acta endocrinologica

acta endocrinologica

Volume 112

May – August 1986

Copenhagen

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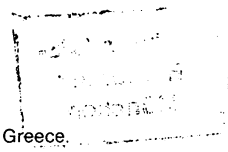
Printed in Denmark
by Bogtrykkeriet Forum
Copenhagen



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Acta Endocrinologica 1986, 112: 494–501

Goitre epidemiology: thyroid volume, iodine excretion, thyroglobulin and thyrotropin in Germany and Sweden

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Abstract. Thyroid volume of 1397 German and 303 Swedish adults were estimated by sonography. Thyroid size of 6–16 year old Germans (n = 619) was determined and compared with findings on palpation. Thyroid volume was more than twice as great in German (21.4 ± 15.6 ml, mean ± SD) than in Swedish adults (10.1 ± 4.9 ml). The echopattern was abnormal in 16% of the Germans and in 3.6% of the Swedes. German children have a thyroid volume ranging from 1.8 ± 0.4 ml at 6 years to 10.8 ± 6.0 ml at 16 years of age. Palpation is by comparison an unreliable method for determining thyroid size. In Germany, the iodine excretion was less in children (n = 619, 39.5 ± 30.5, 34.1 µg I/g creatinine, mean ± SD, median) than in adults (n = 1193, 83.7 ± 94.4, 62.6), ($P < 0.001$) and much lower than that observed in Sweden (adults n = 98, 170.2 ± 93.3, 141.4; 13 year olds n = 113, 172.9 ± 224.1, 124), ($P < 0.0001$). Serum thyrotropin concentration was significantly higher ($P < 0.001$) in Sweden (n = 62, 1.49 ± 0.82 mU/ml), than in Germany (n = 91, 0.97 ± 0.52 mU/ml), while serum thyroglobulin was increased in Germany (n = 91, 72.6 ± 50.6 µg/l) as compared to Sweden (n = 62, 23.5 ± 17.4), ($P < 0.0001$). These results indicate the goitrogenic effect of iodine deficiency and the continuing need for an effective iodine prophylaxis in the FRG.

Alimentary iodine supply in Germany is insufficient and goitre is endemic (Horster et al. 1975). There are, however, no iodine excretion measurements for adults available. Urinary iodine excretion is generally considered to be equivalent to alimentary iodine intake. Habermann et al. (1975) found an iodine excretion of 25–35 µg I/g creatinine in 13–15 year olds. This was far below the iodine intake recommended by WHO with an optimum of 150–300 µg iodine daily (Dunn et al. 1974).

Previous epidemiological studies on goitre in adults were obtained by evaluating chest-X-rays from public health service screening programmes, (Finger et al. 1982; Schoknecht & Barich 1975), as well as by palpation of military recruits' necks (Horster et al. 1975). Goitre prevalence studies for children were solely based on palpation (Habermann et al. 1975; Stubbe & Heidemann 1983). A representative study of the general population has not yet been undertaken.

Sonographic volumetry is now considered the most reliable method to determine thyroid volume (Brunn et al. 1981; Gutekunst et al. 1985; Hedegüs et al. 1983). Since iodine supply in Sweden is sufficient (Gutekunst et al. 1985) a comparison of iodine excretion, thyroid size and thyroid function in Germany and Sweden was carried out. In this study we examined the reliability of palpation for goitre epidemiological studies in children. Furthermore, we attempted to gain new data about alimentary iodine supply and goitre prevalence.

Dedicated to Prof. Dr. med. E. Buchborn, Munich, at the occasion of his 65th birthday.

Subjects and Methods

Thyroid volume from 1397 German adults in 7 towns (from north to south, Kiel n = 46, Lübeck n = 70, Berlin n = 111, Wolfsburg n = 313, Frankfurt n = 226, Tutzing n = 339, Penzberg n = 293), from 619 children, 6–16 year old from two schools near Göttingen and from 303 adults from Stockholm, Sweden, were determined by ultrasound. Length, width, and thickness of both thyroid lobes were measured with portable ultrasound equipment (Sonoline 1300, Siemens, Erlangen, FRG; transducer 4 MHz). Echo structure deviations were recorded and reported to the subjects' physicans. The volume was estimated by multiplication of thickness, width, length and a corrective factor (0.479) (Brunn et al. 1981). There was no selection process for the adult volunteers who were employees of large companies.

Children's necks were palpated for estimation of thyroid size according to WHO staging (Dunn et al. 1974), by an independent experienced paediatrician.

Spot urine samples were collected from 1812 Germans (adults, n = 1193, children, n = 619) and 211 Swedes (adults n = 98, 13 year old children n = 113). The determination of urinary iodine excretion was performed by a modified ceric arsenious acid wet ash method according to Wawschinek, (1985). The kinetic determination of creatinine followed Jaffe's method (Beckman creatinine analyser, ASTRA-IV).

Serum thyrotropin (TSH) from a random selection of 91 German adults and 62 Swedes was measured by a hypersensitive immunoradiometric assay (IRMA) from Behring company (Wood et al. 1985), and serum thyroglobulin by an immunoluminometric assay (ILMA) (Gadow et al. 1984).

Finally, the use of iodized salt (20 mg iodine as potassium iodate per kg), which is available only on a voluntary basis in the FRG, was investigated by interrogation.

Results

1. *Thyroid volume*

Among Swedish adults, women have a thyroid volume of 7.7 ± 4.3 ml (mean ± SD) with a range of 2.5–34.0 ml and a median of 6.9 ml; and men 11.1 ± 4.7 ml (range 3.3–27.4 ml) and median 9.1 ml. German adults had much larger volume: women, 16.5 ± 12.2 ml, median 13.3 ml, range 2.6–124.1 ml; men 26 .9 ± 17.0 ml, median 23.1 ml, range 3.8–105.0 ml. The difference between the thyroid volume in Swedes and Germans is highly significant ($P < 0.0001$). Fig.1 shows the distribution of volume in both countries. The frequency distribution in Germany as compared

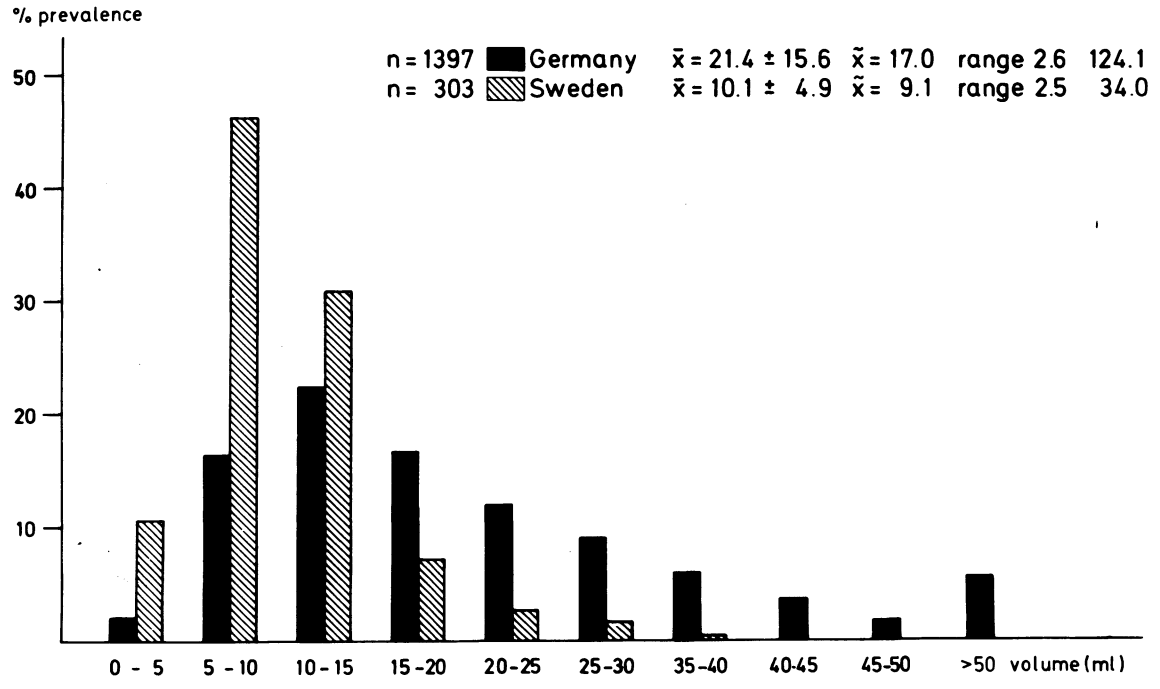

Fig. 1.
Frequency distribution of thyroid volume (ml) in Germany and Sweden.

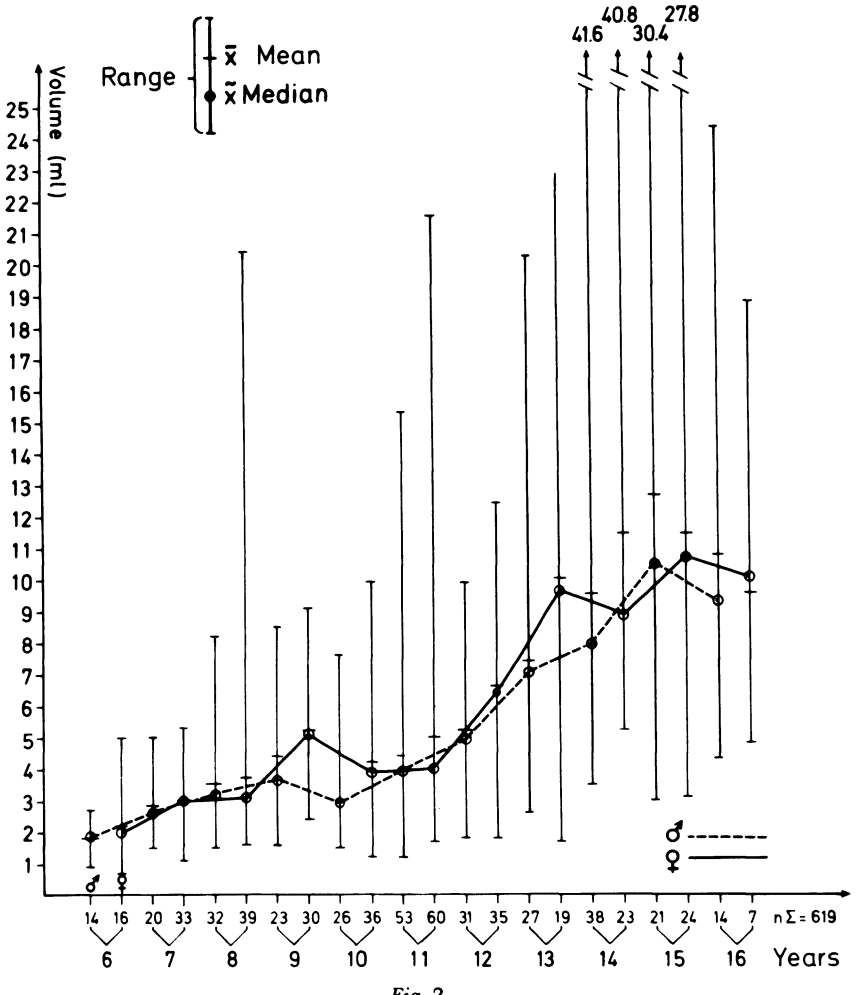

Fig. 2.
Thyroid volume (ml) in 6 – 16 years old from Göttingen, FRG.

to Sweden is shifted toward larger volume ($P < 0.0001$).

Six year old German children had volume of 1.8 ± 0.4 ml which progressively increased to 10.8 ± 6.0 ml at age 16 years ($P < 0.001$) (Fig. 2). Palpation in children for thyroid size is rather unreliable. As seen in Figs. 3 and 4, ranges of thyroid volume determined sonographically overlap widely in the respective age groups with volume estimated by palpation (goitre 0, I, II).

2. *Echopatterns* (Table 1)

Eighty-four per cent of the German adults had a normal echopattern; 2.5% had a scattered sonolucent pattern and 0.1% a scattered echocomplex pattern; 13.4% had unifocal and/or multifocal echo alterations; 5.9% had cysts; 2.1% had calcifications; 3.2% had sonolucent nodules; 2.1% had echosolid nodules; and 0.1% had echocomplex nodules.

Ninety-six per cent of the Swedes had a normal echopattern; 1% had scattered sonolucent thyroids; 0.3% had calcifications; 1.3% had cysts; 0.3% had sonolucent nodules; and 0.7% had echosolid nodules.

3. *Iodine excretion*

Adults. Urinary iodine excretion was significantly lower in Germany as compared to Sweden (83.7 ± 94.4, 62.6 µg I/g creatinine, vs 170.2 ± 93.3, 141.4, mean ± SD, median), ($P < 0.0001$). Thirty-one urine samples from German subjects were contaminated with iodine (> 1063.5 µg I/g creatinine). Fig. 5 illustrates the frequency distribution

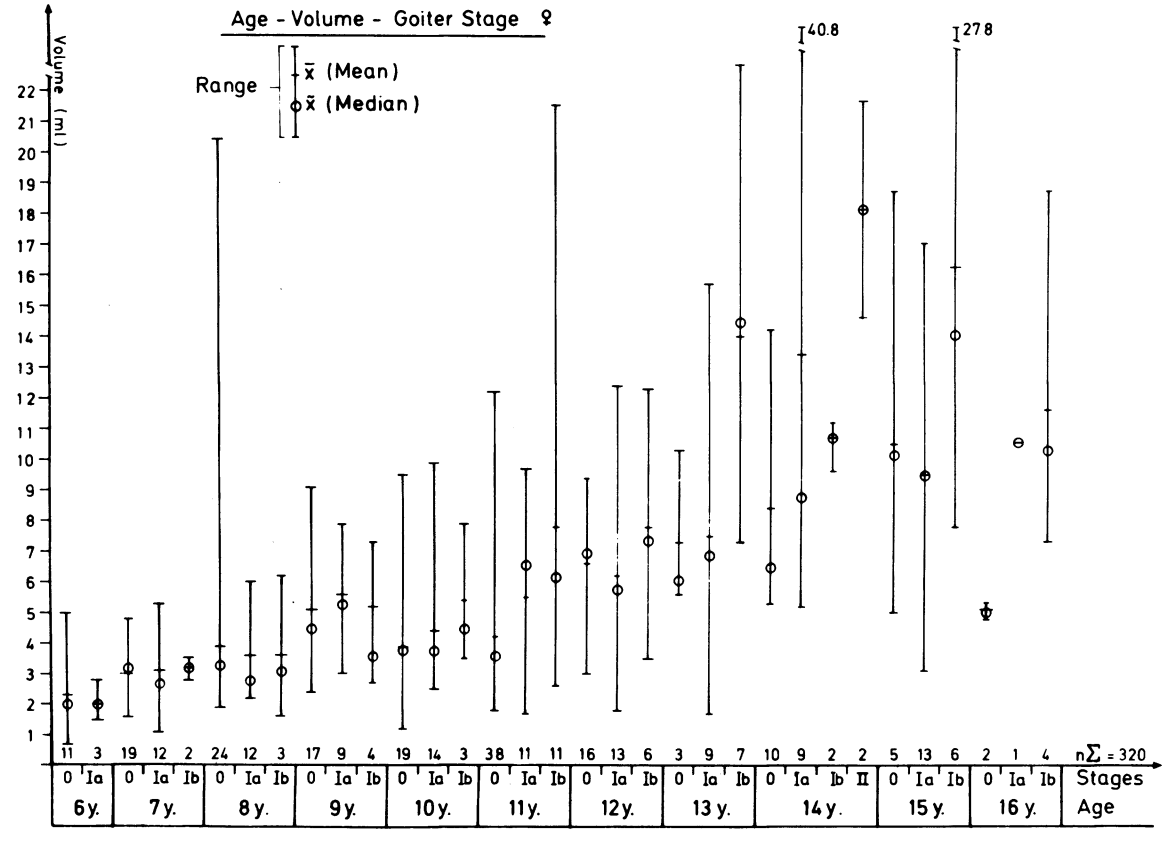

Fig. 3.
Sonographically determined thyroid volume as compared with respective palpatory goitre stages for girls 6–16 years old.

for iodine excretion in both countries. The Swedish distribution shows clearly higher values.

Children. Urinary iodine excretion was low in all age groups in Germany (39.6 ± 30.5, 34.1 µg I/g creatinine, mean ± SD, median) and more than twice as high in Sweden (172.9 ± 224.1, 124), ($P < 0.0001$).

4. *Comparison of iodine excretion to thyroid volume in German adults*

Table 2 shows the median iodine excretion and thyroid volume from cities extending from north to south. The variation from north to south is hardly noticeable, although iodine excretion is higher and thyroid volume is smaller in coastal towns compared to the rest of Germany.

5. *Iodized salt*

There is little difference between iodine excretion of subjects (children and/or adults) using iodized salt and those not ingesting iodine salt ($P > 0.05$). Thyroid volume also did not differ.

6. *TSH and TG levels* (Table 3)

Surprisingly, basal serum TSH levels were lower in German adults (0.97 ± 0.52 mU/ml) than in Swedes (1.49 ± 0.82; $P < 0.001$), whereas the mean serum thyroglobulin concentrations in German adults (72.6 ± 50.6 µg/l) was more than twice as high as in the Swedes (23.5 ± 17.4; $P < 0.0001$).

Discussion

The observation that iodine deficiency has a goitrogenic effect was again supported by the comparison of thyroid volume and iodine excretion between Germans and Swedes. The German adults' thyroids are more than twice as large as those observed in Swedish adults. These findings

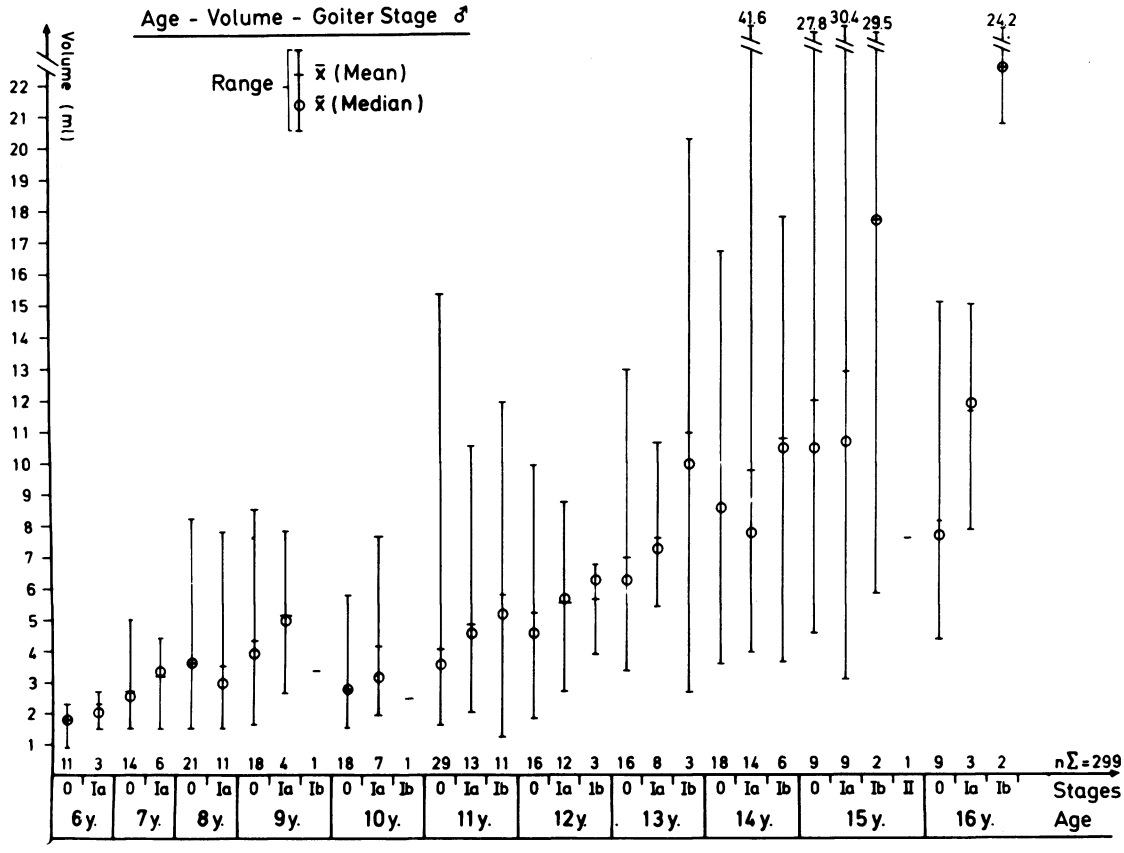

Fig. 4.
Sonographically determined thyroid volume as compared with respective palpatory goitre stages for boys 6–16 years old.

confirm the results of our previous study of 2468 13 year old children in Germany and Sweden, (Gutekunst et al. 1985). In this study, 9 year old German children already exhibited larger thyroid volume compared to those in 13 year old Swedish children. Since it is impossible to define normal thyroid volume in Germany, goitre prevalence cannot be determined on the basis of thyroid volumetry. However, almost one third of the German thyroids are larger than those observed in Sweden (99% range, mean + 3 SD). Thirteen per cent of the German thyroids are above the largest measured Swedish volume. Accordingly, a thyroid volume larger than 20 ml for women and 25 ml for men should be treated or at least controlled. Forty-two per cent of the German men and 25% of the women studied belong in this category. Similarily, 'normal ranges' were defined by Olbricht et al. (1982) and Hegedüs et al. (1983).

The traditional view that goitre is predominantly a problem in Southern Germany can no longer

Table 1.
Echopatterns in Swedish and German adults.

Echopattern	Sweden	Germany
Normal	96.4% (n = 292)	84.0% (n = 1174)
Scattered sonolucent	1.0% (n = 3)	2.5% (n = 35)
Scattered echocomplex	–	0.1% (n = 1)
Uni- and/or multifocal alterations	2.6% (n = 8)	13.4% (n = 187)
Cyst(s)	1.3% (n = 4)	5.9% (n = 82)
Calcification(s)	0.3% (n = 1)	2.1% (n = 29)
Sonolucent nodule(s)	0.3% (n = 1)	3.2% (n = 46)
Echosolid nodule(s)	0.7% (n = 2)	2.1% (n = 29)
Echocomplex nodule(s)	–	0.1% (n = 1)

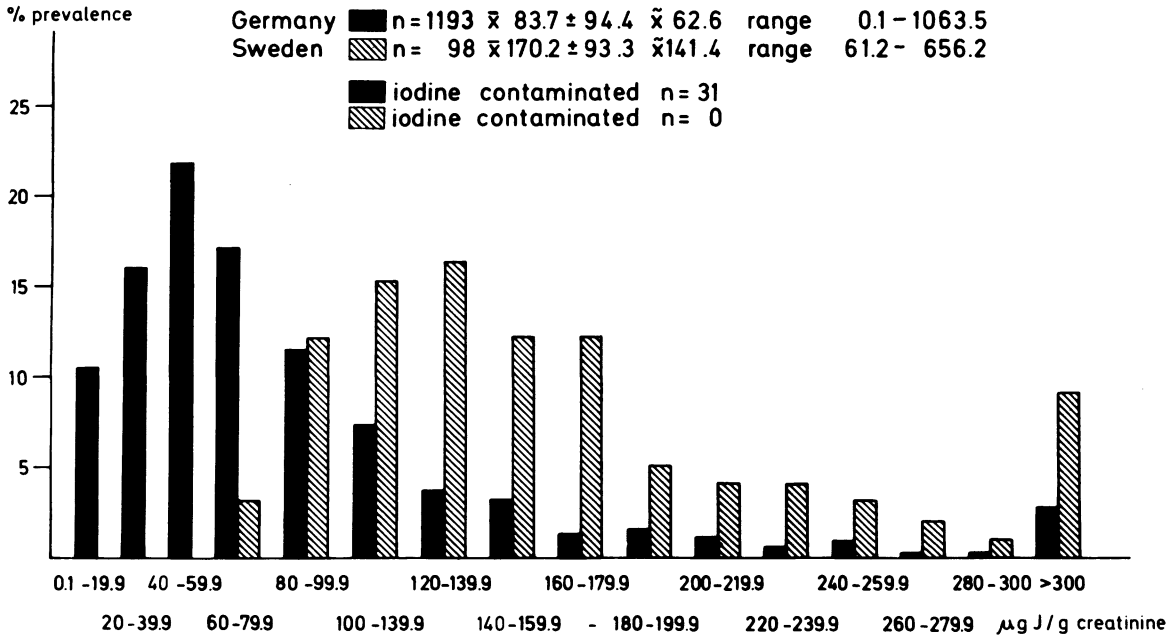

Fig. 5.
Frequency distribution of iodine excretion in Germany and Sweden.

be maintained. As previously found with children in 23 German towns, (Gutekunst et al. 1985), there is likewise no clear-cut increase of thyroid size in adults from north to south. Similarily, endemic nests have to be expected especially in the central region of the FRG. However, in order to obtain a satisfactory mapping of goitre prevalence and iodine deficiency in the FRG, and extensive investigation at further locations would be necessary.

In the German population, 12.4% more abnormal sonographic echopatterns – a sign of diffuse or focal alteration of the gland – were observed than in the Swedish population. These findings are in accordance with the well-known fact that nodular goitre is mainly the consequence of thy-

Table 2.
Comparison of medians of iodine excretion (µg I/g creatinine) and thyroid volume (ml) from Northern to Southern Germany.

	Iodine (µg I/g creatinine)	Thyroid volume (ml)
Kiel	67.3 (n = 46)	14.3 (n = 46)
Lübeck	104.7 (n = 63)	12.5 (n = 70)
Berlin	61.9 (n = 98)	15.2 (n = 111)
Wolfsburg	48.2 (n = 230)	18.7 (n = 313)
Frankfurt	64.2 (n = 201)	18.8 (n = 224)
Tutzing	64.8 (n = 291)	18.5 (n = 339)
Penzberg	66.0 (n = 264)	14.5 (n = 293)
Total	62.6 (n = 1193)	17.0 (n = 1397)

Table 3.
Comparison of TSH and TG serum levels in Germany and Sweden.

	Germany (n = 91)	Sweden (n = 62)
TG (µg/l)	$\bar{x} = 72.6 \pm 50.6$ $\tilde{x} = 43$ range 1.6–234.7	$\bar{x} = 23.5 \pm 17.4$ $\tilde{x} = 21.2$ range 15.0–86.0
TSH (mU/l)	$\bar{x} = 0.97 \pm 0.52$ $\tilde{x} = 0.9$ range 0.02–2.82	$\bar{x} = 1.49 \pm 0.82$ $\tilde{x} = 1.55$ range 0.08–3.98

roid enlargement following iodine deficiency, (Hedinger 1980).

From our present observations and those in an earlier study (Gutekunst et al. 1985) it is apparent that thyroid palpation is of limited value for epidemiological goitre studies. Palpation is even less reliable in younger subjects. It is almost useless in children below 10 years of age. Although the sensitivity of palpation in adults was acceptable (91%), the specificity decreased dramatically to 63.5%.

There is no statistical relation between thyroid volume and iodine excretion in Germany, since all Germans are similarily iodine deficient. Furthermore, iodine excretion is very close to the minimum daily iodine excretion, i.e. individuals with increased tendency to develop goitre cannot be distinguished from the normal population.

This is also true for children and adults who use iodized table salt. The iodized salt in Germany contains 20 mg iodine per kg. To counteract this iodine deficiency, a salt intake of 5 g per person per day is necessary. Since iodized table salt can only be added by the individual to his own food, 5 g daily is obviously unrealistic. Hintze et al. (1985) reported in a 4 year follow-up that there is no significant difference in iodine excretion and goitre stages in children who use iodized salt compared to those who do not. The study of Kersting et al. (1985) suggests that a daily additional intake of more than 1–3 g salt is impractical.

As expected, serum thyroglobulin concentration was higher in German subjects than in those living in Sweden. This is probably due to abnormal thyroid metabolism of thyroglobulin during iodine deficiency, (Pezzino et al. 1978) as well as a greater thyroglobulin leak in degenerative goitre (Gebel et al. 1983).

The surprisingly lower TSH levels in Germany could partially be explained by a higher prevalence of 'preclinical autonomy'. This is a well-known consequence of iodine deficiency (Fenzi et al. 1985; Pickardt et al. 1972). Our results concur with those of Delange et al. (1971) who observed no relationship between serum TSH and thyroid volume. Pickardt et al. (1972) also found no difference in serum TSH in an endemic goitre area in Bavaria. A rise in serum TSH is only observed when iodine deficiency leads to inadaequate production of T_4 and T_3 as has been reported in severe endemic goitre areas (Chopra et al. 1975). Studies in the rat have shown that iodine depleted thyroids are much more sensitive to TSH than those with normal iodine content (Bray 1968). Possibly, the reduced TSH level is a physiological response to protect the thyroid from additional growth. It is currently disputed whether TSH is indeed a growth factor for the thyroid cell (9th Int. Thyroid Congr. 1985).

However, these explanations do not conclusively explain the significantly lower levels of serum TSH in the German population. Further investigation with supersensitive TSH-immunoassays will be necessary.

Conclusions

It is evident from the present study and those reported earlier that the iodine supply in Germany is insufficient. Goitre prevalence can be substantially decreased by an effective program of iodine prophylaxis. Since compulsory iodination of salt is at this time not possible there must be a gradual increase to 50 mg iodine per kg table salt. Further ways to supply people with appropriate iodine should be considered. Increased public awareness of this problem is essential.

Acknowledgments

We thank the following companies for giving the employees time to participate in this study: Boehringer Mannheim, Brunnengräber Lübeck, Ferring Kiel, Henning Berlin, Hoechst Frankfurt, LKB Stockholm and Volkswagenwerk, Wolfsburg.

We are grateful for the support of the Freunde und Förderer of the Medical University of Lübeck.

We thank Prof. Dr. Kl. Lorentz and Dr. E. Kraas for the technical advice to measure creatinine.

The authors gratefully acknowledge the critical reading and help with the manuscript by Prof. L. Braverman, Worcester, MA, USA.

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Received December 2nd, 1985.
Accepted February 17th, 1986.