Treatment of Endemic and Sporadic Goitre

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Goitre and Iodine Deficiency in Europe – A Review

Extended Report of the Subcommittee for the Study of Endemic Goitre and Iodine Deficiency of the European Thyroid Association[1,2]

P. C. SCRIBA

"The scientific community of the ETA has the obligation to contribute to the eradication of endemic goitre and iodine deficiency in Europe. With the available knowledge it seems an anachronism that endemic goitre in Europe still prevails." This was the conclusion of A. QUERIDO, the former chairman of the "ETA subcommittee for the study of endemic goitre and iodine intake in Europe" in his 1981 report (Pisa). The information so far collected by the subcommittee has been summarized in four European maps (Fig. 1 – 4), and in an additional table (Table 1). The list mentioned is unfortunately still incomplete with respect to some European countries.

In general, epidemiologic information in a strict sense is scanty for most European countries. Vastly, there are just regional data available with relatively good information concerning the population sample studied (age, sex); however, it is frequently difficult to conclude which part of the whole population of a given area is represented by the sample studied, what its relation to the other groups is, and which percentage of the total inhabitants of a country live in the areas studied. Undoubtedly, the methodological approach used for the review therefore deserves epidemiological criticisms. However, it was felt justified to present this imperfect information now, as even with the above limitations the data is alarming enough.

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(2) Presented in part at this meeting; official publication: The Lancet *I*: 1289 – 1293 (1985).

Table 1. Endemic goitre, iodine deficiency and prophylaxis in the individual European countries.

		Epidemiological information			*Information on*	*Urinary iodine excretion*		*Prophylaxis*
		Goitre prevalence on average, % ∅ = no endemic goitre	*Sample* from population (year)	*PAHO* goitre staging applied	*regional goitre prevalence,* %	µg per g creatinine or 24h [ ] = regional values	Population sample	m = mandatory or > 90% v = voluntary n = none
A	Austria	3	recruits (1976) N = 47,576	(+)	12; 25 students	[65]; [47]	N = 80; Northern Tyrol N = 293; Salzburg	m
B	Belgium	1.8	recruits (1956) N = 54,237	–	3 –	[51] [50]	N = 38; Brussels N = 178	v (?)
BG	Bulgaria	12 (decreasing)	whole population (1961); N > 65,000	+	–	–	–	m
CH	Switzerland	0-B: 14 I: 1	recruits (1983) N = 425 Canton of Geneva	+	34 Bern; N = 2,916	[93];	N = 770 Bern; whole population	> 90%
CS	CSSR	< 10 age dependent steady decline of RT-values	> 2% of whole population	+	+	100	adult women N = 2,484	m continued
D	Fed. Rep. Germany	15	recruits (1974) N ~ 5.4 mio.	(+)	+	20–35 South to North	school children N = 1,945 adults N = 5,678	v
DDR	German Dem. Rep.	12	recruits (1978) N > 600,000	(+)	+	25–37	whole country 16–50 y. N = 645	m (?)
DK	Denmark	∅	children (1970) N = 364,593; (7–17y)	(+)	–	62	whole country 17–20 y., N = 6000	n

		Epidemiological information			*Information on*	*Urinary iodine excretion*		*Prophylaxis*
		Goitre prevalence on average, % ∅ = no endemic goitre	*Sample* from population (year)	*PAHO* goitre staging applied	*regional goitre prevalence,* %	µg per g creatinine or 24h [] = regional values	Population sample	m = mandatory or > 90% v = voluntary n = none
E	Spain	several areas of severe endemia, see text		+	86 Las Hurdes	[16µg/l]	school children N = 156; cretinism!	v
F	France	no information obtained		–	10	[33]	–	v
GB	Great Britain	no information obtained		–	8	–	–	n (?)
GR	Greece	see text –		(+)	30 several areas affl.	[20]	–	v
H	Hungary	< 11	school children (1965) N > 670,000	–	+	still iodine deficient despite prophylaxis		m
I	Italy	Some heavily populated areas are free of endemic goitre, see text		+	11–>50 several areals cf. BASCHIERI et al.	[26] – [76] [51] – [19]	mostly school children	v
IRL	Ireland	see text –			12, emigrants 68 → 12, school ch.	– [11] – [15]	– N = 128 school children	v
N	Norway	∅		–	1.5	[133] 100–300	N = 460	v
NL	The Netherlands	see text –		+	2–13	[70] – [120]	young adults	m
P	Portugal	see text –		+	51 → 9.3 40	[12]	[cretinism!] school children	v

		Epidemiological information			*Information on*	*Urinary iodine excretion*		*Prophylaxis*
		Goitre prevalence on average, % ∅ = no endemic goitre	*Sample* from population (year)	*PAHO* goitre staging applied	*regional goitre prevalence,* %	µg per g creatinine or 24h [ ] = regional values	Population sample	m = mandatory or > 90% v = voluntary n = none
PL	Poland	see text –			31–50 adolescents, Cracow	–	–	m
R	Romania	no information obtained			60 Carpathian mount.	iodine deficiency despite prophylaxis		?
S	Sweden	∅	?	–	∅ (?)	200	–	m
SF	Finland	∅		+	< 6	250	school ch. (1979) N = 1,275	v > 90%
SU	Soviet Union	no information obtained			27 Taschkent	–	school children	?
T	Turkey	see text –			+ Black Sea coast Anatolia	[55]	–	?
Y	Yugoslavia	no information obtained			25 Bosnia, Herzegovina (1959); N > 34,000	–	–	m

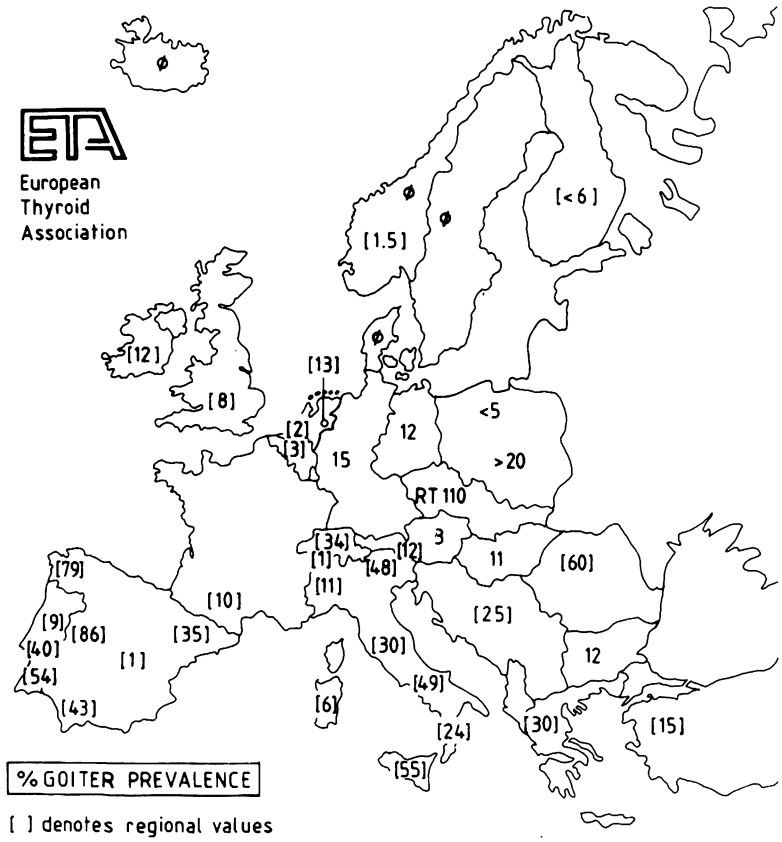

Fig. 1. The goitre prevalence in Europe. See text and Table 1 for more detailed information.

Methodological Remarks

The information provided in this report was extracted

1. from the literature as cited and
2. from individual reports to the chairmen of the ETA goitre subcommittee in response to repeated questionaires.

The techniques for the study of endemic goitre have been established earlier. According to PAHO 1974 (DUNN and MEDEIROS-NETO, 1974), the goitre stages were defined stage 0-A to stage III. A note of caution appears necessary with regard to the assessment of the size of small goitres. Studies implying the technique of sonographic volumetry have revealed, that approximately 4.3 % false positive results were obtained by experienced investigators when the diagnosis was based on palpation when compared with a volume of 30 ml considered as the debatable upper

normal value for adults (GUTEKUNST et al., 1983). The risk of overestimating small goitres particularly in school children has received attention in earlier reports (DUNN and MEDEIROS, 1974; SILINK and CERNÝ, 1966). These limitations for staging should be kept in mind, when surveys for endemic goitre are evaluated.

In an area with a suspected goitre prevalence of more than 10%, examination of school children is recommended as a first step (DUNN and MEDEIROS-NETO, 1974). However, when the goitre prevalence in the school population exceeds 10%, more than 1% of the total population should be sampled. The latter procedure is particularly recommended in areas with a recent increase of iodine supply, since the goitre prevalence can be remarkably high in elder age groups in such regions, when compared with adolescents. If the goitre prevalence in the general population exceeds

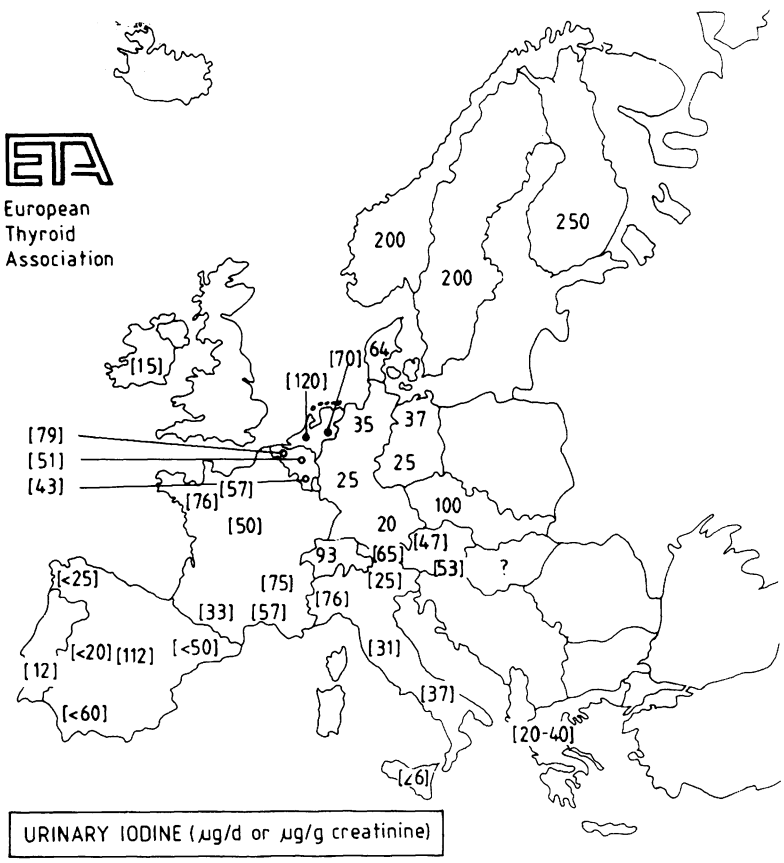

Fig. 2. The urinary iodine excretion in Europe. See text and Table 1 for more detailed information. Values for Belgium und France were derived in part from LAGASSE et al. (1976). Values for Spain were given in µg/l, see text.

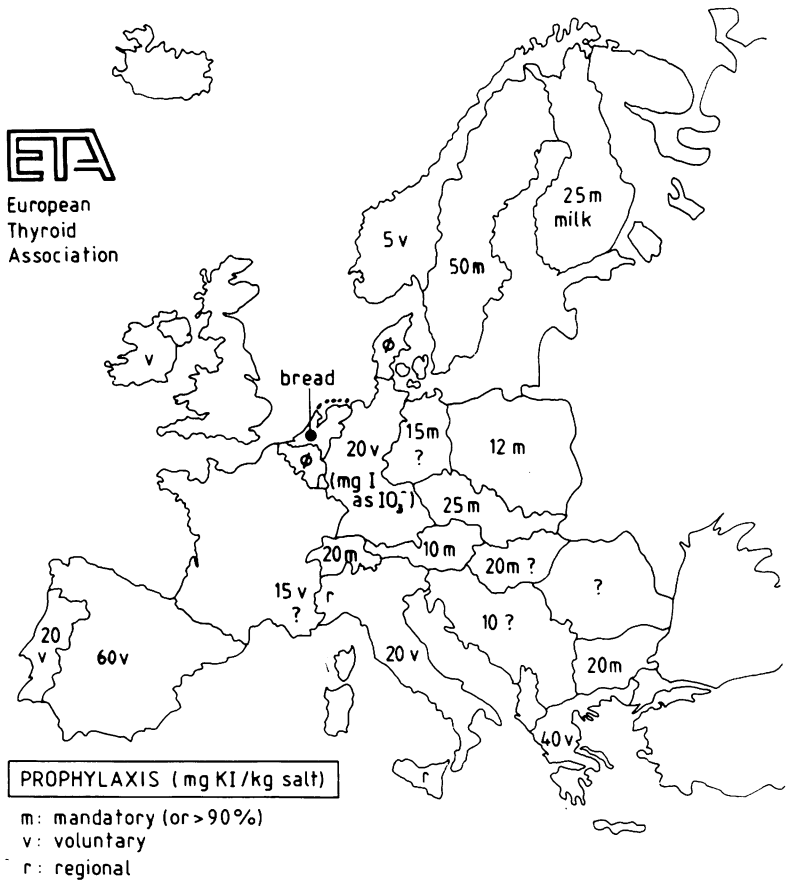

Fig. 3. Goitre prophylaxis in Europe. See text for more detailed information.

10% the urinary iodine excretion must be examined in specimens from 20 of every 1000 persons examined. School children of both sexes 10–14 years of age are the group recommended for this purpose (DUNN and MEDEIROS-NETO, 1974).

The daily urinary iodine excretion was considered equivalent to the iodine excretion per g creatinine in most European countries. However, in one Spanish area (ESCOBAR DEL REY et al. 1981) protein malnutrition resulted in a decreased creatinine excretion per day, invalidating the µgI/g creatinine ratio. Nutritional factors for goitrogenesis other than iodine deficiency (INGENBLEEK et al., 1980; MATOVINOVIC, 1983) have not been included in this review on the European situation.

It is obvious from the information presented in this review that most data do not meet the criteria mentioned above. Unfortunately, legal obstacles for epidemiological research in some countries make the complete application of the "tech-

niques for the study of endemic goitre" (DUNN and MEDEIROS-NETO, 1974) almost not feasible. Remarks about the information on individual European countries not available to the committee are therefore included in this report.

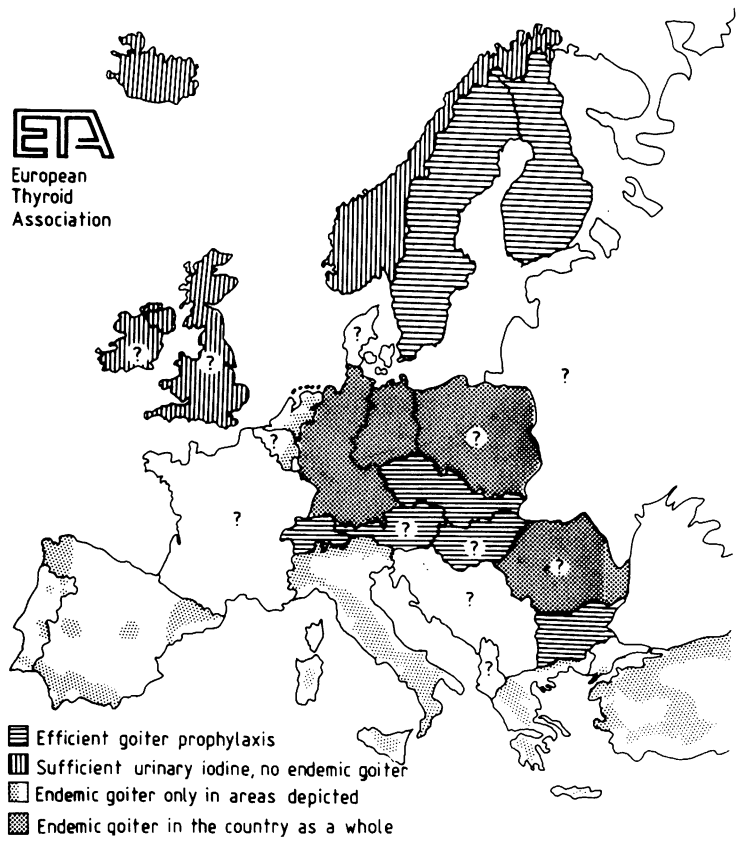

Fig. 4. Current status of effectiveness of goitre prophylaxis in Europe.

Survey Concerning the Situation in Individual European Countries

Some reviews relevant to endemic goitre and iodine deficiency are cited since they are referred to repeatedly in this report (KELLY and SNEDDEN, 1960; KOUTRAS, 1980; LANGER , 1980; BECKERS and DELANGE, 1980). PFLÜGER (1937) published two maps depicting the goitre distribution in central Europe, one of his own and one drawn by H. BIRCHER already in 1883. The European maps presented in this review show the global information on goitre prevalence (Fig. 1), urinary iodine excretion (Fig. 2), and iodine prophylaxis (Fig. 3). A characterization of the current

status of the efficacy of goitre prevention is given in the conclusions paragraph (Fig. 4). The European countries are discussed below alphabetically:

A = **Austria:** Goitre prevalence in army recruits was recently reported to be 3.3% (STEINER and ZIMMERMANN, 1978). However, after 17 years of mandatory (90%) iodine prophylaxis in Austria, RICCABONA et al. (1981) reported a decrease of the goitre prevalence from 50 to 35% in the population as a whole and from 45.9% to 12% in school children of three towns in Northern Tyrol. The authors therefore suggest raising the content of potassium iodide in the salt from 10 to 20 mg per kg. Currently, the urinary iodine excretion is 65.3 µg/g creatinine in this area. –GRUBECK-LOEBENSTEIN et al. (1982) observed a selected group of 80 patients with "ordinary" goitre in Vienna with only 48% of the patients having an iodine excretion of less than 70 µg per 24 h. –A further appeal for an increased iodine content of the table salt was published by GALVAN et al. (1982) after demonstration of an average urinary iodine excretion of 46.6 µg per g creatinine in 293 students in Salzburg; 73 of these students had a palpable goitre. Likewise, GOEBEL et al. (1983) reported a decrease of the mean radioiodine uptake rates from 52.4% in 1972 to 30.5% in 1981 for Graz, where the mean urinary iodine excretion is currently 53.3 µg/g creatinine.

AL = **Albania:** No information was obtained.

B = **Belgium:** The population has a marginally low iodine intake (BECKERS et al., 1962; DE CROMBRUGGHE et al., 1963; DELANGE et al., 1978; KOUTRAS, 1980). The study of 54,237 males aged 18 years (recruits to the army) showed that the mean prevalence of goitre (criteria not defined) was 1.8%. It increased from the north-western to the south-eastern parts of the country (BRULL and DEWART, 1956). More recent epidemiological data for the country have not been forwarded.

In 18 normal adults, the mean urinary excretion of iodine was found to be 65.6 ± 5.10 µg/day (DE CROMBRUGGHE et al., 1964), a finding later confirmed in 12 adults by DELANGE and ERMANS (1967), who found a mean urinary iodine of 58.8 ± 6.1 µg/d. Studies on the seasonal variation of stable iodine in non-toxic goitre performed more recently by JONCKHEER et al. (1982) in the Brussels area indicate a mean excretion of 50 µgI/g creatinine. The first collaborative report on iodine deficiency in Europe was published only in abstract form (THILLY et al., 1973). Table 2 showes the 24 h radioiodine-uptake in some European countries; the mean value was 46% for Europe as a whole. This type of information permitted the authors to calculate regional mean iodine intake values according to the

Table 2. Synoptic survey of 24 h ^{131}I thyroidal uptake values for seven countries. The mean (± SEM), the mode and the median were reported by LAGASSE et al. (1976).

Country	Number of subjects	Number of centers	24 h ^{131}I thyroidal uptake		
			mean ± SEM	mode	median
Switzerland	162	2	32.6 ± 0.8	28	32
The Netherlands	411	3	39.9 ± 0.5	40	37
France	938	8	40.9 ± 0.6	38	38
Italy	1510	10	42.2 ± 0.4	40	37
Belgium	1232	14	47.0 ± 0.5	44	46
Luxembourg	69	1	52.3 ± 1.5	55	53
Germany	1055	7	59.6 ± 0.5	62	60
Total	5377	45	46.2 ± 0.2	40	42

method of ODDIE et al. (1970). The latter values have been transformed into urinary iodine values (see Fig. 2) by multiplication with f = 0.66 according to HABERMANN et al. (1975).

Preliminary observations in 29 adolescents, 8–15 years of age indicated a urinary excretion of iodine of 42 ± 4.5 µg/d. In this group, the thyroid clearance rate of iodine was 27 ± 3.4 ml/min, and with a plasma-inorganic iodine of 1.1 ± 0.14 µg/l, the absolute iodine uptake was 37 ± 4.7 µgI/24 h (MALVAUX et al., 1965). This finding was confirmed by DELANGE and ERMANS (1967) who found in adolescents, 10–15 years of age (n = 23) a 24 h urinary excretion of iodine of 43.9 ± 5.7µg/d. BECKERS and NOEL (1972) observed the urinary iodine excretion in 483 healthy school children and adolescents. Minimal values typical of iodine deficiency were found among subjects aged 9–10 and 13–15 years. Iodine balance studies in 26 nongoitrous children and adolescents gave a mean iodine intake of 32 ± 1.94 µg/d (MALVAUX et al., 1969). All these results clearly stress the insufficient iodine intake in the Belgian population.

BG = **Bulgaria:** A survey of 1 million school children in 1957 revealed a goitre prevalence of 19.2%. Thereafter, a reduction of the regional goitre prevalence from 55 to 12% was reported. No endemic goitre is now observed below 15 years of age (LANGER, 1980). 20 mg potassium iodide per kg salt are used.

CH = **Switzerland:** Goitre prevalence in 1975 increased with age: 20% (including stage 0-B) in the age range of 20–39 years, and 60% between 60 and 79 years in general hospital patients. The potassium iodide content of salt was raised from 5 mg/kg to 10 mg in 1962 and to 20 mg/kg in 1980. The

high goitre prevalence in the elderly is probably due to the fact that they suffered from iodine deficiency before the salt was adequately iodinated (STECK et al., 1972; GEISER et al., 1978; SCHMID et al., 1980; BÜRGI et al., 1982; EBERHARD et al., 1983). Among 425 men aged 19 and examined for entry into the army, goitre (all stage I) was found in 4 (1%) in 1983 (B. SELZ and H. BÜRGI, personal communication).

CS = **Czechoslovakia:** A prevalence of goitre of 50% (m) and 70% (f) was observed in more than 370.000 persons examined between 1947 and 1953 (LANGER, 1980), before the introduction of iodine prophylaxis. Correlation to low iodine excretion and to thiocyanate from brassica (PODOBA and LANGER, 1964), respectively was shown. Detailed data on the prevalence of all and nodular goitres and of different sizes of goitres in the men and women according to old districts during the years 1949 to 1953 have been published (PODOBA, 1962; PODOBA et al., 1970).
Iodine prophylaxis was started in 1947 in some selected areas only, but since 1953 it was introduced in the whole territory. At that time, the content of potassium iodide was 12 mg/kg, but in some areas 25 mg/kg were used. Since 1965 the level of 25 mg/kg was used in the whole territory. It is being considered to increase the level up to 35 mg/kg after 1985. – Follow-up studies in 100 000 subjects showed urinary iodine values increasing to 100 µg per 24 h and age-dependent decreases of goitre prevalence reported as RT-value, which stands for relative thyroid weight given in percent with RT = 100 being normal (SILINK and CERNÝ, 1966). The iodine prophylaxis was interrupted for almost 7 years in 2 districts, which clearly showed an increase of radioiodine uptake by the thyroid, an increase of TSH in serum, and a decrease of urinary excretion of iodine from 109.0 to 33.3 mg/24 h (district BK) and of PBI in serum (PODOBA and STUKOVSKY, 1972; PODOBA, 1975; PODOBA and REISENAUER, 1982).

D = **Federal Republic of Germany:** Military conscripts (5.4 million) have an average goitre prevalence of 15%; 85% of the goitrous have goitre stage I (HORSTER et al., 1975). Iodine deficiency (HABERMANN et al., 1975) was documented by chemical analysis in urines of school children and by calculation from radioiodine uptake of adults after ODDIE et al. (1970). Potassium iodine was not sufficiently stable in iodized salts from several European countries (HABERMANN et al., 1978). The iodination of the salt to be used on a voluntary basis was altered in 1981, so that potassium iodate is added to give an iodine content of 20 mg per kg salt (SCRIBA, 1981).

DDR = **German Democratic Republic:** An average goitre prevalence of 12% was

found in recruits. Low urinary iodine excretion was observed in school children. Mandatory iodine prophylaxis will probably be introduced soon (MENG et al., 1981).

DK = **Denmark:** A nation-wide screening of 6000 young men revealed a mean urinary iodine excretion of 64 µg/24 h, but was only published in abstract form (MUNKNER, 1969). The values were higher in Seeland (68–139) than in Jutland (41–68 µg/24h). According to the ETA-questionaire 1981 (T. MUNKNER) and to personal communication (P. LAURBERG) a committee under the Danish Health Department concluded from unpublished data on goitre prevalence in school children, that iodine prophylaxis was not necessary. Further information is lacking (KOUTRAS, 1980).

E = **Spain:** There are some areas with endemic goitre, according to older reports (PFLÜGER, 1937; KOUTRAS, 1980). – All the boys and girls (N = 156; 6–14 y) regularly attending school in three villages from an area in Spain known as Las Hurdes were studied (ESCOBAR DEL REY et al., 1981) with respect to thyroid size, body weight and height. The same survey was carried out in 354 school children from Madrid. Goitre prevalence was very high, the overall frequency being 86% in Las Hurdes. The concentration of iodine in the urine was 20 µg/l in 71% of the school children. The concentration of creatinine in the urine was also half of that found in children from Madrid, and the daily creatinine excretion in children from Las Hurdes was lower than expected from their body weight. Therefore, urinary iodine was not related to g creatinine excretion. Somatic development, as measured by height and weight, was retarded markedly, both as compared to the Madrid reference group and to international charts. Serum T_4 was less than 78 nmol/l (6 µg/dl) in 46% of the children from Las Hurdes, and serum TSH greater than 7.5 mU/l in 40%. A relatively low stature (below the 10th percentile) was associated with either a low serum T_4, an elevated serum TSH, or both in 30% of the children. These results indicate that the persistence of endemic goitre in Las Hurdes is of great significance, and that there is a continuing risk of the birth of cretins. – Meanwhile, injections of iodized oil have been administered in this area (SANCHEZ-FRANCO et al., 1983).

The following areas of endemic goitre (PAHO-classification) and severe iodine deficiency have been identified meanwhile and are currently being investigated: Several hundreds of school children from further villages of the 3 provinces of Cáceres, Salamanca and Guadalajara have been studied by F. ESCOBAR DEL REY et al. (personal communication); thousands of school children were studied in all provinces of Andalucia (Sevilla, Cadiz,

Huelva, Cordoba, Granada, Almeria, Jaen), where goitre grade 0-B + I was found in 17.4 to 45.7% of the school children of the villages; in this area, urinary iodine was below 60 µg/l in 33.1 to 86% (principal investigator: S. DURAN-GARCIA). Iodine deficiency and endemic goitre was also shown in 2500 persons equivalent to 0.6% of the population of villages of the provinces of Cataluña (main investigator L. SERRA I. MAJEM), and in villages of Galicia, where goitre incidence was 79%, with 85% excreting less than 25 µg iodine per liter urine (R. TOJO). – Recently, iodized salt (60 mg KI/kg) available on a voluntary basis was introduced in Spain.

F = **France:** Endemic goitre was reported from the Pyrenees (KOUTRAS, 1980). According to the elder literature (PFLÜGER, 1937), there were several areas of endemic goitre in France.

GB = **Great Britain:** The regional prevalence reported does not permit epidemiological conclusions (KOUTRAS, 1980; TUNBRIDGE, 1977). According to the elder literature (PFLÜGER, 1937), there were several areas of endemic goitre in Great Britain (Derbyshire neck). PHILLIPS et al. (1983) published a map depicting areas of England and Wales, where endemic goitre has been prevalent in the past. The authors showed, that the distribution of mortality from thyrotoxicosis among women in England and Wales during 1968 – 78 correlates with the previous prevalence of endemic goitre. The average British diet was calculated to provide 323 µgI/day. Milk was be most variable as well as the most important individual source of iodine. Summer milk samples contained 70 µg/kg and winter milk 370 µg/kg on average (WENLOCK et al., 1982).

GR = **Greece:** The regional prevalence of goitre and iodine deficiency was repeatedly reported (KOUTRAS, 1980). Endemic goitre is still prevalent in Greece (D. A. KOUTRAS, personal communication). Although the exact prevalence in the whole country is not known, sample studies in many regions as well as the experience of the thyroid centers permit the construction of a map (Fig. 4). In some villages the entire population has been examined, in others as well as in Athens only the school children. In the endemic villages fully studied, prevalence rates up to 50% have been found. An average of 30% for the endemic areas seems to be a good guess. Athens and the big cities are relatively spared, non-endemic.

In Greece, the urinary excretion of iodine in the endemic areas ranges from 20 to 40 µg/g creatinine. In Athens, the urinary iodine excretion rose from 44.9 µg/d (MALAMOS et al., 1966) to 94.5 µg/g creatinine (KOUTRAS et al. 1982). – Iodized salt is used (40 mg KI/kg) on a voluntary basis. Since it

is more expensive, it is used more by the well to do Athenians who are not iodine deficient, than by the poor villagers who are.

H = **Hungary:** A decrease of goitre prevalence from 32 to 11% in school boys from some iodine deficiency areas was reported (G. SZILAGY, ETA-questionaire, 1981). The iodine content of the salt was subsequently increased. However, the supply of iodized salt is somewhat irregular (F. PETÉR, personal communication) and from data in 60 newborns it was deduced, that iodine deficiency may still prevail.

I = **Italy:** The regional prevalence of goitre and iodine deficiency has been extensively studied (BASCHIERI et al. 1978; DELANGE et al., 1978; COSTA and MORTARA, 1981; SQUATRITO et al., 1981; SAVA et al., 1982; VIGNERI et al., 1982). Further goitrogenic mechanisms have been considered. Prophylaxis was first introduced in the valley D'Aosta. Iodized salt is now available on a voluntary basis. Iodized salt consumption, however, is very limited even in areas of severe goitre endemia. Extensive regional information on iodine content of water, kitchen-salt and foods, the urinary iodine output, and goitre prevalence in school children has been published.
A study has been carried out in Sicily where an endemic goitre area involving more than 300.000 inhabitants has been described. Goitre prevalence, evaluated among more than 25.000 school children in this area of Sicily, ranges from 25% to 80% (DELANGE et al., 1978; SAVA et al., 1982; F. TRIMARCHI and A. JANNI, personal communication, 1984). Urinary iodine excretion averages 90–120 μg/24 h in non-endemic areas of Sicily, while it is as low as 18 μg/24 h in the most severe endemic goitre area. Endemic cretinism has been observed in this area (SQUATRITO et al., 1981). – A prophylactic program through water iodination has been carried out in Troina (Sicily) resulting in a nearly complete goitre eradication in 4 years (VIGNERI et al., 1982). – Further endemic goitre areas have been described in Lazio and Calabria (DE LUCA et al., 1966): ^{131}I thyroid uptake at 24 h was as high as 75 – 90% in these areas.
In 1982, the prevalence of goitre (WHO IB–III) was 23.7 ± 14.2% (9.3–37.9%) among 3109 school children of Alto Adige, mean altitude 1106.4 m/sml; regional values of the urinary iodine excretion varied between 4.57 (!) and 18.5 μg per g creatinine (N.CABASSA, F. FRANZELLIN, personal communication). – A detailed survey of current endemic goitre areas in sanitary districts of Tuscany was provided by G. FENZI and A. PINCHERA. In some districts, the goitre prevalence was as high as 63% in school children and 83% in adults. In the Appenin Mountain district 4, where the mean urinary iodine excretion was 44.2 μg per g creatinine, io-

dized salt (KI, 120 mg/kg) is now distributed on a voluntary basis (DOVERI et al., 1981; BARTALENA et al., 1982).

The survey on pathology of the thyroid gland, promoted by the Italian Division of the International Academy of Pathology in the period 1977–1979, through the active participation of about 160 pathologists working in the Universities and Hospitals of 16 Italian Regions covered about 82% of the Italian population (LAMPERTICO 1982; the same issue contains detailed regional reports). 37.016 partial or total thyroidectomies performed represent 1.66% of all the surgical specimens histologically examined with an average incidence of 28 surgical procedures on the thyroid every year for 100.000 people, with great regional variability (from 5.7 in Umbria to 48.4 in Marche). The male/female ratio was 1/4.8 for benign disease. The age distribution was stated in 21.131 benign and 2.125 malignant conditions.

In summary, endemic goitre is widespread all over Italy, especially in most mountain areas, while big cities and some heavily populated areas are apparently free of endemic goitre (Fig. 4).

IRL = **Irland:** A goitre prevalence of 27% and 12% was reported in female and male emigrants, respectively (GREENWALD, 1975; KOUTRAS, 1980). The Tipperary survey revealed an area of endemic goitre (68% among 700 school children) due to iodine deficiency, with an iodine intake as low as 11–15 µg per day in 1946. Goitre prevalence was reduced within 3 1/2 years to 12% by treatment with iodine (2500 µg/d) (O'DONOVAN, 1950). Iodized salt (42 tons) constitutes 1.2% of total salt sales in Ireland, 34 tons being sold in S. Tipperary and N. Cork (P. SMYTH, personal communication). No further information has been obtained.

IS = **Iceland:** There is no endemic goitre (KOUTRAS, 1980). No further information is available.

N = **Norway:** Modum, a Norwegian community, where endemic goitre and iodine deficiency were common before the last war, was reexamined in 1977 (FREY et al., 1981). There is obviously no longer any endemic goitre in Norway. The urinary iodine excretion varies in women und men between 165–364 µg per day. The high iodine intake is mainly due to feeding of cows with seaweed, whereas iodized salt (5 µg KI per kg) contributes only neglegable amounts of iodine (FREY et al., 1974).

NL = **The Netherlands:** There is some regional endemic goitre left in The Netherlands (WHO grade I and II, disregarding grade 0-B). All salt used for baking bread has to be iodized. Iodine intake was considered to be inade-

quate in Doetinchem (A. QUERIDO, personal communication). The report No. 78 of the Ministry of Health (NL) published in 1981 and forwarded by G. HENNEMANN, proposed that struma prophylaxis be improved by raising the KI content of bread salt, (at present 46 mg per kg), to 60 mg, so that one slice of bread would contain 20 µg iodine. It also proposes making the addition of KI to household salt compulsory, at a level of 26.2 mg per kg salt, so that 1 g salt would contain 20 µg iodine. Those who consume four slices of bread and 4 g household salt per day (the nowadays reduced average per capita consumption) would obtain a daily iodine supplement of 160 µg. For the vast majority of the population this will mean a daily iodine intake in the optimal zone of between 150 and 300 µg; more modest eaters will remain outside the danger zone through an average daily intake of 100 to 150 µg iodine, whilst those who consume large amounts of bread and household salt, and thus have an intake of ca. 400 to 500 µg iodine per day, should suffer no harmful effects.

The most recent survey in Leiden and Doetinchem, western and eastern parts of the Netherlands, showed an increase of the urinary iodine excretion and decrease of the goitre prevalence, more clearly for grade I than for grade 0-B, which was still found in 26% of the female school children in Doetinchem (J. W. F. ELTE, D. VAN DER HEIDE, B. M. GOSLINGS, A. QUERIDO, personal communication, 1983).

P = **Portugal:** Most of the population of Portugal lives near the coast, where there is no endemic goitre (L. G. SOBRINHO, E. LIMBERT, personal communication). However, several regions of the interior are severely affected. Some regions were studied locally in detail. In one region of the district of Castelo Branco nearly 16,000 school children and adults were studied in 1963–1966. An average of 51% of the school children had goitre. Of the adult males 35% had grade II goitre and 2% grade III goitre. Prophylaxis with iodized salt (20 mg KI per kg) started in 1971, which reduced the goitre prevalence in school children to 9.3% by 1977 (LOPES DE OLIVERA et al., 1983). An upsurge of Jod-Basedows was detected in the ensuing years (SOBRINHO et al., 1977). – In another region, also in the district of Castelo Branco, the prevalence of goitre in school children approached 40% (1978). Here, the mean urinary iodine from school children lacking iodine prophylaxis was 12 µg/g creatinine. Two further regions, Baixo Alentejo and Algarve and Portalegre respectively were recently shown to house goitre endemia up to 54% locally and some endemic cretinism!

PL = **Poland:** A goitre prevalence of 20 – 40% in adolescents was reported (Z. SZYBIŃSKI, ETA-Questionaire, 1981), despite the use of 8 mg potassium iodide per kg salt (LANGER, 1980). After 20 years of prophylaxis

with currently 12 mg KI per kg salt, the goitre prevalence is still between 31 and 50% in southern parts of Poland as the Carpathian Mountains and Cracow. In addition, the eastern parts of Poland appear to be heavily afflicted in a map published (FALKIEWICZ and PACYŃSKI, 1967).

R = **Romania:** A regional prevalence of more than 60% is reported for the Carpathian mountains (LANGER, 1980). Antiendemic centers have been organized in all endemic regions during the 1949 – 1978 period (S. M. MILCU, personal communication). Iodized salt for the population and, in addition, iodinated tablets for school children and pregnant women, have been used. Unfortunately, the results of this campaign have only been published in Romanian (MILCU, 1957). More recent information is desirable.

S = **Sweden:** There is probably no longer endemic goitre in Sweden (JOHNSSON, 1965, KOUTRAS, 1980). All table salt is iodized (50 mg/kg) for more than 10 years, starting with 10 mg/kg in 1930 and raising in iodine content to 20 mg/kg in 1940. The same salt is used for commercial baby diets. All foods used for animals are iodized (R. GUTEKUNST, personal communication). Further information is lacking.

SF = **Finland:** Endemic goitre is obviously disappearing steadily. There is voluntary but highly distributed use of iodized salt. Milk products are shown as additional iodine sources (LAMBERG et al., 1981; LAMBERG et al., 1982). The average dietary iodine intake is now 340 µg/d/person (VARO et al., 1982). Earlier reports of goitrogens in the milk have to be remembered (KOUTRAS, 1980).

SU = **Soviet Union:** No information about western parts of the Soviet Union has been obtained. An endemic area of Usbekistan with iodine deficiency goitre was described by ISLAMBEKOV et al. (1973); prophylaxis is performed in this area with 1 mg iodine per day.

TR = **Turkey:** Endemic goitre is a problem on the Black Sea shore and in the inner parts of eastern und western Anatolia (ESER, 1966). In some provinces such as Bolu, Bursa, Isparta, Kastamonu, Rize and Trabzon, goitre prevalence is over 15%, in many provinces such as Adiyaman, Artvin, Bilecik, Bingöl, Burdur, Çanakkale, Denizli, Eskisehir, Gümüshane, Izmir, Kars, Konya, Kütahya, Malatya, Mardin, Mus, Sakarya, Samsun, Sinop, Sivas, Tokat, Yozgat and Zonguldak goitre prevalence is 5 – 15%. Those are preliminary results; however, a nation-wide detailed investigation on the pre-

valence of endemic goitre in Turkey is under progress. Screening and grading of goitre by neck palpation has started, beginning from regions with high prevalence of goitre. Urinary iodine excretion will also be determined in those regions (URGANCIOGLU et al., 1982). The information given in Fig. 4 was taken from a preliminary map provided by I. URGANCIOGLU and E. DUREN.

YU = **Yugoslavia:** A persisting regional prevalence of endemic goitre of up to 25% and the mandatory use of iodized salt (10 mg KI/kg) since 1956 were reported (LANGER, 1980; MATOVINOVIC, 1983). The failure completely to eradicate goitre was ascribed to defects in the iodization techniques and/or loss of iodine from the salt (MATOVINOVIC, 1983). Further information has not been obtained.

Though outside of the direct scope of this review, it should be noted, that there are regions of severe iodine deficiency and endemic goitre in North Algeria (BACHTARZI and BENMILOUD, 1983).

Tentative Conclusions

Even when keeping in mind some limitations of this review, which are due to incompleteness of the information obtained, the results of the inquiries performed by the ETA Subcommittee for the Study of Endemic Goitre and Iodine Intake in Europe already permit some conclusions (Fig. 4):

1. There are some European countries where either endemic goitre used to be prevalent within the country as a whole or where areas of endemic goitre (and cretinism) were formerly well described. Iodine prophylaxis either mandatory or voluntary, but accepted by more than 90% of the population was introduced in these countries but had and still has to be intensified in some cases, since it was shown to be formerly insufficient. Nevertheless, eradication of endemic cretinism and a marked reduction of goitre prevalence have been reported particularly for the younger age groups. This description would probably apply to Austria (?), Bulgaria, Switzerland, CSSR, Hungary (?), The Netherlands (?), and Finland.

   Other countries with sufficient iodine intake and probably no endemic goitre are Great Britain (?), Ireland (?), Norway and Sweden. – A third group of countries have documented borderline low or insufficient alimentary iodine intake but fail to report even regional endemic goitre as Denmark and Belgium (?).

   It is notable that the eradication of goitre has not only been achieved through iodine prophylaxis but in some countries is also due to a change in alimentary

habits, e.g. feeding of seaweed to cows and use of iodine containing disinfectants in dairy hygiene. This resembles the situation in the United States and in Tasmania (FREY et al., 1974; ADAMS et al., 1975; STEWART and VIDOR, 1976; LAMBERG et al., 1982).

In fact, a gradual increase of the supply of iodine for goitre prophylaxis over decades was applied in several European countries as Austria, Czechoslovakia, The Netherlands, Sweden and Switzerland. This slow increase of alimentary iodine may help to minimize iodine induced thyrotoxicosis (cf. HALL and KÖBBERLING, 1984) and possibly thyroid antoantibody development, respectively (BOUKIS et al., 1983).

In the group of formerly iodine deficient countries some open questions and continuing tasks are left (DUNN and MEDEIROS-NETO , 1974) which include

- monitoring of iodine prophylaxis, which is to be continued with repetition of goitre prevalence surveys and monitoring of the urinary iodine excretion,
- studies on prevalence of residual goitre and goitrogenic mechanisms other than iodine deficiency, and
- longitudinal studies on the question, whether the sequelae of iodine deficiency and endemic goitre, as nodular goitre in the elder age group, or increased frequency of single toxic autonomous adenomas and disseminated autonomy will gradually subside.

All efforts aiming at these problems have to be recommended for this group of countries.

2. There are some European countries where endemic goitre is still prevalent, when the country is regarded as a whole. The two parts of Germany, Federal Republic of Germany and German Democratic Republic, have convincingly demonstrated endemic goitre and iodine deficiency. Other countries may have to be added. An effective general iodine prophylaxis has to be recommended strongly for these countries.
3. There are some European countries, where only regional prevalence of endemic goitre and iodine deficiency have been documented, the remainder of the country being free of endemic goitre. The information as received up to now does not always allow conclusions as to the epidemiological situation within the country as a whole. Therefore, either general iodine prophylaxis or regional measures are an alternative for these countries. The list of such countries may have to include Spain, France, Greece, Italy, Portugal, Poland (?), Romania, Turkey, and Yugoslavia.

   Possibly, one will have to add some of the following countries: Belgium, Denmark (?), Great Britain (?), Ireland (?) and the Soviet Union (?).

   Further epidemiological studies are strongly recommended for some of these countries (Table 1), since either general or regional iodine prophylaxis appears desirable.

The information provided by this report pertains to goitre prevalence, urinary iodine excretion surveys and prophylactic measures only. Further support for the ETA's effort aiming at the eradication of iodine deficiency and endemic goitre can probably be derived from other data:

1. The study of the iodine supply of the newborn in Europe (ESPE and ETA subcommittees, 1982; cf. DELANGE et al., 1979; HEIDEMANN et al., 1984) provided evidence for iodine deficiency in some European centers, particularly in Germany. The consequences described are e.g. transient effects on thyroid function (increased frequency of elevated TSH values in screening programmes for congenital hypothyroidism) and increased susceptibility to toxic effects of acute iodine loads, as goitre and transient hypothyroidism. The increased frequency of elevated TSH in neonatal screening programmes may be considered as a sensitive parameter for iodine deficiency, indicating changes in iodine supply at the earliest feasible interval (VAN THIEL et al., 1982).
2. Hyperthyroidism is more frequently due to single toxic adenoma or disseminated or multifocal autonomy including non-immunogenic toxic nodular goitre as compared with Graves' disease in iodine deficiency areas, where a particular susceptibility for hyperthyroidism induced by excess iodine loads was reported (ADAMS et al., 1975; STEWART and VIDOR, 1976; EMRICH et al., 1982). For instance, 50.8% and 31.6% of the thyrotoxic patients from Munich referred to surgery (N = 625) and seen in the Medical Department (N = 734), respectively had a single autonomous adenoma as compared to 23% and 28.4% with exophthalmic Graves' disease (HEBERER et al., 1978; LEISNER et al., 1980).These figures are way above data reported for the United States and Canada (WILLIAMS et al., 1984). Recently, BELFIORE et al. (1983) reported an increased frequency of autonomously functioning thyroid nodules in another iodine deficiency area. ADAMS et al. (1975) quote H.D. PURVES (1974) reporting a finally decreased frequency of toxic adenomas some years after the introduction of iodine prophylaxis in New Zealand.

There is an enormous amount of money spent for diagnosis and treatment of thyroid diseases by Public Health systems or insurance companies in our countries. 380 million DM were spent for out-patient diagnosis and medical treatment because of thyroid disorders in 1979 in the Federal Republic of Germany (PFANNENSTIEL and HORSTER, 1982). This amount of money is chiefly spent for endemic goitre and its sequelae. It may help government authorities to make up their minds about iodine prophylaxis, when the public becomes aware of these figures, simple goitre being "the easiest of all known diseases to prevent" (MATOVINOVIC, 1983).

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