consequence of a transient hypothyroidism during the critical phase of the cerebral development which resolved spontaneously.

Iodine deficiency in the neonate

Miscarriages are more frequent in iodine deficient regions. An increased perinatal mortality due to iodine deficiency has been shown in DRC from the results of a controlled trial of iodized oil injections alternating with a control injection given in the latter half of pregnancy. There was a substantial fall in infant mortality with improved birth weight following the iodized oil injection. Low birth weight of any cause is generally associated with a higher rate of congenital anomalies and higher risk of death throughout childhood. Apart from mortality the importance of the state of thyroid function in the neonate relates to the fact that the brain of the human infant at birth has only reached about one third of its full size and continues to grow rapidly until the end of the second year. The frequency distribution of IQ in apparently normal children in such conditions is shifted towards low values as compared to matched controls who were not exposed to iodine deficiency during the critical period of brain development because of correction of the deficiency in the mothers before or during early gestation.

More globally, in a meta-analysis of studies on neuromotor and cognitive functions in conditions of moderate to severe iodine deficiency, iodine deficiency resulted in a loss of 13.5 IQ points at the level of the global population.

Iodine deficiency in the adult

A high degree of apathy has been noted in populations living in severely iodine deficient areas. This may even affect domestic animals such as dogs. It is apparent that reduced mental function due to cerebral hypothyroidism is widely prevalent in iodine deficient communities with effects on their capacity for initiative and decision making. This indicates that iodine deficiency can be a major block to the human and social development of

communities living in an iodine deficient environment and constitutes a major teratogen at the community level. In addition to this impact to brain and neurointellectual development, iodine deficiency at any period in life, including during adulthood, can induce the development of goitre with mechanical complications and/or thyroid insufficiency. Another consequence of longstanding iodine deficiency in the adult but also in children is the development of hyperthyroidism, especially in multinodular goitres with autonomous nodules. It is now accepted that hyperthyroidism is one of the disorders induced by iodine deficiency.

Treatment

The prolonged administration of iodide or of T4 reduces the volume of goitre. Surgical treatment is rarely indicated. Unfortunately, these individual treatments are frequently impossible to apply on the whole population because of the magnitude of the problem and of the lack of medical infrastructure. The logical medical attitude is to focus all efforts on the prevention. The principle is simple: the prevention of iodine deficiency = a regular and stable iodine administration.

Prevention

Diagnosis of endemicity

Several factors can be taken into consideration when determining and quantifying the endemicity of the problems related to iodine deficiency:

1. Prevalence of endemic goitre

Its determination is based on the percentage of people with a goitre in a specific population. During field inquiries, the best method consists in examining the whole population of the region. In case of difficulties, it is allowed to limit these inquiries to children from 6 to 12 years. By palpation, a thyroid is considered goitrous when each lateral lobe has a volume greater than the terminal phalanx of the thumbs of the subject being examined. However, palpation of goitre in areas of mild iodine deficiency has poor sensitivity and specificity. In such areas, measurement of thyroid volume by ultrasound is preferable.

Classification	Description
Grade 0	No palpable or visible goitre.
Grade 1	A goitre that is palpable but not visible when the neck is in the normal position (i.e. the thyroid is not visibly enlarged). Thyroid nodules in a thyroid which is otherwise not enlarged fall into this category.
Grade 2	A swelling in the neck that is visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated.

Revised classification of goitre according to WHO/UNICEF/ICCIDD

2. Dosage of urinary iodine

It is difficult to measure precisely the food iodine content. When in nutritional balance, the intake of iodine equals the urinary excretion of iodine. Urinary iodine excretion is a good marker of the very recent dietary intake of iodine and therefore is the index of choice for evaluating the degree of iodine deficiency and of its correction. Iodine concentrations in casual urine specimens of children or adults provide an adequate assessment of a population iodine nutrition, provided a sufficient number of specimens is collected. Twenty four hours samples are difficult to obtain and are not necessary. Relating urinary iodine to creatinine is expensive and unnecessary. However the median urinary iodine is often misinterpreted. Individual iodine intakes and therefore a spot urinary iodine concentration are highly variable from day-to-day, and a common mistake is to assume that all subjects with a spot UI <100 µg/L are iodine deficient.

For epidemiological studies, the population distribution of urinary iodine is required rather than individual levels. Because the frequency distribution of urinary iodine is usually skewed towards elevated values, the median is considered instead of the mean as indicating the status of iodine nutrition.

Median urinary iodine (µg/l)	Iodine intake	Iodine nutrition

< 20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Optimal
200-299	More than adequate	Risk of iodine-induced hyperthyroidism following introduction of iodized salt in susceptible groups
> 300	Excessive	Risk of adverse health consequences: iodine-induced hyperthyroidism, auto-immune thyroid diseases

Table: Epidemiological criteria for assessing iodine nutrition based on median urinary iodine concentrations in school-aged children

3. TSH dosage (thyroid stimulation hormone)

TSH level in the serum are elevated in cases of iodine deficiency. However difficulties are often encountered in obtaining venous blood samples in populations due to apprehension about blood collection and operational difficulties. Therefore these measurements are not routinely recommended in routine assessment and monitoring. In spite of the difficulties in blood collection, it has to be kept in mind that the final objective of correction of iodine deficiency is not only to increase the access of the population to iodized salt and to normalize the urinary iodine concentration but mostly to normalize thyroid function tests. Elevated serum TSH, unless exceptional pathological situations, indicates an insufficiency in the saturation of the T3 receptor in the brain, whatever the level of serum thyroid hormones. Therefore, elevated serum TSH constitutes an indicator of the potential risk of iodine deficiency on brain development. Serum T4 and T3 are less specific indicators of iodine deficiency because they are modified usually only in conditions of at least moderate iodine deficiency. Moreover these levels are largely influenced by age and sex. Elevated serum T3 in spite of low serum T4 is considered as a protective mechanism to most parts of the body, except the brain, where T3 is produced locally and not derived from the circulating T3.

The use of whole blood from finger pricks spotted on filter paper cards can be used at least for the measurement of serum TSH as indicators of thyroid hyperstimulation. A frequency distribution of serum TSH in neonates shifted to high values is a particularly sensitive index of the risk of potential damage of the developing brain due to iodine deficiency. In normal conditions, less than 3 % of neonatal TSH are above the critical threshold of 5 mU/L whole blood. However because of technical and financial limitations the use of this variable has been recommended only in countries and areas where a program of systematic neonatal hypothyroid screening is already implemented.

4. Prevalence of cretinism

The study of the prevalence of cretinism can be completed by a study of the light forms (deaf muteness) when necessary. The prevalence of the cretinism can be up to 10 % of the whole population in certain regions.

Criteria on the intervention level

An operational definition of endemicity based on the experiences and a consensus between the experts has been refined and allows identification of the need for interventions in a formal manner. A zone is arbitrarily defined as affected by endemic goitre when more than 10 % of the children between 6 to 12 years suffer from goitre.

Iodine Deficiency	Severe	Moderate	Mild
Number of cases of goitre among school children Visible goitre Total goitre	 > 50 % > 10 %	 20-49 % 5-9 %	 10-19 % 1-5 %
Urinary iodine (median, µg/l)	< 20 %	20-49 %	50-99 %
Prevalence of cretinism	> 1 %	< 1 %	0 %

Indicators of iodine status at population level

In case of suspicion of endemic disease a fast inquiry on the prevalence among school children from 6 to 12 years old will give a first approximation of the magnitude of the problem. The consultation of a specialist is recommended for the following stages which will consist in refining the endemicity diagnosis and in deciding if an intervention is a good idea and what sort of intervention is needed.

Intervention strategies

1. Iodized salt

The iodination of salt is one of the most simple, least expensive and most efficient measures, in nutrition as well as in public health. It was used for the first time in 1917 in the United States. Since then its efficiency has been recognized in several countries: Guatemala, Argentina, Brazil, and Switzerland. It is a simple technology with an ignorable risk for toxicity. Iodine is added to the salt under the form of potassium iodide or, in humid tropical regions, potassium iodate because of its increased stability. The proposed concentration varies between 1/25.000 and 1/100.000 in function of certain criteria like the consummation of salt by the population and the severity of the deficiency. The cost averages 0.20 US$/person/year and the efficiency of the program depends on:

- the control and monitoring of the iodine quantity
- the resistance of the producers of salt
- the geographical distribution of the production sites
- the distribution in the risk zones
- the accessibility of the iodized salt and the by-passes

Iodized salt is considered as the most appropriate measure for iodine supplementation. The advantage of supplementing with iodized salt is that it is used by all sections of a community irrespective of social and economic status. It is consumed as a condiment at roughly the same level throughout the year. Its production is often confined to a few centres which means that processing can occur on a larger scale and with better controlled conditions. However this is often not the case in developing countries.

The packaging of the iodized salt is very important. Jute bags have been used extensively but

in humid conditions salt absorbs moisture. The iodate dissolves and will drop out of the bag if it is porous with a heavy loss. This has been found to reach 75% over a period of nine months. To avoid this waterproofing is required, achieved by a polythene lining inside the jute bag or else a plastic bag. The additional cost of a plastic bag (50-80% more) would be justified by reduced losses and their resale value.

2. Iodination of water

Water is really a good means of transportation with a large distribution and it is easy to adjust. There are no negative effects and costs are moderate. It can be done by iodizing the water distribution system or wells with slow release capsules. As salt, it is a daily necessity and thus the iodization will reach the most vulnerable groups.

3. Iodized oil

An iodized oil supplementation program is necessary when other methods have been found ineffective or can be considered to be inapplicable. Iodized oil can be regarded as an emergency measure for the control of severe IDD until an effective iodinated salt program can be introduced. Spectacular and rapid effects of iodized oil in reducing goitre can be expected. Iodized oil can be given in injections (Lipiodol®) or orally. Protection of an oral dose is around one year, that of an injection four to five years.

The possibility of linking up an iodized oil program with childhood vaccination and antenatal care has been considered in the past. Diversification and modification of food habits in endemic zones is another preventive measure, but is challenging as it often requires importation of sea food to remote areas.

Monitoring

In the countries that have begun iodized salt programs, sustainability is a major focus. These programs are fragile and require a long-term commitment from governments. In several countries where iodine deficiency had been eliminated, salt iodization programs fell apart and iodine deficiency recurred.

The indicators used in monitoring and evaluating IDD control programs include:

1) Indicators to monitor and evaluate the salt iodization process (Process indicators)
2) Indicators to monitor the impact of salt iodization on the target populations (Impact indicators).

The impact indicators include in order of priority the determinations of urinary iodine, of the prevalence of goitre and of the serum levels of TSH and thyroid hormones. It is now considered that iodine deficiency has been eliminated from one particular country when the access to iodized salt at household level is at least 90 %, together with a median urinary iodine of at least 100 µg/L and with less than 20 % of the samples below 50 µg/L.

Side effects of iodine supplementation

The effect of iodine on the thyroid gland is complex with a U shaped relation between iodine intake and risk of thyroid diseases as both low and high iodine intake are associated with an increased risk. It is stated that normal adults can tolerate up to about 1000 µg iodine/day without any side effects.

However this upper limit of normal is much lower in a population which was exposed to iodine deficiency in the past. The optimal level of iodine intake to prevent any thyroid disease may be a relatively narrow range around the recommended daily intake at 150 µg.

The possible side effects of iodine excess are as follows:

1. Iodide goitre and iodine-induced hypothyroidism

When the iodine intake is chronically high, as for example in coastal areas of Japan and China due to the chronic intake of seaweeds rich in iodine such as laminaria or in Eastern China because of the high iodine content of the drinking water from shallow wells, the prevalence of thyroid enlargement and goitre is high as compared to normal populations and the prevalence of subclinical hypothyroidism is elevated. The mechanisms behind this impairment of thyroid function are probably both iodine enhancement of thyroid

autoimmunity and reversible inhibition of thyroid function by excess iodine (Wolff-Chaikoff effect) in susceptible subjects. However, this type of thyroid failure has not been observed after correction of iodine deficiency, including in neonates after the administration of huge doses of iodized oil to their mothers during pregnancy.

2. Iodine-induced hyperthyroidism

Iodine-induced hyperthyroidism (IIH) is the main complication of iodine prophylaxis. It has been reported in almost all iodine supplementation programs. Iodine deficiency increases thyrocytes proliferation and with the development of multifocal autonomous growth. These nodules become autonomous and can result in hyperthyroidism after iodine supplementation. A multicentre study conducted in seven African countries, including Zimbabwe and Congo showed that the occurrence of IIH in the last two countries was due to the sudden introduction of poorly monitored and excessively iodized salt in populations which had been severely iodine deficient for very long periods in the past.

The conclusion of the multicentre study was that the risk of IIH is related to a rapid increment of iodine intake resulting in a state of acute iodine overload.

It thus appears that IIH is one of the Iodine Deficiency Disorders. It appears to be largely unavoidable in the early phase of iodine supplementation. It affects principally the elderly with long lasting autonomous nodules. Its incidence reverts to normal or even below normal after one to ten years of iodine supplementation.

3. Iodine-induced thyroiditis

Another possibility is the aggravation or even the induction of autoimmune thyroiditis by iodine supplementation. However, no large surveys have been performed which have analyzed the impact of large scale programs of iodine supplementation on the occurrence of clinically significant iodine-induced thyroiditis with public health consequences on thyroid function.

4. Thyroid cancer

Although in animal studies the chronic stimulation of the thyroid by TSH is known to produce thyroid neoplasms, in humans correction of iodine deficiency rather decreases the risk of and morbidity from thyroid cancer.

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