Iodine Deficiency in the World: Where Do we Stand at the Turn of the Century?

François Delange,1 Bruno de Benoist,2 Eduardo Pretell,3 and John T. Dunn1,4

Iodine deficiency is the leading cause of preventable mental retardation. Universal salt iodization (USI), calling for all salt used in agriculture, food processing, catering and household to be iodized, is the agreed strategy for achieving iodine sufficiency. This article reviews published information on programs for the sustainable elimination of the iodine deficiency disorders and reports new data on monitoring and impact of salt iodization programs at the population level. Currently, 68% of households from areas of the world with previous iodine deficiency have access to iodized salt, compared to less than 10% a decade ago. This great achievement, a public health success unprecedented in the field of noncommunicable diseases, must be better recognized by the health sector, including thyroidologists. On the other hand, the managers and sponsors of programs of iodized salt must appreciate the continuing need for greatly improved monitoring and quality control. For example, partnership evaluation of iodine nutrition using the ThyroMobil model in 35,223 schoolchildren at 378 sites of 28 countries has shown that many previously iodine deficient parts of the world now have median urinary iodine concentrations well above 300 μg/L, which is excessive and carries the risk of adverse health consequences. The elimination of iodine deficiency is within reach but major additional efforts are required to cover the whole population at risk and to ensure quality control and sustainability.

Introduction

IODINE DEFICIENCY is the leading cause of potentially preventable mental retardation in childhood (1–3). Its elimination is within reach and would constitute an unprecedented public health success in the field of noncommunicable diseases (4). These statements result from a long series of events.

Goiter is the most visible sign of the disorder but has only recently been appreciated as the tip of the iceberg of iodine deficiency disorders (IDD). It belongs to the history of mankind in the parts of the world where the soil is iodine deficient because of active erosion by recent melting of the glaciers, intense rainfalls, or flooding (5–8).

In 1960, the World Health Organization (WHO) presented the first comprehensive review of the extent of endemic goiter worldwide, underlying the severity of the problem (9). However, despite the successful elimination of IDD in a number of industrialized countries, progress in the developing world was slow during the next 15 years.

A concept introduced in 1983 stated that a population not receiving the daily requirements of iodine (Table 1) experiences developmental abnormalities in all age groups. These include not only goiter with impaired thyroid function but also decreased fertility, increased perinatal mortality, retarded growth, and impairment of mental development, including its extreme form, endemic cretinism. These abnormalities are grouped under the general heading of IDD (10), replacing the older term endemic goiter and focusing mostly on mental retardation as the most important consequence of iodine deficiency.

In 1985, with the support of the United Nations Children’s Fund (UNICEF), WHO, and the Australian government, the International Council for Control of Iodine Deficiency Disorders (ICCIDD) was founded in order to bridge the gap between available knowledge on IDD and its application, and to achieve the sustainable elimination of IDD (8).

In 1987, the United Nations Sub-Committee on Nutrition established an IDD Working Group to provide an annual report on the progress towards elimination.

The next important milestone was the 1990 World Health Assembly resolution to eliminate iodine deficiency as a major public health problem. In the same year, the United Nations World Summit for Children, attended by 71 heads of state and representatives of 159 governments, endorsed the

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goal of the virtual elimination of IDD by the year 2000. In 1992, the goal was reaffirmed by the International Conference on Nutrition jointly convened by WHO and the UN Food and Agriculture Organization (FAO) (11).

The last decade has seen enormous efforts and investments toward reaching this goal. The governments of the affected countries mobilized their resources to implement programs for IDD control, aided by coordination from WHO and UNICEF, technical support of ICCIDD, and the combined efforts of many other partners including international and bilateral cooperation agencies, national and international nongovernmental organizations (NGOs) such as the Micronutrient Initiative (MI), and private foundations such as Kiwanis International. Moreover, an effective partnership with the salt industry also played a major role, recognized during the 8th World Salt Symposium, “Salt 2000,” held in The Hague, The Netherlands.

The progress achieved during the last decade is remarkable. In 1990, an estimated 1.572 billion people (28.9% of the world’s population) were at risk of IDD, 655 million (12%) were affected by goiter, up to 11.2 million (2%) by cretinism, the extreme form of mental retardation due to iodine deficiency, and another 43 million people had some degree of mental impairment (3). By 1999, 81% of the 130 countries where IDD was a public health problem had a national intersectoral coordinating body, 78% had an action plan for IDD control, 75% had salt iodization legislation in place, and another 9% had it in draft form, 65% had laboratory facilities for program monitoring, 68% of households had access to iodized salt, 73% of countries were monitoring salt quality, and 61% were monitoring iodine nutrition in the population (4).

These results constitute an unprecedented success in the control of noncommunicable diseases and especially of nutrition diseases. The achievement can be attributed at least partly to the fact that IDD is universally recognized as a major cause of preventable mental retardation and that IDD is one of the rare nutritional disorders which can be controlled easily and at low cost by nutritional measures.

However, despite the efforts of IDD experts, salt specialists, policy makers, health care providers, communication specialists, and consumer associations, collaboration between all these players is often insufficient, especially with regard to the health sector, including the thyroidologists (12).

The present article critically reviews world data on IDD control, to promote better understanding and collaboration among the different stakeholders, especially between the donors and health professionals. We discuss public health significance of IDD, the current status of IDD control programs and their implementation, monitoring and impact of the programs of salt iodization at the population level, and how to ensure sustainability of the ongoing programs of iodine supplementation.

Reevaluation of the Public Health Significance of IDD

New concepts during recent years have enlarged the concept of IDD.

Maternal hypothyroxinemia and brain damage to the offspring

Extensive studies on perinatal thyroidology and feto-maternal thyroid relationship (13–19) have thrown new light on the pathogenesis of endemic cretinism and mental retardation (20) by indicating very clearly that part of the fetal thyroxine (T4) is of maternal origin, disproving the old concept that maternal thyroid hormones do not cross the placenta. On the contrary, maternal T4 is crucial for brain development in early fetal life, including the first trimester, before the onset of fetal thyroid function (20–24). This issue has recently been extensively reviewed (25).

Hyperthyrodism as a disorder induced by iodine deficiency

Areas of mild to moderate iodine deficiency have more nonautoimmune (sub)clinical hyperthyroidism in the elderly (26–28) and even in schoolchildren (29) than do iodine replete areas. On the other hand, the correction of iodine deficiency can induce, almost systematically in all endemic areas, so called iodine-induced hyperthyroidism (IIH) in susceptible individuals. It occurs commonly in adults with autonomous nodular goiters (30). In both cases, the chronic thyroid hyperstimulation due to iodine deficiency tends to induce a heterogeneous multifoccal polyclonal abnormality of the thyroid. Both cold and hot nodules develop. Some of the hot nodules are monoclonal and associated with activating mutations of the thyrotropin (TSH)-receptor (31,32). Under these conditions, hyperthyroidism may develop spontaneously or as a consequence of a sudden increment in iodine intake (33–35). Thus both spontaneous and IIH fit into the family of iodine deficiency disorders.

Goiter as maladaptation to iodine deficiency

Early studies on the physiopathology of endemic goiter (see reviews in Ermans [36] and Delange [37]) culminating with the outstanding report by Stanbury et al. (38), considered goiter as an adaptation to iodine deficiency. Subsequent studies, including from adjacent areas with the same degrees of iodine deficiency but differing in goiter prevalence, challenged this view and showed that goiter represents rather maladaptation to iodine deficiency (39,40).

Current Status of IDD Control Programs: Public Health Issues

Seaweed has been used to prevent goiter in China for centuries (8) but it is only in the years 1910 to 1920 that systematic programs of salt fortification with iodine were introduced as a strategy for the elimination of IDD almost simultaneously in the United States (41) and in Switzerland (42,43). In the latter country, the level of salt iodization be-

<table>
<thead>
<tr>
<th>TABLE 1. RECOMMENDED DAILY INTAKE OF IODINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–59 months</td>
</tr>
<tr>
<td>6–12 years, schoolchildren</td>
</tr>
<tr>
<td>&gt;12 years, adolescents and adults</td>
</tr>
<tr>
<td>Pregnant and lactating women</td>
</tr>
</tbody>
</table>

gan at only 1.9 to 3.75 ppm, then increased progressively up to 15 ppm in later years, in response to close monitoring of the program’s impact on the population.

Starting in the early 1950s with pioneering studies in New Guinea (44-46), supplementation with iodized oil was introduced in severely affected populations in Asia (47), Africa (48), and Latin America (49). Initially, iodized oil was administered intramuscularly, more recently by the oral route. Follow-up studies of these programs demonstrated the following.

Goiter prevalence decreased rapidly and thyroid function reverted to normal and remained so for up to 7 years after injections of iodized oil and for up to 1 to 2 years after oral administration (47-53). Key factors in this success were normalization of the thyroid’s iodine stores (48) and the level of iodization of thyroglobulin, the determining factor in impairment of thyroid function (36).

Endemic cretinism was prevented, both in its neurological and myxedematous forms, provided that iodine deficiency was corrected before or during early pregnancy, at least for the prevention of neurological signs. This result indicates that the neurological damage of cretinism stems mostly from lack of maternal thyroid hormones for the developing brain during early gestation and even before the fetal thyroid started to function (reviewed in Delange [20]).

A meta-analysis of 18 studies on mental development in endemic goiter areas (17 severe and 1 mild) showed that even noncretins and clinically euthyroid individuals had a mean loss of 13.5 IQ points compared to controls from nearby iodine-sufficient areas after correction of iodine deficiency by iodized oil (54). Corresponding data are not available from areas with only mild endemic goiter or after the correction of iodine deficiency by iodized salt.

The frequency of still births and the perinatal mortality decreased and the birthweight increased (55-57).

In summary, the studies using iodized oil unquestionably demonstrated that correction of iodine deficiency greatly reduced or eliminated its consequences: brain damage, mental retardation, goiter, impaired thyroid function, and perinatal morbidity.

These facts were subsequently much less clearly evidenced when correction of iodine deficiency occurred on a large scale using iodized salt, which is nevertheless the universally adopted strategy aiming at the sustainable elimination of IDD.

As a matter of fact, it has been recognized that in order to move from pilot studies using iodized oil to ambitious national programs of iodine supplementation, the strategy of choice is Universal Salt Iodization, that is iodization of all human and livestock salt, including salt used in the food industry (4,58,59).

The choice of this approach is based on the following: salt is one of the few commodities that is consumed by virtually everyone; salt consumption is fairly stable throughout the year; salt production is usually limited to a few geographical areas; salt iodization technology is easy to implement and available at reasonable cost (0.4-1.5 US cents/kg or 2-8 US cents per person per year); the addition of iodine to salt does not affect its color, taste or odor; and the quality of iodized salt can be monitored at production, retail and household levels.

The level of salt iodization in order to provide 150 μg of iodine per day in adults via iodized salt is influenced by several factors: (1) the consumption of salt per capita, (2) the degree of iodine deficiency, and (3) the loss of iodine from producer to consumer. Consequently, the optimal level of salt iodization will vary from country to country. The initial levels of salt iodization in different countries varied markedly from one country to another (Table 2). North America has always had one of the highest levels. Recent epidemiological studies (35) and improvement of the salt technology (60), have led to the present recommendation that the iodine concentration in salt at the site of production should be within the range of 20 to 40 mg of iodine per kilogram of salt, i.e., 20 to 40 ppm (61). This range is based on iodine loss of 20% from salt production to household, another 20% during cooking and an average daily salt intake of 10 g.

Over the last decade, countries have made enormous progress in introducing access to iodized salt for iodine-deficiency populations.

Table 3 provides the latest information of iodized salt coverage in IDD-affected countries. Of the 130 countries having iodine deficiency as a public health problem, nearly half provide access to iodized salt for more than 50% of the households and 20 countries for more than 90%. The 90% figure is one of the criteria used to assess IDD elimination (3,62). In 1999, 68% of households in affected countries had access to iodized salt, compared to 5% to 10% in 1990 (63). The proportion varies from 27% in Europe to 90% in Latin America, with the other four regions ranging from 63% to 76%.

The figures in Table 3 should be interpreted cautiously because they refer only to the amount of iodized salt available to households and not its actual intake. In addition, the countries where such data are available are few and the data are usually derived from local surveys that are not representative of the overall IDD-affected populations. This lack of precision exists because iodized salt has been introduced in most countries within the past decade and there has not been enough time for systematic dietary salt surveys. Therefore,
in many countries, the proportion of households having access to iodized salt was reached only by estimation on a theoretical basis from the amount of iodized salt imported or produced, as reported by the salt industry, divided by the total population of the country.

Monitoring and Impact of the Programs of Salt Iodization

Monitoring procedures

The social process for successfully implementing a national IDD control program includes the following components (11): situation assessment; communication of results to health professionals, political authorities and the public; development of an action plan; implementation of a program; and finally, evaluation of its impact at population level. This last phase, monitoring, is often neglected not only because it is the last phase in the process but because it may be overshadowed by other components of the program such as implementation, which is considered as the main or occasionally even the single component to be considered. In addition, many countries affected by IDD belong to the group of countries with low income that therefore do not have the financial or technical resources for the laboratory facilities necessary to proper monitoring of salt quality and iodine status.

And yet, monitoring is crucial because IDD is a disease and its prevention and therapy require trained professionals to prescribe the therapy and verify its effects. This absolute ethical duty applies equally to a single individual and to a global population.

Table 4 defines the criteria recommended by WHO, UNICEF, and ICCIDD for monitoring progress towards the elimination of IDD (3).

The adequate level of salt iodization has been discussed earlier. A detailed description of the procedures for assessing progress in iodized salt production, (the product), in program implementation (the process) and in coverage by iodized salt (the progress) is given elsewhere (64).

The second indicator is urinary iodine, to assess the present iodine intake. There is an agreement that casual urine samples from a representative fraction of the population provide accurate information on the status of iodine nutrition.

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Number of IDD-affected countries</th>
<th>Number of countries categorized by percent of households having access to iodized salt</th>
<th>Percentage of households having access to iodized salta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>44</td>
<td>8, 6, 8, 19, 3, 10, 63%</td>
<td></td>
</tr>
<tr>
<td>Americas</td>
<td>19</td>
<td>0, 0, 3, 6, 10, 90%</td>
<td></td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>9</td>
<td>0, 1, 5, 7, 70%</td>
<td></td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>17</td>
<td>5, 2, 6, 66%</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>32</td>
<td>10, 12, 4, 27%</td>
<td></td>
</tr>
<tr>
<td>Western Pacific</td>
<td>9</td>
<td>0, 4, 3, 76%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>130</td>
<td>23, 13, 31, 43, 68%</td>
<td></td>
</tr>
</tbody>
</table>

aTotal population of each country multiplied by the percentage of households having access to iodized salt. Number then totalled for each region and divided by the total regional population.

IDD, iodine-deficiency disorder.

The daily collection of 24 hours urine is not necessary and relating urinary iodine to creatinine excretion does not add significantly. The frequency distribution of urinary iodine is usually asymmetrical and presentations by box plots showing the median and the upper and lower quartiles (P25 and P75) provide the most adequate visualization (62).

Table 5 shows the latest epidemiological criteria for assessing iodine nutrition, based on median urinary iodine concentrations in school-age children. These introduce a clear distinction between iodine intake and its impact, i.e., the status of iodine nutrition. It was agreed that the optimal status of iodine nutrition corresponds to a median urinary iodine concentration in schoolchildren situated between 100 and 200 μg/L (62).

The third indicator is thyroid size (Table 4). The prevalence of goiter reflects a population's history of iodine nutrition but does not properly reflect its present iodine status, in contrast to the urinary iodine. Palpation is obviously the simplest method for measuring thyroid size. WHO, UNICEF, and ICCIDD have recently updated and simplified the classification of goiter by palpation. The previous definition that

### Table 4. Criteria for Monitoring Progress Toward Eliminating IDD as a Public Health Problem

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Salt iodization</td>
<td>Proportion of households consuming effectively iodized salt</td>
</tr>
<tr>
<td>2. Urinary iodine</td>
<td>Proportion below 100 μg/L</td>
</tr>
<tr>
<td></td>
<td>Proportion below 50 μg/L</td>
</tr>
<tr>
<td>3. Thyroid size</td>
<td>Proportion with enlarged thyroid, by palpation or ultrasound</td>
</tr>
<tr>
<td>4. Neonatal TSH</td>
<td>Proportion with levels &gt;5 mU/L whole blood</td>
</tr>
</tbody>
</table>

From WHO/UNICEF/ICCIDD (3). IDD, iodine-deficiency disorder; TSH, thyrotropin.
the thyroid gland will be considered goitrous when each lateral lobe has a volume greater than the terminal phalanx of the thumb of the subject being examined, has been maintained but the classification has been simplified into grade 0 (no goiter), grade I (a goiter palpable but not visible when the neck is in normal position), and grade II (visible goiter) (62). Goiter prevalence by palpation is subject to important interobserver variability, especially when the prevalence is low and thyroids are small. Therefore, the actual measurement of thyroid volume by ultrasounds now receives more attention (65–72). A European study (73) led WHO and ICCIDD to propose normative values for thyroid volume measured by ultrasound in school-age children based on gender, age, and body surface area (74). A series of investigators from other parts of the world have questioned these values (68,69,72) and a recent study on interobserver and interequipment variability of thyroid size on ultrasonography suggests that these normative values were overestimated by a factor of about 30% (75).

Neonatal thyrotropin (TSH) is the last variable recommended for monitoring. Its major advantage is its reflection of brain cell receptor saturation by thyroid hormones, and consequently, the risk of damage to the developing brain and subsequent impairment of intellectual development. Pilot and regional studies have demonstrated the accuracy and sensitivity of neonatal thyroid screening as a monitoring tool (76,77), but it is recommended only if a national program of systematic screening for permanent sporadic congenital hypothyroidism is already in place.

The WHO/UNICEF/ICCIDD recommendations for monitoring and assessing progress indicate that two blood constituents, TSH and thyroglobulin (Tg), can serve as surveillance indicators but that determining serum concentrations of thyroid hormones, T4, and triiodothyronine (T3) in schoolchildren is usually not recommended for monitoring iodine nutrition because these tests are more cumbersome, more expensive and less sensitive indicators (62).

However, it has to be clearly understood that the ultimate goal of any program of iodine supplementation is to normalize thyroid function at the individual level. It is not only to organize access to iodized salt nor to increase the urinary iodine.

<table>
<thead>
<tr>
<th>Median urinary iodine (µg/L)</th>
<th>Iodine intake</th>
<th>Iodine nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>Insufficient</td>
<td>Severe iodine deficiency</td>
</tr>
<tr>
<td>20–49</td>
<td>Insufficient</td>
<td>Moderate iodine deficiency</td>
</tr>
<tr>
<td>50–99</td>
<td>Insufficient</td>
<td>Mild iodine deficiency</td>
</tr>
<tr>
<td>100–199</td>
<td>Adequate</td>
<td>Optimal</td>
</tr>
<tr>
<td>200–299</td>
<td>More than adequate</td>
<td>Risk of iodine-induced hyperthyroidism (IIH) in susceptible groups</td>
</tr>
<tr>
<td>&gt;300</td>
<td>Excessive</td>
<td>Risk of adverse health consequences (IIH, autoimmune thyroid diseases)</td>
</tr>
</tbody>
</table>

From WHO/UNICEF/ICCIDD (62).

Impact of the programs of salt iodization

Currently, we have much less information about the impact of the salt iodization programs on IDD than on the implementation of the programs themselves. It is beyond the scope of this article to review all these monitoring data, but they are summarized country by country on the websites of ICCIDD (http://www.iccidd.org) and WHO (http://www.who.int/nut). As assessed by measurements of urinary iodine, many countries have achieved the elimination of iodine deficiency, e.g., Algeria, Kenya, Cameroons, Tanzania (Africa), Iran, Lebanon, Tunisia (Eastern Mediterranean), Bhutan, China, Indonesia, India, Thailand (Asia) and Venezuela, Peru, Ecuador (Latin America) (4).

However, as shown in Table 6 and in spite of the tremendous improvement of the implementation of programs of iodized salt, the percentage of the world population affected by goiter has not changed between 1990 and 1999. This situation is at least partly explained by the fact that the denominator of the fraction has changed during the last 9 years: the figure for 1999 includes a number of countries from Central and Eastern Europe and from Africa which are often severely affected and that were not considered in the 1990 figures.

Also, surprisingly enough, few longitudinal or case control studies address the influence of USI on the other main

Table 6. Comparison of the Percentage of the World Population Affected by Goiter per WHO Region in 1990 and 1999

<table>
<thead>
<tr>
<th>Region</th>
<th>1990%</th>
<th>1999%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>15.6%</td>
<td>20%</td>
</tr>
<tr>
<td>Americas</td>
<td>8.7%</td>
<td>5%</td>
</tr>
<tr>
<td>Eastern Med.</td>
<td>22.9%</td>
<td>32%</td>
</tr>
<tr>
<td>Europe</td>
<td>11.4%</td>
<td>15%</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>13.0%</td>
<td>12%</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>9.0%</td>
<td>8%</td>
</tr>
<tr>
<td>Total</td>
<td>12.0%</td>
<td>13.0%</td>
</tr>
</tbody>
</table>

aFrom WHO/UNICEF/ICCIDD (3).
disorders induced by iodine deficiency such as impairment of thyroid function, low birthweight, perinatal mortality and morbidity, and the prevention of endemic cretinism and mental retardation. The oft-quoted statement that correction of iodine deficiency protects 85 million neonates from brain damage and mental retardation annually was reached by extrapolating the 13.5 points of IQ reduction with iodine deficiency (54) to populations at risk for iodine deficiency.

Many countries want partnership evaluation of their national programs, not only by nationals but also by experts from international organizations such as WHO, UNICEF, and ICCIDD. Some hope that the joint national and international team will conclude that IDD has been eliminated. Frequently, the joint survey has been conducted with support of the ThyroMobil model (73) in which a van, equipped with an ultrasound, deep freezer for urine samples, and computer, circulates from place to place and measures thyroid volume by ultrasound and collects samples for urinary iodine determination from selected samples of schoolchildren. The advantage of this approach is that its methodology is standardized and allows comparisons among all places in the world. Another advantage is that the physical presence of such a vehicle gives a valuable opportunity for increasing awareness and social mobilization on IDD.

Table 7 summarizes the present achievement of the ThyroMobil program. The surveys included so far 35,223 schoolchildren from 378 sites in 28 countries. The frequency distribution of the median urinary iodine in the different sites varies extensively among countries: only 28% to 46% of these medians are in the normal range of 100 to 200 μg/L. In Europe, 59% are below the threshold of 100 μg/L, indicating persisting iodine deficiency. By contrast, Latin America and Indonesia, show only 8% to 11% of their values below normal but 46% to 52% are above the upper limit of normal, indicating more than adequate iodine intake and its risks. In West Africa, the situation is more heterogeneous, only 28% of the medians are within the normal range, with 31% below and 41% above.

This heterogeneous situation is further illustrated in Table 8 which shows detailed results obtained in the 10 sites investigated in Burkina Faso. Only 1 site has insufficient iodine in the salt; it also has a very low median urinary iodine and a high prevalence of goiter, so these indicators are consistent in showing iodine deficiency. In the 9 other sites, the level of salt iodization is satisfactory with a mean of 48 ppm, but the median urinary iodine varies widely, from too low to too high, and the prevalence of goiter is normal in only 2 of these 9 sites. This indicates that a right level of iodine in salt does not guarantee either a normal urinary iodine or a normal prevalence of goiter in previously iodine deficient countries.

Table 9 offers more details from the 11 Latin America countries investigated. All previously had varying degrees of iodine deficiency, but by 1999, 90% of the households had access to iodized salt. Now, with the exception of Guatemala, all have a median urinary iodine above the lower limit of normal, a remarkable achievement. The frequency distribution of individual values shows that 62.3% of the cases in

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of</th>
<th>Percentage of median urinary iodine (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Countries</td>
<td>Sites</td>
</tr>
<tr>
<td>Europe</td>
<td>12</td>
<td>68</td>
</tr>
<tr>
<td>Latin America</td>
<td>11</td>
<td>142</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1</td>
<td>129</td>
</tr>
<tr>
<td>West Africa</td>
<td>4</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>378</td>
</tr>
</tbody>
</table>

Compiled from Delange et al. (73, 83), Pretell, Djokomoeljanto and Ntambwe (unpublished; with permission).

<table>
<thead>
<tr>
<th>Sites</th>
<th>Mean iodine content of salt (ppm)</th>
<th>Median iodine content of urine (μg/L)</th>
<th>Prevalence of goiter (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>4</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>90</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>108</td>
<td>14</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>248</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>138</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>190</td>
<td>27</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>183</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>51</td>
<td>69</td>
<td>34</td>
</tr>
<tr>
<td>10</td>
<td>47</td>
<td>283</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>114</td>
<td>22</td>
</tr>
</tbody>
</table>

From Ntambwe and Jooste (unpublished; with permission).
Guatemala and from 3.0% to 45.5% in the 10 other countries have values below the cutoff point of 100 mg/L. But a striking finding is that from 5.8% to 79.1% of the values in these 10 countries are now above 300 mg/L, indicating excessive iodine intake and the risk of adverse health consequences.

**Table 9. Distribution of Urinary Iodine in the Eleven Latin America Countries Investigated by the ThyroMobil Model**

<table>
<thead>
<tr>
<th>Country</th>
<th>Median Urinary iodine mg/L</th>
<th>% values outside the normal range</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>180</td>
<td>17.9</td>
<td>40.6</td>
</tr>
<tr>
<td>Peru</td>
<td>202</td>
<td>12.2</td>
<td>45.8</td>
</tr>
<tr>
<td>Venezuela</td>
<td>280</td>
<td>9.8</td>
<td>55.5</td>
</tr>
<tr>
<td>Ecuador</td>
<td>420</td>
<td>4.8</td>
<td>74.3</td>
</tr>
<tr>
<td>Chile</td>
<td>540</td>
<td>3.0</td>
<td>82.1</td>
</tr>
<tr>
<td>Bolivia</td>
<td>100</td>
<td>45.5</td>
<td>55.8</td>
</tr>
<tr>
<td>Mexico</td>
<td>176</td>
<td>27.6</td>
<td>48.6</td>
</tr>
<tr>
<td>Honduras</td>
<td>240</td>
<td>22.0</td>
<td>57.1</td>
</tr>
<tr>
<td>El Salvador</td>
<td>176</td>
<td>29.1</td>
<td>43.4</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>116</td>
<td>39.0</td>
<td>44.8</td>
</tr>
<tr>
<td>Guatemala</td>
<td>72</td>
<td>62.3</td>
<td>65.1</td>
</tr>
</tbody>
</table>

Adapted from Pretell et al. (84).

Guatemala and from 3.0% to 45.5% in the 10 other countries have values below the cutoff point of 100 mg/L. But a striking finding is that from 5.8% to 79.1% of the values in these 10 countries are now above 300 mg/L, indicating excessive iodine intake and the risk of adverse health consequences. Figure 1 illustrates the situation in Chile, where the median urinary iodine is 540 mg/L and where the frequency distribution of urinary iodine is shifted toward elevated values with as much as 17.5% of the values above the potentially toxic level of 1,000 mg/L.

**Discussion**

This article describes remarkable success toward the elimination of iodine deficiency in the world. Within a decade, the proportion of households with access to iodized salt has increased from less than 10% to 68%. This great achievement against the world’s most frequent thyroid disease has not been fully recognized by either the public health community or even thyroidologists.

However, this optimism needs to be tempered for at least two reasons:

1. Thirty-six affected countries have not yet introduced iodized salt or still have an household coverage below 10%. As a result, one-third of the population from affected countries cannot get iodized salt.
2. Quality control and monitoring have to be markedly improved and maintained: in too many places, iodine deficiency has now been replaced by a state of iodine excess. Sudden iodine excess following a long period of iodine deficiency can have damaging consequences (78–80). The most important of these because potentially lethal is IH (30), well documented in some parts of Africa (33–34) and elsewhere. Its diagnosis by clinical evaluation alone is unreliable. Biochemical screening of populations is much more accurate but is too rarely performed.

Several concepts and priorities need emphasis to advance the goal of IDD elimination. We must constantly remember that the final objective of iodine supplementation is not only to correct iodine nutrition and urinary iodine but to correct thyroid function. This has been substantially demonstrated by using iodized oil but much less clearly by iodized salt.

**FIG. 1.** Frequency distribution of iodine concentration in 565 children from 10 sites (September 1998).
Iodized oil has corrected or eliminated other key signs and symptoms of iodine deficiency, but similar results from iodized salt need more conclusive demonstration; these include the elimination of endemic cretinism, the prevention of less obvious blunting of intellectual and socio economic potential and reduction in perinatal morbidity and mortality.

Finally, the long-term sustainability of IDD control programs needs special attention; political authorities and their affected populations must maintain awareness and commitment. Iodine deficiency is a disease of the soil that will relapse soon after the preventive measures are abandoned. Guatemala (12) and, to a much larger extent, Russia and the Commonwealth of Independent States (CIS) (81) offer spectacular examples of this point.

With these considerations in mind, we recommend the following actions:

1. To maintain and even reinforce advocacy and training on IDD at the local, national, and regional levels, with particular emphasis on quality control, monitoring and sustainability.
2. To encourage the assessment of IDD magnitude and evaluation of intervention programs, and maintain global databases on IDD as a means of assessing progress toward eliminating IDD.
3. To provide support to the implementation of universal salt iodization, focusing on countries still facing obstacles in meeting the goal of IDD elimination. This implies:
   - To ensure availability and coordination between salt plants and importers of iodized salt.
   - To standardize the techniques and regulations on salt iodization (compounds, levels, trade, taxes).
   - To standardize and implement the quality control of iodized salt from the producer to the consumer.
4. To introduce temporary alternative strategies in communities where iodized salt is not yet available:
   - Supplementation with iodized oil where IDD is severe, concentrating at least on women of childbearing age and young infants.
   - Supplementation with tablets of potassium iodide at physiological doses during gestation, lactation, and early childhood up to 3 years where IDD is mild or moderate, as often reported in industrialized countries.
5. To strengthen or set up effective monitoring systems for salt quality control at all levels and encourage the development of reliable test kits for measuring iodine levels in salt. The promotion of iodized salt should not result in an increase of salt intake. The necessary monitoring of iodized salt intake is a unique opportunity to evaluate and monitor the salt intake and to respect the WHO recommendation to maintain or decrease the salt intake to healthy levels.
6. To strengthen or set up effective monitoring systems for iodine status. This implies:
   - To agree on the indicators, epidemiological, clinical, and biochemical (62).
   - To implement and maintain efficient national IDD programs.
   - To organize partnership evaluations of country programs by national and international teams.
   - To develop operational research: kits for urinary iodine, use of neonatal TSH as monitoring tool, measurement of IQ in moderate, mild ID.
   - To reinforce existing iodine laboratories, or support the development of new national, regional or subregional laboratories, able to meet the needs of countries lacking properly equipped facilities and to ensure availability of international reference iodine laboratories. This is a prerequisite for the establishment of effective systems for IDD surveillance and monitoring.

7. To evaluate the possible side effects of iodine supplementation (reviewed in Delange and Lecomle [80]).

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