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Iodine deficiency disorders in Europe

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Abstract

Iodine deficiency disorders (IDD) are related to the degree of iodine deficiency. In european countries, characterized by mild to moderate iodine deficiency, neurological deficits or minor neuropsychological impairments have been described. Urinary iodine excretion (UIE) ranged from 30 to 170 mcg/L, 141 millions of people were at risk of IDD, 97 millions were affected by goiter and 0.9 millions had an impaired mental development.

Iodine prophylaxis is devoid of adverse reactions with the exception of sporadic cases of transitory hyperthyroidism, associated to the severity of iodine deficiency before the prophylaxis. The International Council for Control of IDD recommends an universal iodine prophylaxis, instituted gradually in severe iodine deficient countries. The total cost of universal iodine prophylaxis is very cheap compared to the social cost of goiter and cretinism.

In conclusion, most european countries are still characterized by mild to moderate iodine deficiency. Iodine prophylaxis programs are already operating, its cost is irrelevant with respect to the undebatable beneficial impact on the health. Adverse effects are not observed except in severe iodine deficient areas where iodine intake was abruptly increased.

Keywords
Iodine deficiency
Endemic cretinism
Goiter
Iodine prophylaxis
Iodine intake

Introduction

Iodine deficiency leads to several disorders referred to as 'iodine deficiency disorders' (IDD) (Table 1) that can be prevented by iodine supplementation[1]. The knowledge of the global magnitude of IDD, and its real significance for the health and socioeconomic development, has improved considerably during the last decades. IDD is known to be a significant public health problem in 118 countries. At least 1572 million people worldwide are estimated to be at risk of IDD, who live in areas where iodine deficiency is prevalent (total goiter rates above 5%) and at least 655 million of these are considered to be affected by goiter. The regional distribution of goiter prevalence, and estimated rates of cretinism, are given in Table 2. As shown in Table 2, projections derived from field studies indicate that in Europe 97 millions of people are affected by goiter, while 141 millions are at risk of IDD and 0.9 millions have an impaired mental development.

Iodine exists primarily in the ocean, and it was also present on the earth's crust, but large amounts were leached from the soil by glaciations. The most likely areas to be devoid of iodine are the mountainous areas of the world. As the only source of iodine in humans is through diet, iodine deficiency can be corrected either through iodine supplementation or alternatively through the use in the diet of food produced in iodine sufficient areas. In industrialized societies diversification of the diet is the main reason for adequate iodine intake, thus explaining why today iodine deficiency occurs in poor and more remote areas even of industrialized Europe, for economical reasons more than for geographical location. In industrialized countries the main source of iodine are dairy products, followed by grain and cereal products. These foods are responsible for over half the dietary intake of iodine in U.S.A.

The frequency and severity of IDD manifestations are related to the degree of iodine deficiency that can be assessed according to clinical and biochemical parameters such as prevalence of goiter, urinary iodine excretion and

Table 1 The spectrum of iodine deficiency disorders*

Fetus	Abortion, stillbirths, perinatal and infant mortality cretinism
Infant/Child Adolescent	Goiter Overt or subclinical hypothyroidism Impaired mental and physical development
Adult	Goiter and its complications Hypothyroidism Endemic mental retardation Decreased fertility rate

* Modified from Hetzel[1].

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Table 2 Total number of people and percent of regional population living in areas at risk of IDD, or affected by IDD*

WHO region	Population (millions)	At risk of IDD		Affected by goiter		Affected by impaired mental development	
		millions	%	millions	%	millions	%
Africa	550	181	32.8	86	15.6	1.1	0.2
Americas	727	168	23.1	63	8.7	0.6	0.9
Eastern Med	406	173	42.6	93	22.9	0.9	2.3
Europe	847	141	16.7	97	11.4	0.9	1.1
South-East Asia	1355	486	35.9	176	13.0	3.2	1.3
Western Pacific	1553	423	27.2	142	9.0	4.5	2.9
Total	5438	1572	28.9	655	12.0	11.2	2.0

* Modified from WHO/NUT[2].

TSH level in newborns (Table 3). The impact of iodine deficiency on the health of humans is indeed well established for some manifestations: goiter is the most frequent manifestation and is closely related to the frequency of mental defects[1–5].

Neuropsychological defects and iodine deficiency in Europe

The most serious complication of iodine deficiency is endemic cretinism, characterized by irreversible and severe mental retardation associated with either a predominant neurological syndrome (neurological cretinism) or hypothyroidism (myxedematous cretinism) or a combination of both. Several theories have been hypothesised to explain the pathogenesis of neurological versus myxedematous cretinism. Recently, the role of combined selenium and iodine deficiency has been stressed. Selenium is present in high concentration in the normal thyroid and is essential for selenoenzymes such as glutathione peroxidase (GPX), that acts as antioxidant, and type I 5′-deiodinase[4]. The mechanism would be the following: iodine deficiency causes thyroid hyperstimulation by TSH that leads to increased production of H2O2 within the thyroid follicular cells; selenium deficiency also results in accumulation of H2O2 due to GPX deficit. Excess of H2O2 can induce thyroid cell destruction and myxedematous cretinism. On the other hand deficiency of the selenoenzyme 5′-deiodinase causes decreased catabolism of T4 to T3 with increased availability of T4 for the fetal brain and prevention of neurological deficits[6].

Cases of overt myxedematous, neurological or mixed endemic cretinism are reported in areas of severe iodine deficiency such as Africa and Asia[1,3,4]. However, in European countries, characterized by slight to moderate iodine deficiency, large goiters and cretinism were no longer observed. Several reports have described cases of neurological deficits[7–11] (Table 4) or minor neuropsychological impairments. In Tuscany neuropsychological performance was tested in 107 children living in a village characterized by mild iodine deficiency (urinary iodine excretion, UIE 64 mcg/L) by a block design subtest of the Wechsler Intelligence Scale for Children and simple reaction times to visual stimuli[7]. The results obtained in these children were compared with those obtained in children born and living in an iodine sufficient area. The block design test was not different between the two groups of children, while reaction times were significantly delayed in children living in the iodine deficient village. These data indicate that mild iodine deficiency may impair the rate of motor response to perceptive stimuli even in the absence of general cognitive defects.

Goiter and iodine deficiency in Europe

The status of iodine nutrition in Europe has been recently reviewed in a meeting in Bruxelles that resulted in a publication 'Iodine Deficiency in Europe', by Delange *et al.*[12]. A review of the iodine nutrition status in some European countries was made also in Munich in 1997[13]. Reported here are summaries of data collected in each country.

Table 3 Classification of goiter endemias by severity*

Indicator	Target population	Mild	Moderate	Severe
Goiter grade >0	Schoolchildren	5.0–19.9%	20.0–29.9%	>30.0%
Thyroid volume >97th centile by ultrasound	Schoolchildren	5.0–19.9%	20.0–29.9%	>30.0%
Median urinary iodine level (μg/L)	Schoolchildren	50–99	20–49	<20
TSH >5 mU/l whole blood	Neonates	3.0–19.9%	20.0–39.9%	>40.0%
Median Tg (ng/mL serum)†	Children/adults	10.0–19.9	20.0–39.9	>40.0

* Modified from WHO/NUT[2].
† Different assays may have different normal ranges.

Table 4 Neuropsychological defects in infants and schoolchildren residing in mild to moderate iodine deficient areas* of Europe

Regions	Tests	Findings	Authors
Spain	Locally adapted Baylely McCarthy Cattell	Lower psychomotor ability and mental development	Bleichrodt *et al.*
Italy			
Sicily	Bender-Gestalt	Low perceptual integrative motor ability Neuromuscolar and neurosensorial abnormalities	Vermiglio *et al.*
Tuscany	Wechsler Raven	Low verbal IQ, perception and motor ability	Fenzi *et al.*
Tuscany	Wisc	Low velocity of motor response to visual stimuli	Aghini-Lombardi *et al.*

* Modified from Delange[4].

Austria[12]

Austria was a classical endemic goiter country due to iodine deficiency with UIE of 35 mcg/day and goiter prevalence in adolescents of almost 50% in the 1960s. In 1923 a prophylactic program with iodized salt was made, but then discontinued a few years later. In 1963 iodized salt at the level of 10 mg/Kg was reintroduced. Goiter prevalence was still elevated, but huge goiter and cretinism had gone.

Belgium[12]

The data over these last 30 years showed that there is no severe endemic goiter in Belgium, but the iodine intake remains marginally low. In a survey carried out in 1980 goiter prevalence was 10% in the eastern part of the country. The UIE in adults in 1990 was around 50 mcg/day and in children was 43 mcg/day.

Denmark[13]

In Denmark a large survey of UIE in 6000 adolescents from different parts of the country was performed in the 1960s. It was shown that UIE was relatively low with an average value of 64 mcg/day. In 1988 in Copenhagen the UIE was from 73 to 100 mcg/day in the age group from 20 to 80 years. Denmark is thus an area of mild to moderate iodine deficiency and the level of UIE has not changed in the last 30 years[17].

Eastern Europe and Central Asia[13]

For a long period of time, iodine deficiency disorders have been greatly underestimated in eastern European countries. Only surveys carried out in the 1980s clearly showed the persistence of moderate or even severely affected areas in several countries of eastern Europe and in Baltic States. The latest available data show that IDD is virtually eliminated in only one country, i.e. the Slovakia. Several countries have marginal or mild IDD. In Czech Republic and Hungary the majority of the subregions have moderate IDD. In some areas iodine prophylaxis programs through salt iodization are already implemented. In Poland two well defined endemic goiter areas have been known for years (Carpathian and Sudeten). Iodine prophylaxis is started in 1935. In the survey carried out from 1949 to 1977 other endemic areas were found.

In the period of time from 1993 to 1997, a survey was carried out by the European Thyro-Mobil action (Table 5). In schoolchildren population UIE was less than 100 mcg/day. Prevalence of goiter ranged from 5 to 41% depending on the area. Poland is characterized by a moderate or, only in seaside area, mild degree of iodine deficiency.

Finland[12]

Iodized salt was introduced in the late 1940s but endemic goiter was found all over the country specially in the inland and in the east[16]. In the 1960s the iodine content of table salt was increased to 25 mg/Kg and the median UIE increased to about 300 mcg/day. In the most recent surveys at the end of 70ies the prevalence of goiter in schoolchildren was $<5\%$.

France[12]

The French Society of Endocrinology carried out a survey in 10–14 years old schoolchildren between 1984 and 1986 in 13 over 25 educational districts. Goiter prevalence was from 10 to 30% in the majority of districts and only in a few of them was $<5\%$. The UIE was comprised between 55 and 174 mcg/g creatinine being >100 only in 2/13 districts.

Table 5 Recommended dietary allowance of iodine*

	Iodine (mcg/day)
Adolescent/adult	150
Pregnant and lactating women	200
Children	
1–6 yr	90
7–10 yr	120
Infants	
<1 yr	90

* Modified from Delange[12].

Germany[12]

Germany is an iodine deficient region and goiter is endemic. Initially, the prophylactic measures gradually introduced since the beginning of 1980s differed in East and West Germany. In East Germany 'general prophylaxis' was able to achieve an improvement of iodine supply until 1989. Adoption of the principle of voluntary action after the reunification of Germany, however, led to a decrease of iodine intake. Endemic occurrence of goiter was detected and iodine deficiency identified as its cause in the 1970s. Surveys carried out in both parts of Germany showed that the prevalence of goiter was about 4–10% in the North and about 10–35% in the South. UIE was 31–37 mcg/g creatinine in North and 18–29 mcg/g creatinine in South.

Greece[12]

Endemic goiter is present in Greece and has been studied extensively. UIE ranged from 17 to 45 mcg/day). The prevalence of endemic goiter ranged from 22 to 59%. After the iodine prophylaxis the prevalence of goiter decreased.

Ireland[12]

In studies carried out during the years 1938–39 areas of endemic goiter were found in Ireland. In a most recent survey UIE showed a seasonal variation due to the different iodine content in the milk according to the season. Ireland was shown to be characterized by slight to moderate iodine deficiency with 22% of 2740 subjects having UIE below 50 mcg/day.

Italy[12]

The existence of goiter in Italy has been known since the age of the ancient Romans. A clear relationship between endemic goiter and endemic cretinism was recognized in 1848 by an 'ad hoc' committee appointed by the king of Sardinia. Iodine deficiency in endemic areas was first documented in the early 20th century in Piemonte and Valle d'Aosta. The manufacture of iodized salt was allowed by law in 1972 and distributed on request to selected endemic areas. In 1977 the distribution was extended to the whole country. In 1991 the amount of iodine has been raised from 15 to 30 mg/Kg of salt by a Public Ministry Decree. In a series of surveys carried out from 1978 and 1991 the goiter prevalence ranged from 14 to 73% and was roughly inversely correlated with iodine excretion (UIE 10–122 mcg/g creatinine)[14].

In a recent survey conducted in 1994 the impact of iodine deficiency on thyroid disease was studied in the whole population of a village of southern Italy, Pescopagano, characterized by mild to moderate iodine deficiency and never submitted to iodine prophylaxis[15]. 1411 people were studied. The history of thyroid disease was collected and thyroid size was determined by palpation and ultrasound. UIE was evaluated and thyroid function was assessed by measuring free thyroid hormones (FT4, FT3), thyroid stimulating hormone (TSH) and thyroid autoantibodies (TgAb, TPOAb). Median UIE was 55 μg/L. The overall prevalence of goiter was 16.0% in children and progressively increased with age up to 74.6% in the 56–65 class of age. Thyroid nodularity progressed from 0.5% in children up to 28.5% in the 56–65 age group. In subjects more than 15 yr-old nontoxic diffuse and nodular goiter were 41.8% and 17%, respectively. The prevalence of hyperthyroidism was 2.9% with a nonautoimmune: autoimmune ratio of 2.2:1. The occurrence of thyroid functional autonomy increased from 0.7% in children up to 15.4% in older subjects, with no difference between nodular and diffuse goiter. The prevalence of overt and subclinical hypothyroidism was 0.2% and 3.8% respectively. The prevalence of serum TgAb and TPOAb was 12.6%, being more frequent in females (17.3%) than in males (7.0%) and progressively increased with age from 2.4% in children to 21.9% in the 46–55 age class, with little change in older age groups. The prevalence of diffuse autoimmune thyroiditis was 3.5%, as assessed by thyroid antibody assays and by ultrasound. Median TSH progressively decreased with age from 2.2 μU/ml up to 0.9 μU/ml, being significantly lower ($p < 0.001$) in goitrous than in nongoitrous subjects. Thyroid cancer was found in 0.1% of the adults.

The conclusion of this study was that in an iodine deficient community a progressive increase of goiter prevalence occurred with age with a high proportion of nodularity and functional autonomy in the adult population. Hyperthyroidism was twice as high than that reported in iodine sufficient areas, the difference being mainly due to an increased frequency of toxic nodular goiter, while the prevalence of hypothyroidism and thyroid cancer showed no difference. Serum TgAb and TPOAb were more frequently detectable with respect to iodine sufficient areas, while the prevalence and age distribution of diffuse autoimmune thyroiditis was relatively low.

Data obtained from single epidemiological surveys carried out in the years 1978–1991 were recently reviewed[14]. A total number of 72.112 schoolchildren (6–14 years) was examined, including 5046 controls residing in urban areas and 66.066 subjects residing in extraurban endemic areas. Surveys were performed to a large extent in predominantly hilly and mountainous districts known or suspected to be endemic and were distributed throughout Italy. Mean UIE was between 50 and 75 mcg/g creatinine. In the control areas UIE ranged from 85 to 175 mcg/g of creatinine. The prevalence of goiter in schoolchildren of endemic areas ranged from 14% to 73% and was roughly inversely correlated with iodine excretion. Generally, goiter prevalence was greater in Central and Southern Italy. In the control areas goiter prevalence was below 10%. In some areas with moderate or severe iodine deficiency cases of cretinism and mental

defects were found. Minor neuropsycological impairements were detected in schoolchildren residing in moderate iodine deficiency such as Val Tiberina (Toscana) and Sicily (see above).

Netherlands[12]

Iodized salt was introduced in the Netherlands in 1928 and the use was voluntary. In 1968 iodized bread salt was introduced. In 1974 the Ministry of Public Health decided that the iodized household salt was no longer necessary and sale was stopped. The main conclusion of this study carried out in 1976 was that iodine supplementation was insufficient to prevent endemic goiter especially in females and adolescents. In 1982 iodized household salt with a higher content of iodine (23–29 mg/Kg) was reintroduced and the iodine content of bread salt was raised from 46 to 60 mg/Kg. UIE was much lower in females than in males. Goiter prevalence in females was 29–25% and in males 17%. The existence of endemic goiter in the Netherlands can be attributed to an iodine supplementation that is marginal for large parts of the population.

Portugal[12]

Severe endemic goiter and cretinism had been known to exist in Portugal since the beginning of the century. The mean UIE ranged from 12 to 129 mcg/g creatinine in different areas. The median UIE in schoolchildren in Lisbon was 71 mcg/g creatinine and in the adult population was 46 mcg/g creatinine. In 1971 the most affected areas were defined and prophylaxis with iodized salt was started. Iodine prophylaxis was followed by cases of iodine induced thyrotoxicosis.

Spain[12]

Iodine deficiency is still widespread throughout Spain, mostly of mild to moderate degree, but with areas still existing with severe iodine deficiency. In particular, in different regions of Spain the goiter prevalence was from 18 to 25% in schoolchildren. UIE was from 30 to 120 mcg/day. In several areas of Spain minor neurological deficits resulting from iodine deficiency were described in schoolchildren[11]. Health authorities showed interest in the eradication of iodine deficiency disorders and in 1982 a law was promulgated for the production of iodized table salt at 60 mg of iodine per Kg. However the availability of iodized salt was not accompanied by a sustained campaign for promotion of its use.

Switzerland[13]

Switzerland was formerly a severely iodine deficient area. The results of goiter prevalence was high and in 1922 iodine salt has been introduced at 1.9–3.75 ppm on a voluntary basis. In 1962, the iodine content of salt was raised from 3.75 to 7.5 ppm and in 1980 to 15 ppm. UIE increased from 20 mcg/g creatinine to 150 mcg/g creatinine. The prevalence of goiter decreased gradually. The two Swiss manufactures actually produce salt at 15 ppm iodide. Salt both for household and food industry (meat, bakeries, instant food) is iodized. In 1989 92% of household salt and 78% of all salt for human consumption was iodized.

United Kingdom[12]

Studies of the 1960s showed that UIE in United Kingdom was around 100 mcg/day. The main iodine sources were established to be fish products (26%), milk and milk products (19%) cereals (14%), vegetables (12%). Current average iodine intake in United Kingdom is approximately 255 mcg/day. United Kingdom can thus be considered not iodine deficient, although there are wide variations in iodine intake due to the variability of the milk content of iodine.

Updated situation of iodine intake in Europe[18]

The recommended dietary allowance of iodine for European countries (Table 5), was recently agreed upon in the meeting held in Bruxelles in 1992[12]. Most European countries recently participated in an extensive survey aimed at assessing the status of iodine nutrition in Europe. Seven thousand five hundred fifty nine children were examined by thyroid ultrasonography and UIE was measured (Table 6). The conclusion of this study was that iodine nutrition in schoolchildren has markedly improved in many European countries and is presently normal in the Netherlands, France and Slovakia. Iodine intake remains unchanged in other countries such as Belgium. Goiter occurs at UIE below 10 mcg/dL. The prevalence of goiter is still up to 10–40% in some European areas stressing the necessity of universal salt iodine prophylaxis.

Efficacy and safety of iodine prophylaxis

In countries of severe iodine deficiency such as African countries iodate oil was shown to reduce the prevalence

Table 6 Range of the median urinary iodine excretion (UIE) in European schoolchildren*

Country	No. of sites	UIE (mcg/dl)
The Netherlands	3	14.1–16.3
Slovak Republic	4	13.0–14.3
Germany	2	10.3–12.6
Austria	4	9.8–12.0
France	15	8.5–13.1
Luxemburg	1	9.0
Czech Republic	2	8.5–8.7
Italy	2	5.4–8.4
Hungary	3	5.2–11.5
Belgium	3	5.0–5.8
Romania	7	3.4–14.0
Poland	3	20.–3.2

* Modified from Delange[18].

of goiter and endemic cretinism. In developed countries the commonly used method of iodine prophylaxis is iodization of table salt. In countries where iodoprophylaxis was introduced many years ago (i.e. North American states, Switzerland and Scandinavian countries) the prevalence of iodine deficiency disorders was dramatically reduced. A clear example of efficacy of iodized salt was obtained in a study in which 453 schoolchildren born before iodine prophylaxis and 399 children born after iodine prophylaxis were examined[19]. Before iodine prophylaxis urinary iodine excretion (UIE) was 47 mcg/g creatinine and goiter prevalence 60%; after iodine prophylaxis UIE was 130 mcg g/creatinine and goiter prevalence 8%. Also neuropsychological performances were improved by optimization of iodine intake[7,8]. In a study performed in a severe iodine deficient region of China iodized oil administered to pregnant women was shown to prevent microencephaly and neurological disturbances in the newborns[20].

Iodine prophylaxis is devoid of adverse reactions with the exception of sporadic cases of transitory hyperthyroidism (iodine induced hyperthyroidism, IIH) first described in Tasmania after administration of iodized bread[21,22]. Recently cases of IIH were observed in Zimbabwe after salt iodization[23]. In agreement with these data Bourdeoux *et al.*[24] observed IIH in 14/190 subjects after institution of iodine prophylaxis in Kivu, Zaire. A possible explanation of this phenomemon is the rapid increase of iodine intake in a severe iodo-deficient population. This hypothesis is supported by the observations made in Switzerland[25] where the iodine content of salt was progressively increased from 3.75 mg/Kg in 1923 to 15 mg/Kg in 1980. A transitory and negligible increase of cases of IIH has been observed in 1980, while the incidence of hyperthyroidism decreased in the following years. To better understand the problem of IIH the WHO and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) undertook a study in 7 African countries in which iodine prophylaxis was recently introduced. The conclusion of this study[26,27] was that IIH is relatively rare and associated to the severity of iodine deficiency before the prophylaxis. This problem has been judged to be not relevant for European countries characterized by mild to moderate iodine deficiency. Thus, ICCIDD recommends an universal iodine prophylaxis, that has to be instituted gradually in severe iodine deficient countries[26,27].

Cost of iodine prophylaxis

The costs of salt iodization include several components, i.e. the cost of the chemical (potassium iodate), processing and packing. The total cost of salt iodization was estimated to be 3.95 to 14.8 USA dollars per ton with an average of 7.40. This amounts to 0.4–1.2 cents per Kg or 1–6 cents per person per year based on an estimated annual consumption of 3 to 5 Kg[28]. This is very cheap taking into account the beneficial impact on the health of a correct iodine intake at the population level.

Conclusions

In conclusion, most European countries are still characterized by mild to moderate iodine deficiency, although in several of them iodine prophylaxis programs are already operating. The cost of iodization of salt is irrelevant with respect to the undebatable beneficial impact of a correct iodine intake on the health. Adverse effects of universal iodine prophylaxis are very rare and observed mainly in severe iodine deficient populations in whom iodine intake was abruptly increased.

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