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REVIEW ARTICLE

# Goiter and iodine deficiency in Europe. The European Thyroid Association report as updated in 1988.

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## INTRODUCTION

This review is based on the report of the subcommittee for the study of endemic goiter and iodine deficiency of the European Thyroid Association (1-4). Epidemiologic information on the prevalence of goiter and alimentary iodine supply is scanty for most European countries. Although regional data are available, these do not necessarily reflect the situation throughout the country from which they originate. The regional data give relatively good information concerning the population sample studied; however, it is frequently difficult to conclude which part of the whole population of a given area is represented by the sample studied and which percentage of the total inhabitants of the country live in the areas studied. Most surveys have used the standard classification of goiter size according to Pan American Health Organization from 1974 (5), which is associated with a significant risk of overestimation in children and underestimation especially in older adults as sonographic volumetry has shown (5, 6-9). Daily urinary iodine excretion or iodine excretion from spot urine samples have widely been accepted as a satisfactory index of iodine intake (10, 11). Since Europe, except one Spanish region (12), is not considered to suffer from protein malnutrition, the urinary iodine/creatinine ratio is acceptable (13). Hardly any data are available about potential effects of dietary goitrogens (14-16). Limitations of the study of endemic goiter and iodine deficiency are partly due to legal obstacles for epidemiology and the widespread disinterest in iodine supplementation programs of European health administrations (17).

Information on goiter prevalence (Fig. 1), iodine supply (Fig. 2) and supplementation programs (Table 1) is listed in alphabetic order for each European

country. For the older literature, the reader is referred to references (3, 4, 15, 18-31).

### *Albania:*

No information is available.

### *Austria:*

Iodine prophylaxis has been mandatory since 1963. Due to this, endemic cretinism had disappeared. The incidence of hypothyroidism of newborn is 1:4600, goiter prevalence in 6 years old 1.1 - 1.5%. Goiter prevalence rises with growing age up to 13.4% in 18 years old. Up to 1/3 of the adult population have a goiter. Iodine excretion in 2262 patients from 5 cities show an iodine excretion slightly below 100  $\mu\text{g}$  iodine/g creatinine. In Graz and Oberwölz, iodine excretion is still below 70  $\mu\text{g}$  iodine/g creatinine, though according to the decrease of radioiodine uptake from 52.4% in 1972 to 30.5% in 1981 (32) iodine intake must have improved. In Sieldorf, a mean iodine excretion of 132.6 iodine/g creatinine was found. Compared with the epidemiological data before 1963, the situation had drastically improved, however, a rise of potassium iodide from 10 mg to 20 mg/kg salt has been recommended and is in legislative planning (33-37).

### *Belgium:*

A prevalence of goiter of 1.8% had been noted in over 50.000 male army recruits in 1956 (18). A study on the seasonal variation of stable iodine in non-toxic goiter indicated a mean excretion of 50  $\mu\text{g}$  iodine/g creatinine. Data from the 1960th indicate similar figures (19, 38-42). In 1986, the median urinary iodine concentration ( $\mu\text{g}/\text{dl}$ ) in 196 healthy full-term infants born in Brussels was 4.8 and thus lower than in Helsinki, Finland (11.2), but higher than in Göttingen, FRG (1.5) (43). New and methodologically reliable data on goiter prevalence and iodine supply are urgently needed.

### *Bulgaria:*

In 1957 a survey of 1 million schoolchildren revealed a goiter prevalence of 19.2%. First, iodized salt be-

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creases of goiter prevalence reported as an RT-value of 110, which stands for relative thyroid weight given in percent with RT=100 being normal (48). The iodine prophylaxis was interrupted for almost 7 years in 2 districts, which clearly showed an increase of radioiodine uptake by the thyroid, a rise of serum-TSH, and a decrease of urinary iodine excretion from 109.0 to 33.3 mg/24 h (district BK) and a PBI in serum (30, 49, 50).

Baby foods were sampled in two series - first from February 1977 to January 1979 (46 samples) and second from February 1981 to October 1982 (79 samples). In series one, the content of total iodine in pure milk foods ranged between 20 and 40 µg/l in 6.1%, 40 and 70 µg/l in 72.2%, 70 and 100 µg/l in 12.1%, and 100 and 150 µg/l in 9.1%, respectively. In the second series, the total content of iodine ranged between 20 and 40 µg/l in 6.1%, 40 and 70 µg/l in 24.5%, 70 and 100 µg/l in 36.7%, 100 and 150 µg/l in 30.6%, and above 150 µg/l in 8.2%, respectively. The total iodine content in mixed foods resembled that of pure milk foods. None of the samples exceeded 70 µg/l (51).

In 1985, thyroid volume was examined by ultrasonography in 207 boys and 220 girls aged 15-16 years from East Slovakia. 49.3% of the boys and 52.3% of the girls respectively had slightly enlarged thyroids between 10 and 15 ml. These thyroid volume resemble those found in areas of mild iodine deficiency (i.e. FRG) and are twice as large as those reported from Sweden, where iodine intake is sufficient. Forty years of goiter prophylaxis with iodized salt abolished large and medium sized goiters in all age groups and increased the urinary iodine excretion to approximately 100 µg/24 h. However, goiters grade I are still endemic (52).

#### *Denmark:*

In 1969, a nation-wide screening of 6000 young men revealed a mean urinary iodine excretion of 64 µg l/24 h. The values were higher in Sealand (range 68 to 139) than in Jütland (range 41 to 28) (53). According to the ETA-questionnaire 1981 and to personal communication (P. Lauerberg), a committee under the Danish Health Department concluded from unpublished data on goiter prevalence in school children that iodine prophylaxis was not necessary. Very recent data from Funen showed an estimated daily urinary iodine - based on extrapolations from five hour collections in 505 subjects - of 76 µg/24 h for adult women, 89 for men, and 85 for the whole population, respectively. The median iodine excretion was 58.8 µg/g creatinine (54). The iodine excretion for men was 77% higher than reported in 1969. Further information is lacking.

#### *Federal Republic of Germany:*

In 1984, thyroid size of more than 3000 school children and more than 3000 adults from 25 and 10 German towns respectively were measured by sonography. These data of several authors (6-8, 55-58) reveal a prevalence of enlarged thyroid glands in all age groups of approximately 40%. The iodine excretion from spot urine samples amounts to 60 µg l/g creatinine. In neonates, iodine excretion was between 1.7 and 2.7 µg/dl and thus 3 to 4-fold lower as compared to Swedes. Furthermore, alterations in sonographic echopatterns were found in almost 16% of the healthy adult population (6-8, 55-58). The iodinated salt (15-25 mg l/kg) is used on a voluntary basis by less than 1/3 of the population. Since this salt is only available as additional table salt, and since the mean use of salt was shown to be 1.7 g per day and person, the iodination program has not proven to be effective enough (59, 60). Since compulsory iodination of all salts used is legally not possible, alternatively a gradual increase of iodine content up to 50 mg l/kg table salt and/or a general use of iodized salt in food production are recommended (4). Programs to increase public awareness have been started.

#### *Finland:*

Endemic goiter has declined to less than 6% (61). Iodized salt is voluntarily but widely used. Milk products are further iodine sources (62). The average dietary iodine intake amounts to 340 µg/d/person (63). Earlier reports of goitrogens in milk have to be remembered (64, 65).

#### *France:*

Endemic goiter was reported from the Pyrenees. According to the older literature (1937) there were several areas of endemic goiter in France. In 1982 the examination of 36,308 children from 13 districts showed a goiter prevalence of up to 16.7%. Spot urine samples (n = 3311) revealed a mean of 86 µg l/g creatinine (66). A survey in Languedoc-Roussillon including 3,157 ten to sixteen year old boys and girls revealed a goiter prevalence of 7.4% and a urinary iodine excretion of 71.7 µg l/g creatinine (67).

#### *German Democratic Republic:*

In the last decade several epidemiological surveys were carried out in the GDR. All studies indicated that goiter prevalence was higher than 12% in the whole country in all age groups increasing from North to South. Iodine excretion was often found to be less than 50 µg l/g creatinine. Iodized salt (unreliable and unstable content 5 - 25 mg KI/kg) was used by less than 1/3 of the whole population. By

1985, eighty-four percent of all table salt was iodized by the more stable iodate (32 mg  $KIO_3$ /kg). Urinary iodine excretion increased from less than 30  $\mu\text{g}$  in 1985 to more than 60  $\mu\text{g}$  in 1987. Goiter prevalence in newborns decreased below 1%. In January 1988, mandatory use of iodinated salt has been introduced. An interdisciplinary iodine commission was established to control and coordinate necessary follow up studies (68-72).

*Greece:*

Endemic goiter remains common with prevalence figures as high as 50% in some areas. Iodized salt (40 mg KI/kg) is available but more expensive than non-iodized preparations. They are mainly used by the urban population, but not in the rural areas where ID prevails. Urinary iodine excretion in Athenians has increased to 94,5  $\mu\text{g}$  l/g creatinine in 1982 (24, 73).

*Hungary:*

A decrease of goiter prevalence from 32 to 11% in schoolboys from some iodine deficiency areas was reported in 1981. The iodine content of salt was subsequently increased. However, the supply of iodized salt is irregular. From data of 69 newborns, it was deduced that iodine deficiency may still prevail (3).

*Iceland:*

There is no endemic goiter. In 1960, urinary iodine exceeded 300  $\mu\text{g}$ /day (74).

*Ireland:*

Available figures date back to the 1970s and before. Goiter prevalence of 27% and 12% was reported in female and male emigrants, respectively (24, 75). Random samples taken recently from 411 outpatients in Dublin hospitals showed a mean urinary iodine of 137.5  $\mu\text{g}$ /g creatinine and a median of 110.0; 23.3% had iodine excretion values below 70  $\mu\text{g}$ /g creatinine (76). It is cautioned that these figures cannot be taken as representative of the total Irish population; however, they justify more careful investigation for iodine deficiency. No further information could be obtained.

*Italy:*

Endemic goiter is widespread in Italy, especially in the mountain areas, while big cities and heavily populated areas are apparently free of endemic goiter (77). Iodized salt is available in some regions although its use remains limited (78-87). In Sicily, 25 to 80% of the school children had goiter, before prophylactic programs through water iodination have been carried out in Troina, Sicily, resulting in a nearly complete goiter eradication in 1982 (87). In Alto

Adige, the prevalence of goiter was 9.2 to 37.9% among 3, 109 school children, with regional values of iodine excretion between 4.57 and 18.5  $\mu\text{g}$ /g creatinine in 1982. In Tuscany, thyroid enlargement was found in 63% of school children and 83% of adults. TG-concentrations increased and serum TSH-levels decreased with goiter size. Functional autonomy of the thyroid was assumed for the findings of low serum TSH (88).

*Luxemburg:*

According to health authorities, there is no need for iodized salt. The iodination of salt is not permitted by law. Data on goiter prevalence are lacking.

*The Netherlands:*

Endemic goiter has decreased since iodization of breadsalt became mandatory in 1968 (46 mg KI/kg). In 1976 it became clear that the goiter prophylaxis was insufficient. Based on the "Report of the National Health Committee Goiter Prophylaxis" the iodine content of breadsalt was increased to 60 mg KI/kg and iodized table salt (25 mg KI/Kg) for voluntary use was reintroduced. Due to a supreme court verdict the use of iodized bread salt is not mandatory, but only recommended since 1984. Fortunately, the use of iodinated bread salt has hardly decreased so far (17). The median urinary iodine excretion varies in different areas between 96  $\mu\text{g}$ /d up to 138  $\mu\text{g}$ /dl. Goiter prevalence is generally below 3% (2 -4, 89-92). However, areas with endemic goiter still exist. In Doetinchem a goiter prevalence of 35% was found in women. Sixty percent of these women excreted less than 100  $\mu\text{g}$  iodine per day. In 1985 the goiter prevalence in school girls in different regions varied between 19-39% with a median urinary iodine excretion of 110  $\mu\text{g}$  l/g creatinine, and in boys the goiter prevalence was lower (4-31%) with an excretion of 120  $\mu\text{g}$  l/g creatinine (91). Locally occurring goitrogens are discussed, causing the regional differences in goiter prevalence.

*Norway:*

Recent information was gained from 6 towns in Norway where 20 to 70 year old people were examined. No endemic goiter could be found. The iodine excretion ranged between 147 up to 247  $\mu\text{g}$  l a day and has not significantly changes since 1972. The high iodine intake is mainly due to feeding cows with seaweed. Salt is iodized with 5  $\mu\text{g}$  l/kg (13, 93-95).

*Poland:*

Goiter prevalence of 20-40% in adolescents was reported, despite the use of 8 mg potassium iodide per kg salt. After 20 years of prophylaxis with currently 5-12 mg KI per kg salt, the goiter prevalence

ranges between 31 and 50 % in southern parts of Poland as the Carpathian Mountains and Cracow. Eastern parts of Poland were heavily affected in 1967 (45, 96). New data are lacking.

*Portugal:*

Most of the population of Portugal lives near the coast, where no endemic goiter is found. Several regions of the interior are severely affected. Prophylaxis with iodized salt (20 mg KI/kg) in one area in Castel Branco started in 1971 reduced the goiter prevalence in school children from 51% to 9,3% by 1977, whereas in another region of this district goiter prevalence in school children approximated 40%. In Portalegre, Baixo Alentejo and Algarve, goiter endemicity goes up to 54%. Some endemic cretinism was reported (2-4, 97, 98). Since 1981, iodized table salt (60 mg KI/kg) is available but not mandatory and rarely used, particularly in rural areas.

Surprisingly, in the island of S. Miguel (the Azores) the prevalence of goiter in school children varied between 11 and 41%. In the most affected region, 16% of the adult males and 48% of the women had goiter. The median urinary excretion of iodine varied between 10 and 49  $\mu\text{g}$  /g creatinine (99).

*Romania:*

A regional prevalence of more than 60% is reported for the Carpathian Mountains in 1980. Antiendemic centers have been organized in all endemic regions during 1949 - 1978 period (100). Iodized salt for the population and, in addition, iodinated tablets for school children and pregnant women, have been used (43, 100). In 1986, 20,000 children from Mures county representing 91.2% of all enlisted 6-14 years old were examined. Goiter was found in 16.8% (62).

*Soviet Union:*

No information about the European part of the Soviet Union has been obtained. An endemic area of Uzbekistan with iodine deficiency goiter was described (101); subjects in this area receive 1 mg iodine per day as prophylaxis.

*Spain:*

Several surveys from this decade have been published. In Galicia, 2,872 school children revealed a 79% prevalence of goiter with 85% excreting less than 25  $\mu\text{g}$  /l urine. From Andalusia the goiter prevalence of 4,949 school children was 29%; 40% had an urinary iodine excretion of less than 40  $\mu\text{g}$  /l. In Catalonia, a population sample from 255 rural communities showed a goiter prevalence of 35,8% and a mean excretion of 79  $\mu\text{g}$  /g creatinine. In Asturias, 6922 school children had a goiter prevalence of 20% and a urinary iodine excretion of 63  $\mu\text{g}$  /l. In Guadajajara, near Madrid, 58% of school children had goi-

ter and 46% had urinary excretions of less than 50  $\mu\text{g}$ . In the Las Hurdes region, goiter prevalence of 86% was found in school children. In this area cretinism still persists. Prophylaxis with iodized oil has been introduced in this region (12, 102). A thorough review about iodine deficiency and goiter epidemiology has recently been issued by Francisco Escobar del Rey (Endocrinologia [Barcelona] 34, Suppl. 2, 1987).

*Sweden:*

There is probably no endemic goiter in Sweden. Salt has been iodized (50 mg/kg) for more than 10 years, starting with 10 mg/kg in 1930 and rising to 20 mg/kg in 1940. Commercial baby diets are iodized. Foods used for animals are iodized. In Stockholm, a median iodine excretion of 141 was found in adults and 124  $\mu\text{g}$ /g creatinine in 13-years old. Swedish neonates showed a two- or three- to four-fold median urinary iodine excretion, when compared to Swiss or Germans, respectively. The median thyroid volume of adults and 13-years old, respectively, as estimated by sonography was twice as small, when compared with those found in the iodine deficient Germany (6-9, 43, 55). Further mappings of iodine excretion and goiter prevalence figures are lacking.

*Switzerland:*

In 1975, a survey showed a goiter prevalence of 20% in adults aged 20-39 and of 60% in the 60-79 age group. The higher figures in the elderly reflect inadequate iodination of salt before 1980 (103-105). In 1983, a goiter prevalence of only 1% was found in 19-year old male army recruits. The potassium iodide content of table salt has been increased progressively over the last two decades to now 20 mg/kg. Iodination of all salt for human consumption (includes table salt for food industries and restaurants) is practically mandatory (106). In 1983 the mean iodine excretion was 141  $\mu\text{g}$  per day (107).

*Turkey:*

Endemic goiter is a problem at the Black Sea shore and in the inner parts of Eastern and Western Anatolia. In some provinces such as Bolu, Bursu, Isparta, Kastamonu, Rize and Trabzon, goiter prevalence exceeds 15%. In many provinces such as Adiyaman, Artvin, Bilecik, Bingöl, Burdur, Canakkale, Denizli, Eskisehir, Gümüşhane, Izmir, Kars, Konya, Kütahya, Malatya, Mardin, Mus, Sakarya, Samsun, Sinop, Sivas, Tokat, Yozgat and Zonguldak, goiter prevalence is 5-15%. The nation-wide detailed investigation on the prevalence of endemic goiter dates back to the sixties. Urinary iodine excretion was below 70  $\mu\text{g}$  /g creatinine (108-111). New data are urgently needed.

#### *United Kingdom:*

The average British diet provides 250  $\mu\text{g}$  iodine a day. Milk is the most important individual source of iodine but is also the most variable. Regional prevalence of goiter reported in 1924 does not permit epidemiological conclusions for today. There is little evidence that major areas of endemic goiter persist (112-116).

#### *Yugoslavia:*

Persisting regional prevalence of endemic goiter up to 25% and the mandatory use of iodized salt (10 mg KI/kg) since 1956 have been reported. Defects in iodizing techniques and/or loss of iodine from the salt are considered to be responsible for the incompleteness of goiter eradication (15). Further information is lacking.

### DISCUSSION

The data reported above are not uniform; variations between countries represent methodological differences, incomplete information and, in some instances, failure to use the generally accepted classification of thyroid size. Although these data are incomplete, the report elucidates the present status of endemic goiter and iodine intake in Europe and urges for further surveys. Obviously, goiter remains a significant problem (Table 1).

#### *No endemic goiter*

This applies for Iceland, Norway and the United Kingdom, Belgium, Denmark, and Ireland, though borderline ID, probably also belong to this group. In Sweden, and Finland highly effective goiter prophylaxis programs have been established. These countries define the goal which can and should be achieved elsewhere in Europe.

#### *Intermediate*

This group comprises Bulgaria, Czechoslovakia, The Netherlands, and Switzerland. These countries have had major problems with endemic goiter in the past, but have introduced goiter prevention programs. Epidemiological surveys have shown that endemic goiter persists in some adults in these countries, but that it is hardly seen in children.

#### *Endemic goiter persists*

This group contains 13 countries - 50% of the total in this review.

#### *- Iodine prophylaxis mandatory*

This sub-group consists in Austria, The German Democratic Republic, Hungary, Poland, and Yugoslavia; substantial areas of high goiter prevalence persist despite iodine prophylaxis. Dietary iodine in-

take remains borderline and analysis of the iodine content of salt from three of these countries gave values ranging from 4 to 12 mg of I/Kg salt (2). Experience from other countries in which iodine prophylaxis is mandatory has shown that iodine content of salt must be at least 20 mg/kg (preferable in the stable form of  $\text{KIO}_3$ ) to meet the WHO recommended iodine intake (150-300  $\mu\text{g}/\text{d}$ ) in areas where there is little iodine in other components of the diet.

#### *- Iodine prophylaxis not mandatory*

This large group consists of the Federal Republic of Germany, France, Greece, Italy, Portugal, Romania, Spain, and Turkey. Goiter continues to be a major problem in these countries, either nationwide or regionally. Iodine intake is so low in some regions that the risk of cretinism persists. Effective iodine prophylaxis programs are urgently required in these countries.

#### *Adequate information unobtainable*

Albania, Luxemburg and the USSR.

### CONCLUSION

The data of this survey provoke concern rather than complacency. More epidemiological studies, including studies of other goitrogenic mechanisms (117-119) and comprehensive iodination programs are urgently needed. Such programs have to be monitored for their effectiveness. Any iodine-induced hyperthyroidism due to an increased prevalence of thyroid autonomy or immunogenic effects have to receive adequate attention (120-132). Furthermore, the daily intake, as well as the quality and standardization for iodized salt preparations must be checked carefully (133-139). In a recent study, the iodine content of 104 commercial salt samples from 19 European countries was analyzed. The results showed that iodine content was significantly lower than that intended by the manufacturer in approximately 30% of samples (2-4).

In the newborn, iodine deficiency causes transient effects on thyroid function and increased susceptibility to the toxic effects of acute iodine loads (55, 140, 141). The increased frequency of elevated thyrotropin levels in screening programs for congenital hypothyroidism may also be regarded as a sensitive index for iodine deficiency (142).

The German experience suggests that the Societies for Nutrition may be more successful than endocrinologists in persuading health authorities to introduce iodine prophylaxis. In addition, it should be remembered that permission and recommendation to use iodized salt in preprepared food as bread,



sausages, cheese etc. can be particularly successful as experienced in Bulgaria, Finland, the German Democratic Republic, Sweden and Switzerland. Notably, the adequate iodine intake in Finland, Norway and the United Kingdom is at least partly due to an inadvertently high iodine content of the milk, which might be subject to undesirable modification in the future.

Considerable sums are spent on the diagnosis and treatment of goiter by public health systems or insurance companies in many countries - more than 500 million US-Dollars in 1987 in the Federal Republic of Germany (143, 144). Prevention is straight forward and cheap.

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