

## CLINICAL STUDY

## Silent iodine prophylaxis in Western Europe only partly corrects iodine deficiency; the case of Belgium

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### Abstract

**Objective:** Belgium is one of the Western European countries in which no program of iodine-deficiency correction using iodized salt has been implemented, in spite of well-documented mild iodine deficiency. In 1995, the median urinary iodine concentration was 55 µg/l (normal: 100–200) and the prevalence of goiter was 11% (normal: below 5%) in representative samples of schoolchildren aged 6–12 years. Based on these results, the authors of the present study and others had emphasized to health professionals and to the public the necessity for iodine supplementation. The objective of this study was to evaluate as to whether these efforts had resulted in an improvement in the status of iodine nutrition. **Design:** We performed a national survey of the status of iodine nutrition in Belgium based on the determination of thyroid volume, obtained by ultrasonography, and urinary iodine concentrations in schoolchildren.

**Methods:** A mobile van equipped with an ultrasound instrument, a computer and a deep-freeze visited 23 schools selected from across the country. The sample included 2855 schoolchildren (1365 boys and 1490 girls) aged 6–12 years.

**Results:** The results show a homogeneous situation in the whole country, with a median urinary iodine concentration of 80 µg/l and a goiter prevalence of 5.7%. Urinary iodine slightly decreases with age in girls and reaches a critical value of 59 µg/l at the age of 12 years, together with a goiter prevalence of 18.4%.

**Conclusion:** Iodine nutrition has improved slightly in Belgium but mild iodine deficiency continues, with public-health consequences. The improvement indicates silent iodine prophylaxis, as no official salt-iodization measures have been taken. Silent iodine prophylaxis only partly corrects iodine deficiency in Western Europe. Active measures, including the implementation of a program of salt iodization, are urgently required.

*European Journal of Endocrinology* 143 189–196

### Introduction

Iodine deficiency is seen as the world's single greatest cause of preventable brain damage and mental retardation. Universal Salt Iodization (USI), calling for all salt used in agriculture, food processing, catering and household salt to be iodized, is the agreed strategy for its control (1).

Iodine deficiency occurs in regions in which the soil has been depleted of iodine by erosion caused by glacier movements, heavy rain and/or flooding. Therefore, the most severely affected areas are located in high mountains such as the Himalayas and the Andes and regularly flooded low-lying areas such as Bangladesh and Southern China (2).

Central and mountainous parts of Europe used to be

affected (3). Perhaps because of a remarkable program of iodine supplementation that eliminated iodine deficiency from Switzerland (4), some might think that the problem is no longer relevant to Western Europe. However, a review of the situation in Western and Central Europe showed that in 1992, most countries, with the exception of Switzerland, Austria, Finland, Norway and Sweden, still had mild or moderate degrees of iodine deficiency (5). Belgium was one of the affected countries, having an estimated iodine intake of 50–60 µg/day (6), two- to four-fold lower than the recommended intake of 100–200 µg/day (7).

In 1993, joint recommendations by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) were

addressed to all ministries of health of the European region, emphasizing the importance of the problem and recommending action to achieve the sustainable elimination of iodine deficiency in Europe. A follow-up study in 12 European countries two years later evaluated iodine nutrition by measuring, as recommended by WHO, UNICEF and ICCIDD (1), thyroid volume (by ultrasonography) and the urinary concentration of iodine in schoolchildren (8). This study showed obviously improved iodine nutrition, and correction of its deficiency in the Netherlands, Slovakia, France and Germany. In contrast, the situation had not changed in Belgium, where the median urinary iodine concentrations in the three sites investigated were still 58, 50 and 54  $\mu\text{g/l}$  (9) respectively, i.e. it remained unchanged and mild iodine deficiency persisted (1).

Since then, a committee appointed by the Belgian Ministry of Health and chaired by one of us (FD) recommended iodine supplementation in the most critical groups (pregnant and lactating women, infants, and children up to three years of age) and the general use of iodized salt for human and animal nutrition while keeping the salt intake as low as possible. These recommendations were endorsed and supported by the Academies of Sciences of Belgium, but the national authorities did not implement any regulation on iodine supplementation at the national level. However, the Belgian members of the ICCIDD, with the support of the consumers' associations and the salt-, drug- and food industries, spoke and wrote widely on the problem of iodine deficiency in the country to the medical and paramedical professionals and to the public.

The aims of the present study were as follows: (1) to reassess the status of iodine nutrition in Belgium in a national survey, using thyroid volume (measured by ultrasonography) and urinary iodine concentrations in schoolchildren as indicators; (2) to evaluate any improvement in iodine nutrition in Belgium in recent years; and (3) to establish a baseline for possible further recommendations on iodine supplementation in Belgium.

The survey was performed by using a mobile van equipped with an ultrasound instrument, a computer for instantly processing the results of the thyroid measurements, and facilities for the collection and storage of urine samples at  $-20^\circ\text{C}$  (ThyroMobil model (8)). This was the first national survey using this approach in an industrialized country in Western Europe.

### Global organization of the project

The target population comprised male and female schoolchildren aged 6–12 years. The sampling frame was compiled from a list of the approximately 6000 elementary schools in the country. Based on an anticipated prevalence of goiter of about 7% and a desired precision of 1%, the required sample size was about 2500 children.

Two or three schools were selected in each of the country's ten provinces (one in its main town and at least one in other areas). We first requested the assistance of the Medical School Centers (MSCs) responsible for the periodic medical surveys of the schools and, if they agreed, they were asked to contact the school directors. The school directors who agreed to participate were then directly contacted by our team, and arrangements were made for a ThyroMobil visit. A total of 23 schools were investigated. Parents were informed and consented to the objectives and methodology of the study. The protocol was approved by the Ethical Committee of the Faculty of Medicine of the Université Libre de Bruxelles. Any anomalies detected during thyroid ultrasonography were communicated to the MSC and the children were referred to medical facilities for further evaluation and possible therapy.

The fieldwork took place between 1 October and 12 November 1998, during which time the van covered some 3800 km (about 10 times the longest distance between two borders in Belgium).

### Subjects and methods

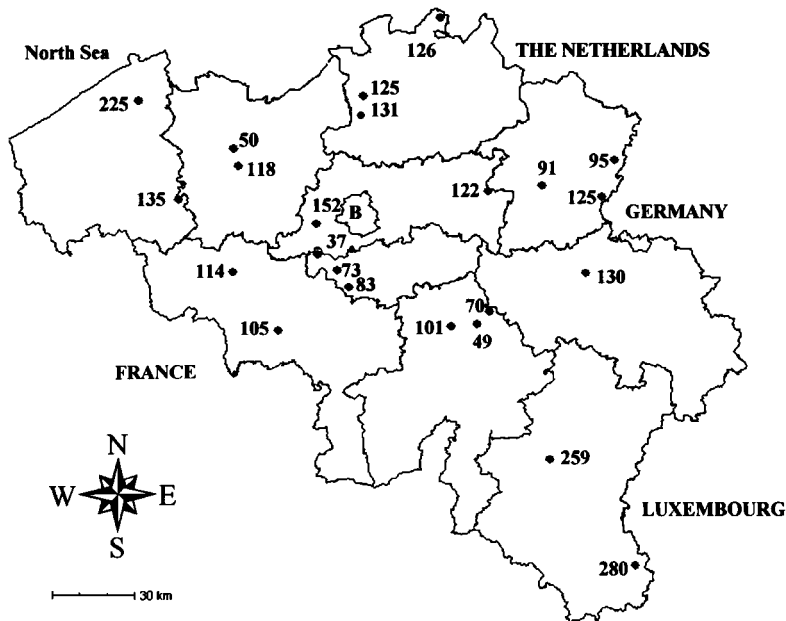
A standardized evaluation was performed according to the recommendations of the WHO, UNICEF and ICCIDD based on the measurements of thyroid volume by ultrasonography and the frequency distribution of urinary iodine concentrations in schoolchildren aged 6–12 years (1). The methodology of the survey was the same as that used previously for surveying Europe (8). Thyroid ultrasonography was performed systematically by one investigator (WS) after intercalibration of the technique with Dr Podoba (Bratislava, Slovakia), who had performed all of the ultrasonography in the European survey.

### Subjects

The investigation included 2855 schoolchildren (1365 boys and 1490 girls) aged 6–12 years. Their distribution by age and gender is shown in Table 1. Figure 1 shows the geographical distribution of the 23 sites and the sample sizes: there were 1–3 sites per province (one

**Table 1** Distribution, by age and gender, of the 2855 school-age children under investigation.

Age (years)	Boys	Girls
6	201	194
7	196	217
8	241	249
9	230	286
10	238	266
11	220	240
12	39	38
<i>Total</i>	1365	1490 = 2855



**Figure 1** Geographical distribution of the 23 sites investigated in Belgium and number of schoolchildren investigated, by site.

site was on the border between two provinces) and from 37 to 280 children per site. Thyroid ultrasound was performed in all children. Urine samples were collected from 2585 children.

## Methods

**Thyroid volume** Thyroid volume was estimated using real-time sonography (Sonoline SI400, Siemens, Erlangen, Germany), according to Brunn *et al.* (10), using a 7.4 MHz linear array transducer. Longitudinal and transverse scans were performed, allowing measurement of the depth (d), width (w) and length (l) of each lobe. The volume of the lobe was calculated by the formula  $v \text{ (ml)} = 0.479 \times d \times w \times l \text{ (cm)}$ . The thyroid volume was the sum of the volumes of both lobes. The volume of the isthmus was not included. The thyroid volumes obtained were compared with the normative values established during the European study in a subsample of iodine-replete European schoolchildren (11). Goiter was defined as the presence of a thyroid volume above the 97th percentile for gender and for age established in the European reference population (8). In normal conditions, the frequency of goiter, using these normative values, should not be higher than 5% (1).

**Urinary iodine** The urinary iodine concentrations were measured by the colorimetric ceric ion arsenious acid wet-ash method based on the Sandell–Kolthoff reaction (12) using an auto-analyzer (Technicon, Tarrytown, NY, USA) (13).

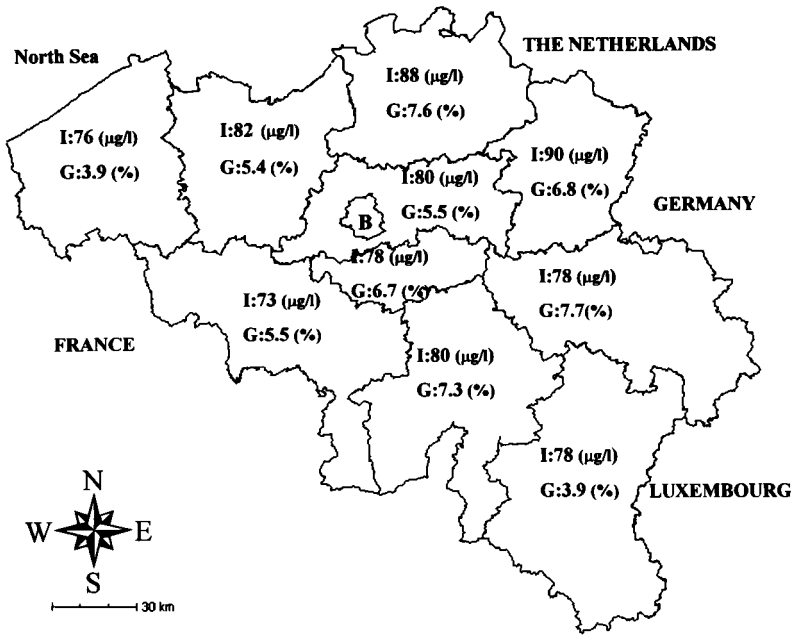
**Statistical methods** Commonly used statistical methods (mean, median and proportions) were applied

to analyze the data. For the prevalence of goiter, the 95% confidence interval (95% CI) was also computed (14). The Kolmogorov–Smirnov test indicated that the distributions of thyroid volumes and urinary iodine were not normal.

For urinary iodine, normalization did not occur after a logarithmic transformation and, as advised by the WHO, UNICEF, ICCIDD recommendations (1), the medians were used rather than means or geometric means. The normal values for urinary iodine in schoolchildren are medians varying from 100 to 200  $\mu\text{g/l}$  (1). The distributions of urinary iodine and thyroid volumes were represented by means of box plots (15), which give the median, the upper (P75) and the lower (P25) quartiles. The ends of the ‘whiskers’ (vertical bars) are the adjacent values defined from the interquartile range (IQR). The upper adjacent value is the largest observation equal to or lower than the top of the box (P75) + 1.5 IQR and the lower adjacent value is the smallest observation equal to or higher than the bottom of the box (P25) – 1.5 IQR. The individual values falling outside the range of the two adjacent values are also represented. Mann–Whitney and chi-squared tests compared the medians of urinary iodine and the prevalence of goiter respectively in both sexes. All analyses were performed using SPSS 9.0 for Windows.

## Results

There were no differences in the prevalence of goiter and in the median urinary iodine concentrations in the different sites of each province. Therefore, the results

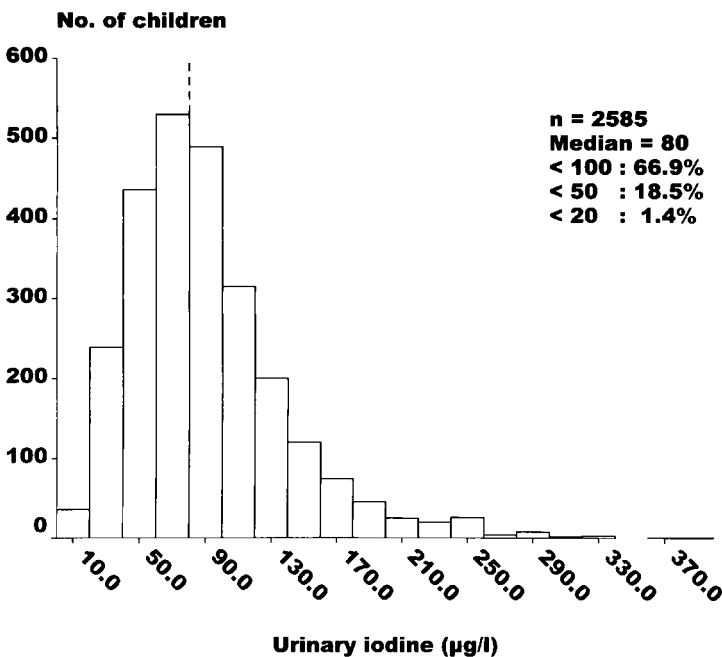


**Figure 2** Prevalence of goiter (G, %) and median urinary iodine concentrations (I, µg/l) in the ten provinces of Belgium.

obtained in each of the ten provinces were pooled. They are shown in Fig. 2. The results were very homogeneous throughout the country. The median urinary iodine varied from 73 to 90 µg/l and the prevalence of goiter varied from 3.9 to 7.7%. There was no relationship between these results and the distance of the 23 sites from the seashore. For the country as a whole, the median urinary iodine was 80 µg/l and the prevalence

of goiter was 5.7% (95% CI: 4.8–6.6%). Figure 3 shows the frequency distribution of urinary iodine in the whole population under investigation. The distribution is skewed towards elevated values: 66.9% of the values were below 100 µg/l, 18.5% were below 50 µg/l and 1.4% were below 20 µg/l.

Figures 4 and 5 show the changes in thyroid volume and urinary iodine concentration respectively, as a



**Figure 3** Frequency distribution of urinary iodine in all children investigated.

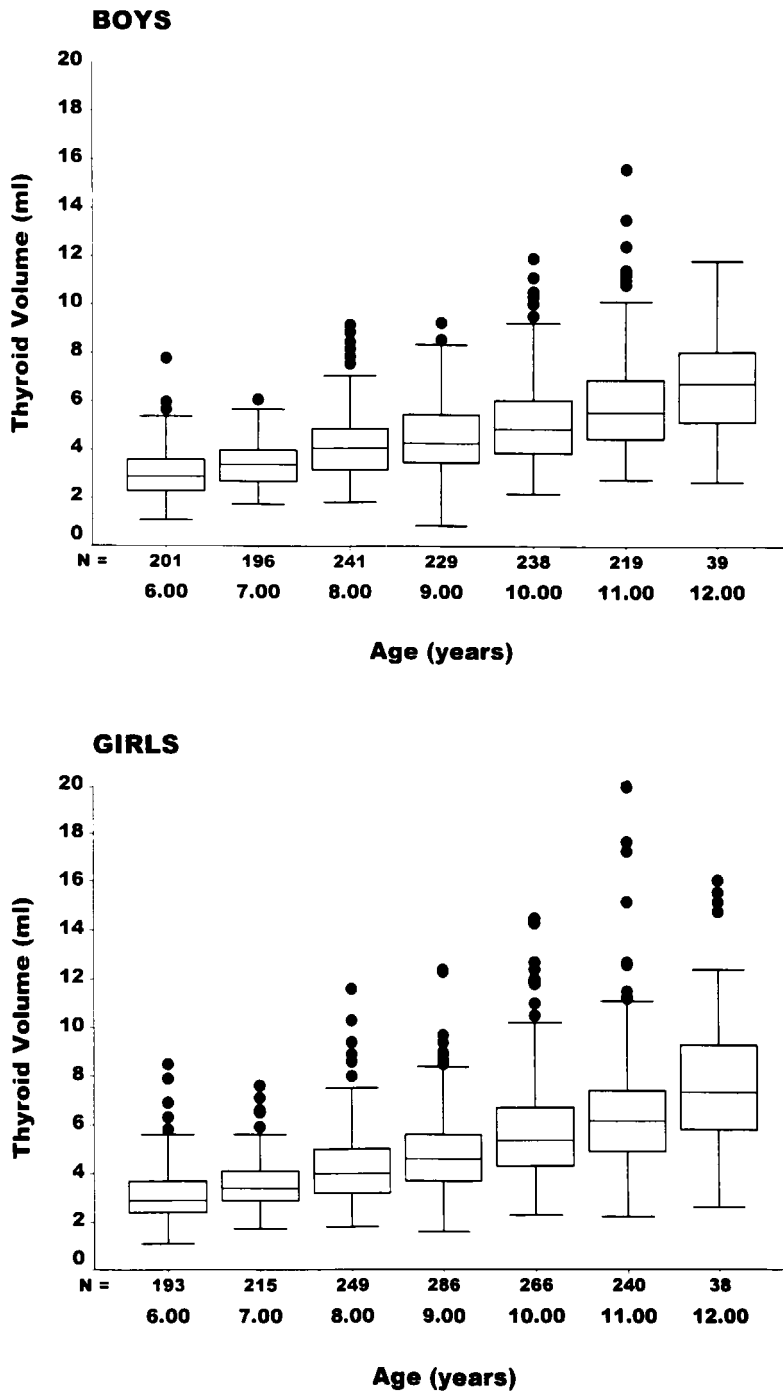


Figure 4 Change in thyroid volume as a function of age and gender. N = number of children.

function of age and gender. In both sexes, thyroid volume progressively increased with age. The variability of the results was slightly higher in girls than in boys, especially from the age of 11 years onwards. Nine children had grossly abnormal ultrasound findings: of these, three had a visible goiter (stage II upon clinical examination (1)) and six had thyroid hemiagenesis of the left lobe. All were forwarded to practitioners

for further evaluation and possible therapy. The goitrous patients were treated with thyroxine. One had chronic thyroiditis and hypothyroidism. Thyroid function was normal in the cases of thyroid hemiagenesis. They were not treated and will undergo longitudinal follow-up. This unexpectedly high prevalence of thyroid hemiagenesis (0.2%) is reported elsewhere (16).

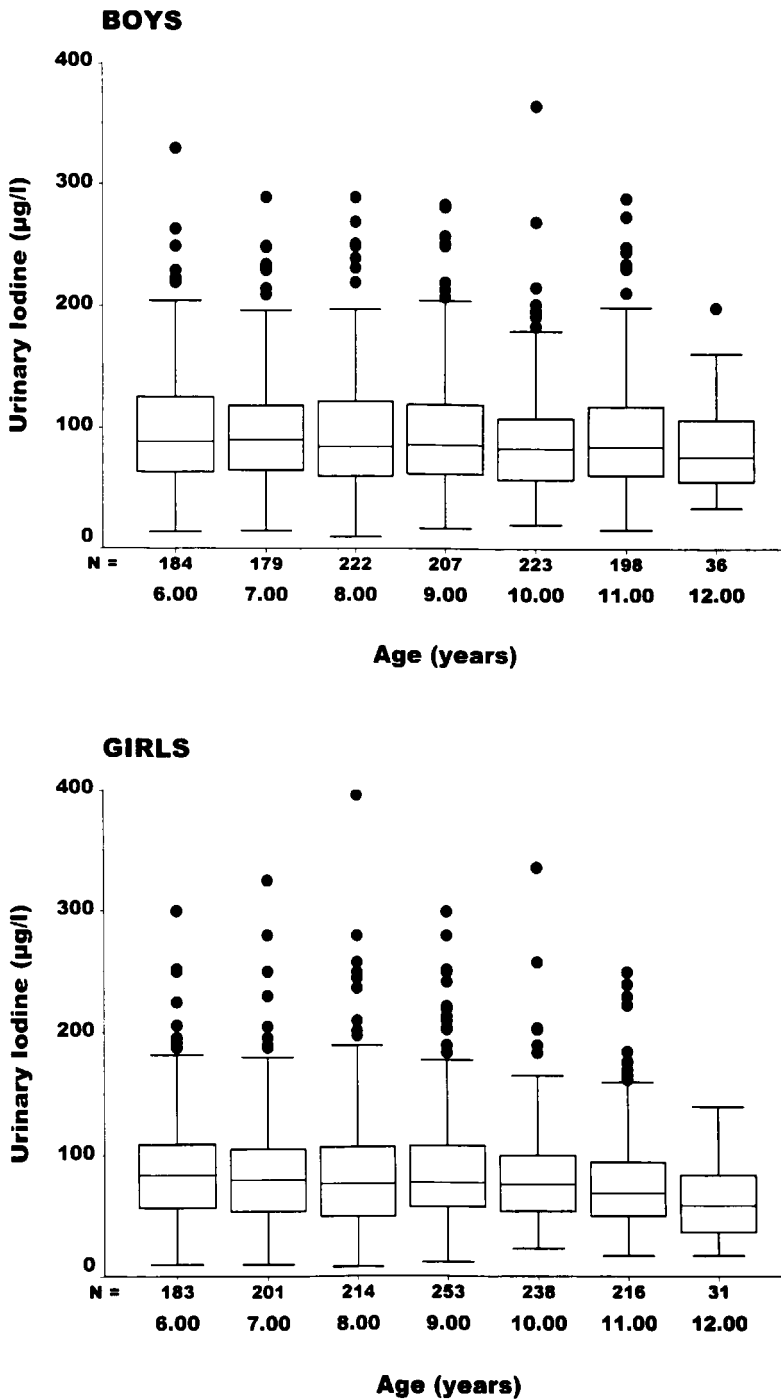


Figure 5 Changes in the concentrations of urinary iodine as a function of age and gender. N = number of children.

Urinary iodine concentrations were relatively stable in boys but decreased slightly and progressively with age in girls. The lowest values were found at the age of 12 years in both sexes.

Table 2 shows the figures obtained for the prevalence of goiter and for median urinary iodine as a function of age and gender respectively. The median urinary

iodine concentration was almost uniformly lower in girls than in boys: for all ages combined, the value was 76 µg/l in girls and 85 µg/l in boys ( $P < 0.001$ ). However, the goiter prevalence did not differ significantly between the sexes and was even slightly higher in boys than in girls at the ages of 6 and 12 years ( $P < 0.05$ ).

**Table 2** Prevalence of goiter (%) and median urinary iodine ( $\mu\text{g/l}$ ) as a function of age and gender in the 2855 schoolchildren examined.

Age (years)	Prevalence of goiter (%)			Urinary iodine ( $\mu\text{g/l}$ )		
	Boys	Girls	Total	Boys	Girls	Total
6	1.8	6.0*	3.9	89	84	86
7	1.0	2.3	1.7	90	80**	84
8	7.1	4.4	5.7	85	77*	80
9	8.6	5.6	6.9	86	78(*)	83
10	8.5	6.7	7.5	83	77	80
11	7.3	5.5	6.4	85	69***	75
12	5.1	18.4*	11.7	77	59*	68
<i>Grand total</i>	6.0	5.5	5.7	85	76***	80

(\*)  $0.05 < P < 0.10$ ; \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

## Discussion

To our knowledge, this is the first national survey of iodine nutrition in an industrialized country carried out using a standardized method involving thyroid volume (obtained by ultrasonography) and urinary iodine concentrations. It shows that in a representative sample of schoolchildren in Belgium, the median urinary iodine concentration is presently  $80 \mu\text{g/l}$  and the prevalence of goiter is 5.7%. These figures indicate mild iodine deficiency (1).

Three years ago, a study using a similar methodology, but covering only three sites, produced a median urinary iodine concentration of  $55 \mu\text{g/l}$  and a goiter prevalence of 11% (8, 9). Consequently, a partial correction of iodine deficiency has taken place during the last three years. During this period, the Ministry of Health took no official measures to implement a program of salt iodization but the authors and others have emphasized (to health professionals and the public) the necessity for iodine supplementation. We hope that these efforts resulted in a process of silent iodine prophylaxis and have contributed to the improved iodine nutrition of Belgian schoolchildren.

This study confirms that puberty is a critical period for thyroid function, since it is during this phase that goiter frequently develops, especially in girls (17). The low urinary iodine concentrations that we found could reflect either a decrease in iodine intake or an increase in the thyroid gland's avidity for iodide characteristic of this age period (18).

The figure of  $80 \mu\text{g/l}$  for urinary iodine in Belgium corresponds exactly to the figure reported recently from France (19). Neither country has so far officially implemented a program of universal salt iodization for the sustainable elimination of iodine deficiency. Such programs are definitely required. Meanwhile, the persistence of iodine deficiency incurs major costs in the diagnosis and therapy of the disorders associated with it (20). Moreover, we cannot exclude the possibility that even a mild degree of iodine deficiency may affect

the neuropsychological development of young infants and children (21, 22).

In conclusion, iodine deficiency persists in Belgium despite 'silent prophylaxis'. Several other Western European countries affected by the deficiency have also not yet adopted and implemented legislation on universal salt iodization. Together with the return of iodine deficiency in Eastern Europe following disruption of previously well-established programs of salt iodization (23), the situation reported in this work explains why Europe as a whole is now the last region in the world to achieve access, by iodine-deficient populations, to iodized salt (24).

## Acknowledgements

This work was supported by the following: the Ministry of Health, Belgium; the Prix Herman Houtman, 1997 (F Delange); Merck KgaA, Germany; Merck Belgolabo, Belgium; and the ICCIDD. The authors wish to acknowledge the support provided by Professors M Jonckheer, B Velkeniers and M Osteaux (Vrije Universiteit Brussel, Brussels, Belgium); Dr J Podoba (Bratislava, Slovakia); Dr M De Spiegelaer, Mrs N Moreau and Mr P De Smet (School of Public Health, Université Libre de Bruxelles); and Mr Y Zwikel.

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Received 8 February 2000

Accepted 28 March 2000