European Journal of Clinical Nutrition (2001) 55, 162–166
 0954–3007/01 $15.00
www.nature.com/ejcn

Monitoring the adequacy of salt iodization in Switzerland: a national study of school children and pregnant women

SY Hess[1], MB Zimmermann[1,2]*, T Torresani[3], H Bürgi[2] and RF Hurrell[1]

[1]*Laboratory for Human Nutrition, Food Science Institute, Swiss Federal Institute of Technology Zürich;* [2]*Fluoride-Iodine Committee, Swiss Academy of Medical Science; and* [3]*Children's Hospital, Zürich, Switzerland*

Background: Several countries with long-standing salt iodization programs, including Switzerland, have recently reported declining and/or low urinary iodine (UI) levels in their populations. In Switzerland, in response to studies indicating low UI levels in children and pregnant women, the salt iodine level was increased in 1998 from 15 to 20 mg/kg.
Objective: Our objective was to evaluate iodine nutrition in a national sample of Swiss school children and pregnant women 8–16 months after the increase in the salt iodine level.
Design: A 3-stage probability proportionate to size cluster sampling method was used to obtain a representative national sample of 600 children aged 6–12 y and 600 pregnant women. We then measured UI in both groups, thyrotropin (TSH) in pregnant women and thyroid volume by ultrasound to determine goiter prevalence in school children.
Results: The median UI (range) of the children and pregnant women was 115 μg/l (5–413) and 138 μg/l (5–1881), respectively. The median blood TSH concentration (range) of pregnant women was 0.6 mU/l (0.2–2.1). Based on the current WHO/ICCIDD normative data for thyroid volume, none of the children were goitrous, using either age/sex-specific or BSA/sex-specific cutoffs.
Conclusions: The iodine status of the Swiss population is once again adequate, illustrating the value of periodic monitoring and prudent adjustments to the iodine level in salt. This approach could serve as a model for countries struggling to maintain dietary iodine intake in the face of shifting dietary habits and changes in the food supply.
Sponsorship: Swiss Foundation for Nutrition Research, Zürich, Switzerland; Foundation for Micronutrients in Medicine, Rapperswil, Switzerland; and Swiss Federal Institute of Technology in Zürich, Switzerland.
Descriptors: salt; iodine; monitoring; Switzerland; children; pregnant women
European Journal of Clinical Nutrition (2001) **55,** 162–166

Introduction

Several countries with long-standing salt iodization programs, including the US, the Netherlands, New Zealand, France and Switzerland, have recently reported declining and/or low urinary iodine (UI) levels among segments of their populations (Hollowell *et al*, 1998; Brussaard *et al*, 1997; Thomson *et al*, 1997; Valeix *et al*, 1999; Zimmermann *et al*, 1998). Because dietary iodine supply is influenced by a number of commercial, agricultural and cultural factors, regular monitoring of iodine nutrition is necessary. Although the World Health Organization/United Nations Children's Fund/International Council for the Control of Iodine Deficiency Disorders (WHO/UNICEF/ICCIDD) has emphasized the importance of periodic monitoring and adjustment of salt iodine levels, few developed or developing countries have established regular and systematic programs (WHO/UNICEF/ICCIDD, 1994; 1999).

Iodized salt was introduced in Switzerland in 1922 and by 1952, iodized salt (3.75 mg/kg salt) was available throughout the country. Periodic monitoring resulted in stepwise increases in the level of iodine in table salt, to 15 mg/kg salt in 1980 (Bürgi, 1998). Although surveys in the 1980s found iodine status in Switzerland to be adequate (Bürgi, 1998; Bürgi *et al*, 1990), in the 1990s, studies began to show marginal to low UI levels among school children and pregnant women (Zimmermann *et al*, 1998; Als *et al*, 1995; Truong *et al*, 1997; Mokhtech *et al*, 1995). In a 1994 survey of pregnant women in Lausanne, the mean UI in the 1st and 3rd trimesters was 100 and 83 μg/g creatinine,

*Correspondence: MB Zimmermann, Laboratory for Human Nutrition, Seestrasse 72/Postfach 474, CH-8803 Rüschlikon, Switzerland.
E-mail: michael.zimmermann@ilw.agrl.ethz.ch
Guarantor: SY Hess.
Contributors: All investigators contributed to the study design. SH coordinated the study, collected data and assisted in writing and editing the paper. TT and HB supervised the completion of the analytic work and edited the paper. MZ and RH initiated and coordinated the study, contributed to data analysis and the writing and editing of the paper.
Received 5 July 2000; revised 20 October 2000;
accepted 30 October 2000

respectively (Mokhtech *et al*, 1995), compared to the estimated requirement of 200 μg/day (WHO/UNICEF/ICCIDD, 1994). In a 1997 study of 5 to 13-y-old children from the Zürich area and the Engadine valley, median UI was 96 μg/l — suggesting mild iodine deficiency (Zimmermann *et al*, 1998). Concerned that iodine intake in Switzerland was falling to levels associated with mild iodine deficiency disorders (IDD), the Federal Government increased the level of iodine (as potassium iodide) in table salt to 20 mg/kg in 1998. Although iodized salt use in Switzerland has always been voluntary and manufacturers must offer both non-iodized and iodized salt, it is estimated that 95% of table salt in the country is iodized.

However, it was unclear what effect this increase would have on Swiss iodine nutrition, as dietary habits and food supply patterns in Europe are changing. In industrialized countries, most dietary salt intake comes from processed foods (James *et al*, 1987). Increasing imports of processed foods containing noniodized salt, combined with reluctance of export-oriented Swiss food producers to use iodized salt, has resulted in a significant proportion of salt consumed in Switzerland being iodized at low levels (5–10 mg/kg) or noniodized (Bürgi, 1998; Als *et al*, 1995). In addition, responding to health guidelines, people may be gradually reducing their salt intake.

Therefore, the aim of this study was to evaluate iodine nutrition in a national sample of Swiss schoolchildren and pregnant women, in order to judge the effectiveness of the recent increase in the salt iodine level to 20 mg/kg. To assess iodine status, we measured UI in both groups, thyrotropin (TSH) in pregnant women and thyroid volume by ultrasound to determine goiter prevalence in school children. This study was planned as the first of a regular series of national monitoring surveys of iodine nutrition in Switzerland.

Subjects and methods

A 3-stage probability proportionate to size (PPS) cluster sampling method was used to obtain a representative national sample of 600 children aged 6–12 y and 600 women in the 2nd and 3rd trimester of pregnancy. PPS cluster sampling is the recommended method for monitoring national salt iodization programs (WHO/UNICEF/ICCIDD, 1994). The sample size was based on an estimated 35% prevalence of UI < 100 μg/l, a 95% confidence interval for the true prevalence of UI < 100 μg/l, a design effect of 2, and a relative precision of 15%. Current census data was used to provide a systematic sampling of urban and rural communities based on the cumulative population.

In stage 1 of the sampling, 30 primary schools and 30 obstetric clinics were recruited using stratified random selection. If a school or clinic declined participation, a replacement was randomly selected from the same stratum. The proportion of pregnant women in Switzerland who receive their prenatal care in hospitals *vs* private clinics is approximately 1:2 (written communication, 1999, Swiss Society for Obstetrics and Gynecology). Therefore, we selected 10 hospitals and 20 private clinics. In the second stage, 2 classrooms were randomly selected from each school. Finally, the teachers randomly selected students to participate, and a clinic physician randomly selected pregnant women in their 2nd or 3rd trimester. An average of 20 subjects was sampled at each of 30 clusters. Data were collected between April and December 1999. Ethical approval for the study was obtained from the Swiss Federal Institute of Technology in Zürich. Written consent was obtained from the community school boards and parents of the children, as well as the physicians. Oral consent was obtained from the pregnant women.

The height and weight of the children were measured using the standard anthropometric techniques (WHO, 1995). For the measurements, subjects removed their shoes, emptied their pockets and wore light indoor summer clothing. Height was recorded to the nearest cm and weight to the nearest 100 g. Body surface area (BSA) was then calculated using the formula: weight $(kg)^{0.425} \times$ height $(cm)^{0.725} \times 71.84 \times 10^{-4}$ (WHO, 1997). For the pregnant women, week of gestation and use of vitamin/mineral supplements were recorded. Thyroid gland volume was measured using an Aloka SSD-500 Echocamera (Aloka, Mure, Japan) with a 7.5 MHz 5 cm linear transducer (WHO, 1997). Measurements were performed on subjects sitting upright with the neck extended. SH or MZ performed the ultrasound measurements. To estimate intra- and inter-observer variability, SH measured 20 school children twice and MZ measured the same children once. The mean (s.d.) intra- and inter-observer errors were 4.9 (4.0)% and 3.7 (3.5)%, respectively. Thyroid volumes were compared to both age/sex-specific and body surface area (BSA)/sex specific normative data for thyroid volume in children (WHO, 1997). Spot urine samples were collected from children and pregnant women and stored at −20°C until analysis. UI was measured in duplicate using a modification of the Sandell-Kolthoff reaction (Pino *et al*, 1996). The CV of this method in our laboratory is 10.0% at 47.4 ± 0.6 μg/l and 12.7% at 79.5 ± 0.8 μg/l. Satisfactory agreement in UI was obtained on urine samples measured by our laboratory and the reference laboratory of the ICCIDD in Brussels, Belgium (unpublished). Urinary creatinine measurement was done in duplicate using a modification of the Jaffé method (Clarke *et al*, 1961). Whole blood obtained from venous samples was spotted and dried on filter paper and TSH was measured using immunoassay (Torresani & Scherz, 1986).

Data processing and statistics were done using SPLUS 4.5 (Mathsoft, Seattle, USA) and SAS (SAS Institute Inc., Cary, NC, USA). UI, urinary iodine/creatinine ratio, and TSH were not normally distributed; the distributions by age, sex and trimester were skewed to the right. They were expressed as medians with ranges, and differences between groups were tested using the Mann–Whitney test. Thyroid volumes in the children for each age and BSA group for both sexes were not normally distributed. They were expressed as medians with ranges, and differences were

tested using the Mann–Whitney test. P-values < 0.05 were considered significant.

Results

A total of 610 students aged 6–12 y from 31 schools throughout Switzerland were studied. This represents approximately 1 in 1000 children in this age group in Switzerland (Bundesamt für Statistik, 1996). The sample included 303 females and 307 males; mean age (s.d.) of the children was 9.5 y (1.9). A total of 511 women from 27 obstetric clinics were sampled; 206 women were in the 2nd and 290 in the 3rd trimester of pregnancy. For 15 women, information on gestational age was not recorded. Mean age (s.d.) of the women was 29.5 y (4.8).

Urinary iodine and blood TSH concentrations
Adequate urine samples were obtained from 600 out of the 610 children. The median UI (range) of the children was 115 μg/l (5–413). Overall, 39.5% of the children had UI < 100 μg/l and 8.5% had levels < 50 μg/l. The distribution of UI among the school children is shown in Figure 1. Expressed per g creatinine, the median UI (range) was 123 μg/g (22–2256). There were no significant gender differences in median UI; 35.2% of the boys and 43.9% of the girls had UI < 100 μg/l. There was also no significant difference in median UI when 6 to 9-y-old children were compared to 10 to 12-y-olds. The percentage of children in the 6–9 and 10 to 12-y-old age groups with iodine levels below 100 μg/l was 38.4% and 40.6%, respectively.

The median UI (range) in the pregnant women was 138 μg/l (5–1881). Expressed per g creatinine, the median UI (range) was 207 μg/g (5–4216). The distribution of median UI among the pregnant women is shown in Figure 2. There was no significant difference in median UI when comparing women in the 2nd and 3rd trimester. Although 70% of the pregnant women were taking a daily multivitamin-mineral supplement, only 13% were taking a supplement containing iodine (150 μg iodide as KI). There was a significant difference in median UI between women taking an iodine-containing supplement ($n = 64$) and those not taking an iodine-containing supplement ($P = 0.023$); the median UI (range) in these 2 groups was 194 μg/l (31–990) and 130 μg/l (5–1881), respectively. The median blood TSH concentration (range) of the pregnant women ($n = 396$) was 0.6 mU/l (0.2–2.1); only 3 women had borderline elevated values (1.9–2.1 mU/l).

Thyroid volumes and goiter prevalence
Based on the current WHO/ICCIDD normative data for thyroid volume, none of the children were goitrous, using

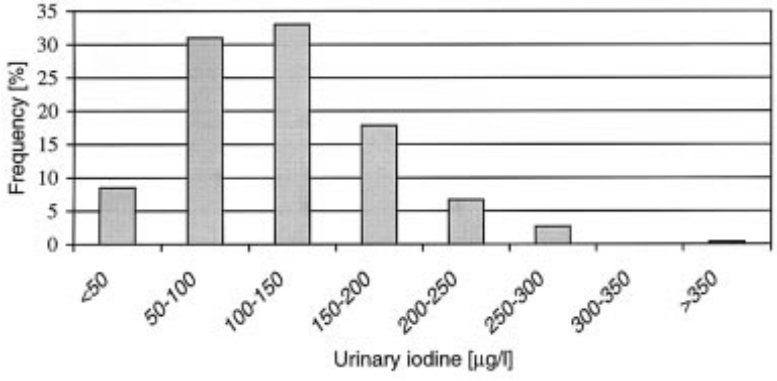

Figure 1 Distribution of spot urinary iodine excretion in a national sample of 600 children aged 6–12 g in Switzerland.

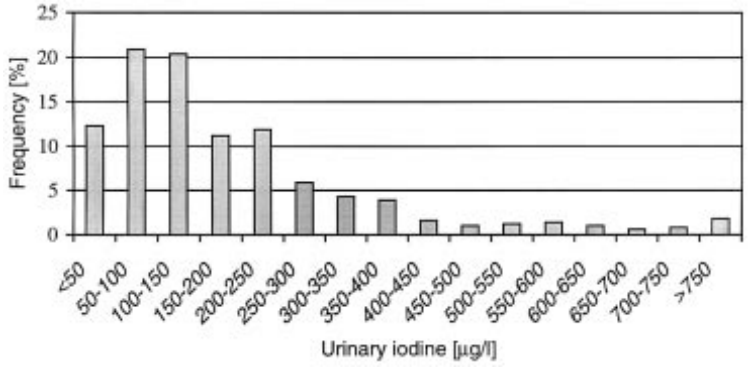

Figure 2 Distribution of spot urinary iodine excretion in a rational sample of 511 pregnant women in Switzerland.

either age/sex-specific or BSA/sex-specific cutoffs (WHO, 1997). We also determined the goiter prevalence in our sample using the older normative data proposed by Gutekuns & Martin-Teichert (1993), and found a prevalence of 3.9% ($n = 23$). There were significant gender differences in median thyroid volume ($P < 0.01$) only at age 12 y, when females had a median thyroid volume 17% greater than males. By BSA, significant differences ($P < 0.05$) between females and males were found only when BSA was $> 1.4\,m^2$. At a BSA of 1.5 and 1.6, females had a median thyroid volume 9% and 10% greater than males, respectively. We have recently published a detailed description and comparison of our thyroid volume data with the current WHO/ICCIDD-recommended reference data (Hess & Zimmermann, 2000).

Discussion

We used schoolchildren and pregnant women as our target groups for IDD surveillance (WHO/UNICEF/ICCIDD, 1994). A strength of our study design was the use of a biological indicator of iodine status — thyroid volume in children and TSH in pregnant women — in addition to UI. Indications of an iodine-sufficient population include a median UI $\geq 100\,\mu g/l$ in school age children, with no more than 20% of samples below $50\,\mu g/l$ (WHO/UNICEF/ICCIDD, 1994). Because this study was done in the summer and fall months, UI was likely measured at a low level in its seasonal variation. Iodine intake tends to be higher during winter months in Switzerland due to higher levels of iodine in cows' milk from feed additives used during wintertime (Schällibaum, 1991). Despite this, the median UI in the school children was $115\,\mu g/l$ and only 8.5% had levels $< 50\,\mu g/l$, indicating iodine sufficiency.

The estimated requirement for iodine during pregnancy is $200\,\mu g$/day (WHO/UNICEF/ICCIDD, 1994). In the pregnant women, the median UI was $138\,\mu g/l$ and, expressed per g creatinine, median UI was $207\,\mu g/g$. Urine volume increases during 2nd and 3rd trimester and the turnover of iodine by the thyroid is estimated to be $60\,\mu g$/day in adults (and may be higher during pregnancy). Therefore, the median UI and the UI expressed per g creatinine in these women suggests their iodine intake is sufficient. Women taking an iodine-containing supplement daily ($150\,\mu g$) had significantly higher median UI compared to women taking a supplement not containing iodine, and those not taking a supplement. These results suggest that $150\,\mu g$ iodine per day as supplemental KI can significantly increase UI during pregnancy. TSH was measured as an additional potential indicator of iodine deficiency. Although generally not sufficiently sensitive to detect mild iodine deficiency in adult populations, it can be valuable as an indicator of early hypothyroidism in areas of moderate to severe iodine deficiency, including in pregnant women (Dunn, 1998). Less than 1% of the pregnant women in this study had borderline elevated blood TSH values. Taken together with the UI data, this suggests that the iodine nutrition of Swiss pregnant women is sufficient.

We have reported UI both in terms of concentration ($\mu g/l$) and per g urinary creatinine. Reporting iodine excretion per g creatinine minimizes variation caused by differences in urine volume and dilution among subjects (Bourdoux, 1988). However, creatinine excretion varies with nutritional status (Delange, 1999). While low creatinine excretion in areas of undernutrition may mask iodine deficiency, high creatinine excretion in affluent, well-nourished populations (such as Switzerland) may overestimate the number of individuals classified as at risk for iodine deficiency disorders (IDD). In the children in this study, UI results were comparable whether reported as concentration or per g creatinine. Because the measurement of creatinine entails additional costs, our findings support the position of the WHO/UNICEF/ICCIDD, which recommend the use of median UI in $\mu g/l$ to monitor iodine status in a population (WHO/UNICEF/ICCIDD, 1994).

To determine goiter prevalence in this study, we used normative thyroid volume data from WHO/ICCIDD (WHO, 1997). Because the WHO/ICCIDD reference cut-off points are the 97th percentiles of thyroid volume in iodine-sufficient European children (Delange *et al*, 1997), applying the WHO/ICCIDD references to this population of iodine-sufficient Swiss children should yield a goiter prevalence of approximately 3%. However, using either the age/sex-specific or the BSA/sex-specific WHO/ICCIDD cut-offs, there were no goitrous children in our sample. Because the WHO/ICCIDD normative data have been recently challenged and may be too high (Hess & Zimmermann, 2000; Delange, 1999), we also determined the goiter prevalence in our sample using the older normative data proposed by Gutekunst & Martin-Teichert (1993), and found a prevalence of 3.9%. One indication of iodine sufficiency in a population is a goiter rate $< 5\%$ in school age children (WHO/UNICEF/ICCIDD, 1994). Together with the median UI of $115\mu g/l$, the goiter rate of $0-3.9\%$ indicates Swiss school children are now iodine sufficient.

To ensure the continued success of an established salt iodization program, regular monitoring of UI and, when indicated, other biological measures of iodine nutrition is critical. As shown in this study, periodic surveillance and prudent adjustments to the iodine level in salt has maintained adequate iodine nutrition in Switzerland. This study was planned as the first of a series of national surveys which will monitor iodine status in the Swiss population every 5 y. Current Swiss legislation is flexible in that it specifies a range of $20-30\,mg/kg$ for salt iodization. Federal decree can quickly adjust the level based on new scientific evidence without the need for a lengthy parliamentary process (Bürgi, 1999). This approach could serve as a paradigm for other countries struggling to maintain dietary iodine intake in the face of shifting dietary habits and changes in the food supply.

Acknowledgements—We thank the subjects, the medical staff of the obstetric centers, and teachers for their participation in the study; and Simon Kollaart and Christina Ammann for their analytical help.

References

Als C, Lauber K, Brandner L, Lüscher D & Rösler H (1995): The instability of dietary iodine supply over time in an affluent society. *Experientia* **51**, 623–633.

Bourdoux PP (1988): Measurement of iodine in the assessment of iodine deficiency. *IDD Newslett*. **4**, 8–12.

Brussaard JH, Brants HAM, Hulshof KFAM, Kistemaker C & Löwik MRH (1997): Iodine excretion among adults in the Netherlands. *Eur. J. Clin. Nutr*. **51**(Suppl 3), S59–S62.

Bundesamt für Statistik (1996): Statististical Yearbook of Switzerland. Zürich: Verlag NZZ.

Bürgi H (1998): Iodine nutrition of the Swiss population. *4. Schweizerischer Ernährungsbericht*, pp 64–73. Bern: EDMZ.

Bürgi H (1999): The Swiss legislation on iodized salt. *IDD Newslett*. **4**, 57–58.

Bürgi H, Supersaxo Z & Selz B (1990): Iodine deficiency diseases in Switzerland one hundred years after Theodor Kocher's survey: a historical review with some new goiter prevalence data. *Acta. Endocrinol*. **123**, 577–590.

Clarke JT (1961): Colorimetric determination and distribution of urinary creatinine and creatinine. *Clin. Chem*. **7**, 271–283.

Delange F (1999): What do we call a goiter? *Eur. J. Endocrinol*. **140**, 486–488.

Delange F, Benker G, Caron Ph, Eber O, Ott W, Peter F, Podoba J, Simescu M, Szybinsky Z, Vertongen F, Vitti P, Wiersinga W & Zamrazil V (1997): Thyroid volume and urinary iodine in European schoolchildren: standardization of values for assessment of iodine deficiency. *Eur. J. Endocrinol*. **136**, 180–187.

Dunn JT (1998): Assessing and monitoring iodine nutrition. In *Iodine in Pregnancy*, eds. JB Stanbury, F Delange, JT Dunn, & CS Pandav, pp 203–210. Delhi: Oxford University Press.

Gutekunst R & Martin-Teichert H (1993): Requirements for goiter surveys and the determination of thyroid size. In *Iodine Deficiency in Europe: A Continuing Concern*, eds. F Delange, JT Dunn, D Glinoer, pp 109–118. New York: Plenum Press.

Hess SY & Zimmermann MB (2000): Thyroid volumes in a national sample of iodine-sufficient Swiss school children: comparison to the WHO/ICCIDD normative thyroid volume criteria. *Eur. J. Endocrinol*. **142**, 599–603.

Hollowell JG, Staehling NW, Hannon WH, Flanders DW, Gunter EW, Maberly GF, Braverman LE, Pino S, Miller DT, Garbe PL, DeLozier DM & Jackson RJ (1998): Iodine nutrition in the United States. Trends and public health implications: iodine excretion data from NHANES I and III (1971–1974 and 1988–1994). *J. Clin. Endocrinol. Metab*. **83**, 3401–3408.

James WP, Ralph A & Sanchez-Castillo CP (1987): The dominance of salt in manufactured food in the sodium intake of affluent societies. *Lancet* **i**, 426–429.

Mokhtech I, Lemarchand T, Hohlfeld P & Portmann L (1995): Evidence of insufficient iodine intake during pregnancy and the post-partum period in the canton of Vaud. *Schweiz. Med. Wochenschr*. **125**(Suppl 69), 57.

Pino S, Fang SL & Braverman LE (1996): Ammonium persulfate: a safe alternative oxidizing reagent for measuring urinary iodine. *Clin. Chem*. **42**, 239–243.

Schällibaum M (1991): Seasonal and regional variation in iodine concentration in milk samples. *Schweiz. Verein Zuchthygiene* **103**, 5–12.

Thomson CD, Colls AJ, Conaglen JV, Macormack M, Stiles M & Mann J (1997): Iodine status of New Zealand residents as assessed by urinary iodine excretion and thyroid hormones. *Br. J. Nutr*. **78**, 901–912.

Torresani T & Scherz R (1986): Thyroid screening of neonates without use of radioactivity: evaluation of time-resolved fluoroimmunoassay of thyrotropin. *Clin. Chem*. **32**, 1013–1016.

Truong TH, Gerber H, Haenel AF & Bürgi H (1997): Iodine nutrition in various life stages and ultrasonographic thyroid volumes in school children in a region of Switzerland. *Schweiz. Med. Wochenschr*. **127**, 715–721.

Valeix P, Zarebska M, Preziosi P, Galan P, Pelletier B & Hercberg S (1999): Iodine deficiency in France. *Lancet* **353**, 1766–1767.

World Health Organization (1995): Physical status: the use and interpretation of anthropometry, 427–429, Geneva: WHO.

World Health Organization & International Council Control of Iodine Deficiency Disorders (1997): Recommended normative values for thyroid volume in children aged 6–15 y. *Bull. WHO* **75**, 95–97.

World Health Organization, United Nations Children's Fund & International Council for the Control of Iodine Deficiency Disorders (1994): Indicators for assessing iodine deficiency disorders and their control through salt iodinization. Geneva: WHO, [WHO/NUT/94.6].

World Health Organization, United Nations Children's Fund & International Council for the Control of Iodine Deficiency Disorders (1999): Progress towards the elimination of iodine deficiency disorders. Geneva: WHO, [WHO/NHD/99.4].

Zimmermann MB, Hess S, Zeder C & Hurrell RF (1998): Urinary odine concentrations in Swiss schoolchildren from the Zürich area and the Engadine valley. *Schweiz. Med. Wochenschr*. **129**, 770–774.