

An epidemiological survey of children's iodine nutrition and goitre status in regions with mildly excessive iodine in drinking water in Hebei Province, China

Shengmin Lv^{1,*}, Jun Zhao¹, Dong Xu¹, Zhengshui Chong¹, Lihui Jia¹, Yonggui Du¹, Jing Ma¹ and Shannon Rutherford²

¹Hebei Provincial Center for Disease Control and Prevention, No. 97, Huai'an East Road, Shijiazhuang 050021, People's Republic of China; ²Centre for Environment and Population Health, School of Environment, Griffith University, Brisbane, Australia

Submitted 30 August 2011: Accepted 6 January 2012: First published online 8 February 2012

Abstract

Objective: To identify children's iodine nutrition and goitre status in areas with mildly excessive iodine in drinking water.

Design: A cross-sectional survey. Probability proportional to size sampling was employed to randomly select children from thirty townships where the median iodine content in drinking water ranged from 150 to 300 µg/l; their urinary iodine concentrations were determined and their thyroid volumes were measured by ultrasound. Drinking water samples and salt samples from the villages where the children lived were collected using a systematic sampling method.

Setting: Hebei Province of China.

Subjects: A total of 1259 children aged 8–10 years (621 boys and 638 girls).

Results: Children's median urinary iodine concentration was found to be 418.8 µg/l, and the iodine concentration was >300 µg/l for 68.3% (248/363) of the urine samples. Children's median urinary iodine concentration in villages with median salt iodine >10 mg/kg was significantly higher than that in villages with median salt iodine <5 mg/kg (442.9 µg/l *v.* 305.4 µg/l, *P* ≈ 0). The goitre rate of 1259 children examined by ultrasound was 10.96%.

Conclusions: The iodine intake of children living in areas with mildly excessive iodine in drinking water in Hebei Province was found to be excessive. The measured iodine excess in the sampled children is exacerbated by consumption of iodized salt. Goitre was identified in these areas; however, due to the limitation of the current criteria for children's thyroid volume, a comprehensive assessment of the prevalence of goitre in these regions could not be made and further study is required.

Keywords
Iodine excess
Urinary iodine
Drinking water
Goitre
Survey

Iodine is an essential trace micronutrient for the human body. Both iodine deficiency and iodine excess can cause thyroid-related health problems. Iodine deficiency has been well studied around the world and is mostly under control in many countries. However, iodine excess and its impacts are still under study. Naturally excessive iodine intake results mainly from consumption of seafood containing a high content of iodine or iodine-rich drinking water. The former has been reported in coastal areas of Japan where seaweed is the staple food of local residents^(1,2). The latter is found in some parts of China where the underground drinking water contains a high concentration of iodine, usually >300 µg/l^(3,4). Hebei is one such province in China. According to a survey conducted in Hebei in 2003–2004, thirty-one counties of six prefectures and 173 townships were identified as having excessive iodine (i.e. iodine content >150 µg/l) in drinking water

based on the National Criteria for Classifying High Iodine Regions⁽⁵⁾. This excess iodine potentially affects nearly 6 million people and has become a prominent public health issue now that iodine-deficiency disorders are more successfully managed in Hebei Province⁽⁶⁾.

Excessive iodine intake can cause iodine overnutrition, goitre and other thyroid disease⁽⁷⁾. Endemic goitre induced by excessive dietary iodine has been reported in coastal areas of Japan where iodine intake from seaweed has been reported as >10 000 µg/d^(1,2). In China, a few studies have revealed that excessive iodine in drinking water, mainly from 300 µg/l to 1300 µg/l, can cause severe iodine overnutrition and high prevalence of endemic goitre in children aged 8–10 years^(3,4,8). However, the impact of mildly excessive iodine content in drinking water, in the range of 150–300 µg/l, on the iodine nutrition and goitre status in children aged 8–10 years remains unclear.

In the present study, a comprehensive survey of urinary iodine concentration and goitre status in children aged 8–10 years was conducted in thirty townships in Hebei Province of China which had median water iodine between 150 and 300 µg/l. The aim of the study was to clarify children's iodine nutrition and goitre status in these areas in order to identify possible harm caused by excessive iodine intake in this vulnerable age group.

Materials and methods

Sampling method and data collection

Sample selection (children aged 8–10 years)

Schoolchildren aged 8–10 years are commonly used subjects in surveys on iodine excess owing to their easy access and sensitivity to iodine intake⁽⁹⁾. A cluster sampling technique, probability proportional to size sampling, in which the probability that a particular sampling unit will be selected in the sample is proportional to the population size of the sampling unit⁽¹⁰⁾, was employed in the present cross-sectional survey.

With township as the sampling unit, first, thirty townships were selected from 111 townships with median water iodine content between 150 and 300 µg/l. One primary school was then randomly selected from each town chosen. Finally forty schoolchildren aged 8–10 years from each school were selected such that a total of 1200 children were selected. Thyroid volume measurement by B-mode ultrasound was conducted for all 1200 children at their schools. Also 360 children from thirty schools (twelve children from each school) were randomly selected for collection of urine samples for measuring urinary iodine concentration. Oral consent for examination of thyroid and urine sample collection was obtained from the headmasters of the investigated schools. The survey was conducted in September of 2009.

Drinking water sample collection

Drinking water samples were collected from households in the thirty villages where the investigated schoolchildren had lived since birth. The population of each of the thirty villages was between 600 and 2000; twenty-four out of the thirty villages had fewer than five wells, the other six villages had more than five wells. The water samples were collected using a systematic sampling method based on their location. The number of drinking water samples depended on the number of water sources. In a village with more than five wells, five households (one in each of the eastern, western, southern, northern and central parts of the village) covered by these wells were randomly chosen to collect water samples. In a village with fewer than five wells, one household for each well was selected. In a village with a centralized water supply (tap water), one household was randomly selected.

Household edible salt sample collection

Edible salt samples were collected at the villages where the investigated schoolchildren were born and lived. A systematic sampling method was used according to their location of east, west, north, south or centre. Two households were randomly selected in each location to collect edible salt to measure iodine content. A total of ten salt samples were collected in each village.

Measurement of thyroid volume by ultrasound

Thyroid volume was measured by using an Aloka SSD-500 echocamera (Aloka, Mure, Japan) equipped with 7.5-MHz linear transducers. The measurement was performed while the child lay on a bed with his/her neck fully exposed. For each thyroid lobe, the maximum perpendicular anteroposterior and mediolateral dimensions were measured on a transverse image of the largest diameter, without including the isthmus. The maximum craniocaudal diameter of each lobe was then measured on a longitudinal image. The thyroid capsule was not included. The ultrasound measurements were done by one experienced examiner who had specialized in thyroid measurement by ultrasound for 5 years.

Thyroid volume was calculated by using the equation of Brunn *et al.*⁽¹¹⁾, in which the volume of each lobe (ml) is equal to anteroposterior diameter (cm) × mediolateral diameter (cm) × craniocaudal diameter (cm) × 0.479, and the lobe volumes are summed.

In accordance with the Chinese national criteria for thyroid measurement, goitre was defined by age-specific thyroid volume. The upper limit of thyroid volume for children aged 8, 9 and 10 years was 4.5 ml, 5.0 ml and 6.0 ml, respectively. If the child's thyroid volume exceeded the relevant value, the child was judged as goitrous⁽¹²⁾.

Data analysis

Biological sample analysis

The iodine concentration of urine samples was measured by the method of ammonium persulfate oxidation in the provincial laboratory⁽¹³⁾. Urinary iodine concentration values from populations are usually not normally distributed. Therefore, the median rather than the mean should be used as the measure of central tendency. Median urinary iodine concentration of a population is a good biochemical indicator for its iodine nutrition. Median urinary iodine concentration of 300 µg/l and above defines a population as having iodine excess⁽¹⁴⁾.

Environmental sample analysis

The iodine content of salt was determined quantitatively by titration in the provincial laboratory. Iodine content was measured by liberating iodine from salt and titrating the iodine with sodium thiosulfate using starch as an external indicator⁽¹⁵⁾. According to the Chinese national standard for iodized salt, edible salt with less than 5 mg iodine/kg is classified as non-iodized salt.

The iodine content in drinking water was determined by the method of arsenic–cerium oxidation–reduction spectrophotometry in the provincial laboratory, in which iodine catalyses the oxidation–reduction between arsenious acid and ammonium cerous sulfate⁽¹⁶⁾. It is stipulated in the Chinese national standard for determination and classification of high water and the endemic areas of iodine excess goitre that drinking water containing more than 150 µg/l iodine/l is classified as excessive.

Data processing and statistical analysis

Data processing and statistical analyses were performed using the statistical software packages Epi-InfoTM 2002 (Centers for Disease Control and Prevention, Atlanta, GA, USA) and SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). Since the distributions of iodine in edible salt, drinking water and children's urine are not normal, the median was employed to describe their central tendency. Differences in children's median urinary iodine concentrations by age, sex and different groups classified on the basis of iodized salt were tested with the Mann–Whitney test.

Results

Iodine content in drinking water and edible salt

A total of eighty-five drinking water samples were collected from thirty villages and analysed for iodine content.

The iodine content ranged from 47.7 µg/l to 945.0 µg/l, with the median iodine content being 166.0 µg/l. Among the thirty villages, the median iodine content in drinking water was >150 µg/l in twenty villages and <150 µg/l in ten villages. Water iodine levels in the thirty villages sampled are listed in Table 1. The number of water samples with iodine content <150 µg/l, 150–300 µg/l and >300 µg/l was thirty-four, forty-seven and four, accounting for 40.0%, 55.3% and 4.7%, respectively.

The overall median iodine content of 301 edible salt samples collected at households in the thirty villages was 28.8 mg/kg. In twenty-three villages the median salt iodine was >10 mg/kg, and in seven villages it was <5 mg/kg. The details of salt iodine in the thirty villages are listed in Table 1.

Iodine concentration in urine samples of children aged 8–10 years

A total of 363 urine samples were collected from children aged 8–10 years and analysed for iodine, with the median urinary iodine concentration found to be 418.8 µg/l. Among the thirty villages investigated, the children's median urinary iodine concentration was >300 µg/l in twenty-three villages and <300 µg/l in seven villages.

Of the 363 urine samples, 184 were from boys and 179 from girls. The median urinary iodine concentration in boys and girls was 436.3 µg/l and 398.5 µg/l, respectively,

Table 1 The iodine content in edible salt and drinking water at thirty villages investigated in Hebei Province, China, September 2009

Village	No. of salt samples	Median salt iodine content (mg/kg)	No. of water samples	Median water iodine content (µg/l)
Dawangcun	10	34.3	5	47.7
Pushang	10	33.5	2	64.8
Zhangerzhuang	10	30.3	2	69.2
Dishiying	10	5.3	5	77.5
Wangdong	10	32.9	5	81.0
Deyi	10	31.7	2	88.6
Cuicun	10	38.0	3	99.9
Biexu	10	34.1	4	138.7
Shilipu	10	2.3	2	147.5
Wangqiao	10	13.8	2	148.0
Datun	10	33.2	2	152.9
Haocun	10	29.4	2	157.3
Fenghuadian	10	2.6	2	159.5
Zangtun	10	32.7	2	162.8
Zaoyuan	10	25.8	2	173.7
Wangjiapu	10	10.6	1	177.0
Chenxiaotun	10	30.1	5	183.3
Louguo	10	27.7	2	196.8
Dongbeiying	10	16.9	1	199.0
Kangzhuang	10	32.9	2	207.5
Xiliang	10	30.6	5	214.0
Wuhu	10	22.5	2	237.1
Changzhuang	10	3.2	5	243.0
Shenzhong	10	0	2	245.0
Luguan	10	3.2	1	246.0
Daying	10	28.1	3	246.2
Yangzhuantun	10	0	4	257.9
Gaozhuang	10	28.6	3	259.3
Xiyuangu	11	31.7	4	260.1
Xinzhuang	10	26.3	3	331.3

with no statistically significant difference identified (Mann–Whitney $U = 15406.0$, $P = 0.288$). The number of urine samples collected from children aged 8, 9 and 10 years was 121, 120 and 122, and their median iodine concentration was $364.3 \mu\text{g/l}$, $425.9 \mu\text{g/l}$ and $441.4 \mu\text{g/l}$, respectively, with no statistically significant difference among them (Mann–Whitney $H = 1.563$, $P = 0.458$).

The iodine concentration was $>300 \mu\text{g/l}$ in 248 out of 363 urine samples, accounting for 68.3% in total. In further classification based on age and sex, the percentage of urine samples with iodine concentration $>300 \mu\text{g/l}$ in each age and sex group varied from 64.2% to 72.1%. The median urinary iodine concentration and frequency distribution of urinary iodine concentration of children aged 8–10 years are included in Table 2.

Impact of iodized salt on children's urinary iodine concentration

Among the twenty villages with median iodine content in drinking water $>150 \mu\text{g/l}$, the median salt iodine in fifteen villages was $>10 \text{mg/kg}$. Five villages had salt supplies with median iodine content $<5 \text{mg/kg}$ or even 0mg/kg . The median water iodine content in the fifteen villages with high salt iodine and the five villages with low salt iodine was $214.0 \mu\text{g/l}$ and $245.7 \mu\text{g/l}$, respectively, and the difference was not significant ($U = 226.0$, $P = 0.34$). The median urinary iodine concentration of children aged 8–10 years in the fifteen villages with high salt iodine was $442.9 \mu\text{g/l}$, while it was $305.4 \mu\text{g/l}$ in the five villages with low salt iodine, and the difference between them was statistically significant ($U = 3810.5$, $P = 0$). Further

analysis based on age and sex showed that the median urinary iodine concentrations of children in different age or sex groups in the fifteen villages with high salt iodine were mostly higher than those in the five villages with low salt iodine. In the group of 9-year-olds, the children's median urinary iodine concentration in the fifteen villages with high salt iodine was significantly higher than that in the five villages with low salt iodine, i.e. $457.3 \mu\text{g/l}$ v. $264.3 \mu\text{g/l}$ ($U = 342.0$, $P = 0.004$). In the group of 10-year-olds, it was $497.8 \mu\text{g/l}$ v. $322.9 \mu\text{g/l}$ ($U = 4444.0$, $P = 0.015$). Comparing female and male children, it was $440.2 \mu\text{g/l}$ v. $249.6 \mu\text{g/l}$ ($U = 843.0$, $P = 0.0$). Further results of statistical analyses are provided in Table 3.

Goitre status of children aged 8–10 years

Among the 1259 children aged 8–10 years examined by ultrasound, 138 were found to have goitre, accounting for approximately 11% of the group. The goitrous cases detected in the 8, 9 and 10 year age groups numbered fifty-six, forty-eight and thirty-four, respectively, with the goitre rate being 13.1% (56/426), 11.6% (48/413) and 8.1% (34/420), respectively. No statistically significant difference was found among the goitre rates across the different age groups ($\chi^2 = 5.8$, $P = 0.06$). In terms of gender, seventy-seven and sixty-one goitrous cases were found in boys and girls, with the goitre rate being 12.4% (77/621) and 9.6% (61/638). The difference between them was not statistically significant ($\chi^2 = 2.08$, $P = 0.15$). The goitre details by age and sex are included in Table 4.

Table 2 Median urinary iodine concentrations and distributions for different age and sex groups of children aged 8–10 years, Hebei Province, China, September 2009

		Urinary iodine concentration						
			<100 µg/l		100–300 µg/l		>300 µg/l	
Group	Total no. of samples	Median (µg/l)	No. of samples	%	No. of samples	%	No. of samples	%
8-year-olds	121	364.3	5	4.2	34	28.0	82	67.8
9-year-olds	120	425.9	1	0.8	42	35.0	77	64.2
10-year-olds	122	441.4	0	–	34	27.9	88	72.1
Boys	184	436.3	5	2.7	52	28.3	127	69.0
Girls	179	398.5	1	0.6	58	32.4	120	67.0
Total	363	418.8	6	1.4	110	30.3	247	68.3

Table 3 Comparison of median urinary iodine concentrations in twenty villages with water iodine content $>150 \mu\text{g/l}$ according to the presence of iodized salt in the village and for different age and sex groups of children aged 8–10 years, Hebei Province, China, September 2009

Group	Villages with iodized salt		Villages without iodized salt		U	P
	No. of samples	Median ($\mu\text{g/l}$)	No. of samples	Median ($\mu\text{g/l}$)		
8-year-olds	62	396.0	19	341.6	466.0	0.17
9-year-olds	60	457.3	20	264.3	342.0	0.004
10-year-olds	59	497.8	23	322.9	4444.0	0.015
Boys	93	483.0	29	322.9	1063.0	0.086
Girls	88	440.2	33	249.6	843.0	≈ 0
Total	181	442.9	62	305.4	3810.5	≈ 0

Table 4 Comparison of goitre status according to iodine content in drinking water and for different age and sex groups of children aged 8–10 years, Hebei Province, China, September 2009

Group	Villages with WI < 150 µg/l			Villages with WI > 150 µg/l			Total		
	No. of children	Goitre cases	%	No. of children	Goitre cases	%	No. of children	Goitre cases	%
8-year-olds	137	17	12.4	289	39	13.5	426	56	13.1
9-year-olds	140	20	14.3	273	28	10.3	413	48	11.6
10-year-olds	139	8	5.8	281	26	9.3	420	34	8.1
Boys	220	25	11.4	401	52	13.0	621	77	12.4
Girls	196	20	10.2	442	41	9.3	638	61	9.6
Total	416	45	10.8	843	93	11.0	1259	138	11.0

WI, water iodine.

The goitre rate in the twenty villages with median iodine content in drinking water >150 µg/l was 11.0% (93/843), while it was 10.8% (45/416) in the ten villages with median iodine content in drinking water <150 µg/l. There was no significant difference between them ($\chi^2 = 0.01$, $P = 0.9$). The goitre comparisons between villages with different water iodine are included in Table 4. The twenty villages with water iodine >150 µg/l were further broken down into two subgroups based on the status of iodine content in salt. The goitre rate in the group with median salt iodine >10 mg/kg was 12.1% (71/587) compared with 8.6% (29/339) in the group with median salt iodine <5 mg/kg. However, the difference was not statistically significant ($\chi^2 = 2.8$, $P = 0.094$).

Discussion

Based on the results of the present survey, the median urinary iodine concentration of children aged 8–10 years in townships in Hebei Province with mildly excessive iodine (150–300 µg/l) in drinking water was 418.8 µg/l, and 68.3% (248/363) of children's urine samples had iodine concentration >300 µg/l. These results indicate that the iodine intake of local children is excessive. Similar findings were also reported by other researchers in other parts of China with mildly excessive iodine in drinking water. When median water iodine content varied from 90 to 300 µg/l, children's median urinary iodine concentration fluctuated from 300 to 800 µg/l^(8,17–19).

Children's median urinary iodine concentration found in the present survey was at the lower end of this range. There are two possible reasons for this. One is that the median water iodine in many of the villages investigated was quite low. The median water iodine content in seven villages, accounting for 23.3% of the total villages investigated, was <100 µg/l, ranging from 47.7 µg/l to 99.9 µg/l. The other reason is that the supply of iodized salt in some villages, especially those with higher water iodine content, was very poor. The median salt iodine content in six villages was <5 mg/kg, varying from 0 to 3.2 mg/kg, which could provide only <30 µg iodine to the local residents' daily intake, given their average daily salt consumption was estimated to be 10 g⁽²⁰⁾ and children's daily salt consumption was even less.

Among the twenty villages with median water iodine >150 µg/l, iodized salt is likely to have played some role in children's iodine excess. Children's urinary iodine concentration in the fifteen villages with median salt iodine >10 mg/kg was significantly higher than that in the five villages with median salt iodine <5 mg/kg, implying that iodized salt increased children's iodine excess.

According to the present survey, the goitre rate of children aged 8–10 years in areas with mildly excessive iodine in drinking water was approximately 11%. This rate is similar to 13.1% in Shanxi Province found by Jia *et al.*⁽²¹⁾ and 12.7% in Inner Mongolia found by Zhang *et al.*⁽²²⁾, but is much higher than 5% reported by Zhao *et al.* in Jiangsu Province⁽⁸⁾, where the median iodine content in drinking water was also in the range of 150–300 µg/l in those investigated areas. There is no doubt that excessive iodine in drinking water can cause goitre in the general population when it is >300 µg/l, and the goitre is more easily detected because of its remarkable enlargement^(23,24). However, when the median water iodine content is <300 µg/l, more study needs to be undertaken to determine whether it can cause epidemic goitre in sensitive populations, like young children aged 8–10 years, given the recognized limitations of the criteria on children's normative thyroid volume.

There is still some disagreement on the normative thyroid volume by ultrasound. WHO recommended a set of age-specific normative values for thyroid volume in 1997⁽²⁵⁾, which Zimmerman argued were too high. In 2004, Zimmerman *et al.* proposed much lower normative thyroid volume values based on samples in iodine-sufficient regions in six countries in Asia, Europe, Africa and America⁽²⁶⁾. However, they also admitted that population-specific references for thyroid volume in countries with long-standing iodine sufficiency may be more accurate than a single international reference. Moreover, normative thyroid volume also closely relates with children's age and body surface area, which is due to genetic differences in their growth and development⁽²⁶⁾.

The normal thyroid volume criteria employed in the present study were formulated in 1996 and were only age-specific. They may be too old and ignore differences in children's development between the present and over 10 years ago in China. Since children's bodies develop

earlier now than in the 1990s, they may have bigger thyroids than their peers in 1990s and in turn be judged incorrectly as goitrous. The goitre rate obtained in the present study could be amplified by these criteria. Consequently, it is difficult to measure the exact prevailing magnitude of children's goitre with the employed criteria. Therefore, the prevalence of goitre in areas with mildly excessive iodine in drinking water, i.e. 150–300 µg/l, needs to be further researched, in particular identifying more accurate criteria of normal thyroid volume in the future.

The impact of iodine content in the range of 150–300 µg/l in drinking water on the iodine nutrition and goitre status in children aged 8–10 years remains unclear. The present study aimed to clarify to what extent mildly excessive iodine in drinking water influences children's iodine nutrition and goitre status. It revealed that the iodine intake of children living in these areas in Hebei Province was excessive, which was exacerbated by consumption of iodized salt. Goitre was identified in these areas, with children's goitre rate being 10.96%. The study adds to Chinese research about dietary iodine exposure. In some parts of China, Chinese public health officials are facing dual challenges relating to both iodine deficiency and iodine excess. These challenges call for good health risk assessment approaches to identify hazardous iodine levels (either too low or too high) in different geographical settings with differing access to iodized salt and differing water iodine levels in order that prevention and control strategies for iodine deficiency or iodine excess can better be designed to meet the needs of each geographic area.

Acknowledgements

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector. The authors declare no conflict of interest. S.L. was responsible for the study design, data analysis, paper writing and field investigation. J.Z. was in charge of the laboratory detection of iodine. D.X. did the thyroid measurements by ultrasound. S.R. was responsible for the paper revision and English polishing. Z.C., L.J., Y.D. and J.M. took part in the field investigation.

References

1. Suzuki H, Higuchi T, Sawa K *et al.* (1965) 'Endemic coast goiter' in Hokkaido, Japan. *Acta Endocrinol* **50**, 161–176.
2. Katamine S, Mamiya Y, Sekimoto K *et al.* (1986) Iodine content of various meals currently consumed by urban Japanese. *J Nutr Sci Vitaminol* **32**, 487–495.
3. Li M, Liu D, Qu C *et al.* (1987) Endemic goiter in Central China caused by excessive iodine intake. *Lancet* **2**, 257–259.
4. Zhao I, Chen Z & Maberly G (1998) Iodine-rich drinking water of natural origin in China. *Lancet* **352**, 2024–2025.
5. Ma DR, Zhou RH, Jia LH *et al.* (2006) Survey on the distribution of the areas with excessive iodine in drinking water in Hebei plain. *Chin J Endem Dis* **21**, 237–238 (in Chinese).
6. Lv SM, Xie LJ, Zhou RH *et al.* (2009) Control of iodine deficiency disorders following 10-year universal salt iodization in Hebei province of China. *Biomed Environ Sci* **22**, 472–479.
7. Hans B (2010) Iodine excess. *Best Pract Res Clin Endocrinol Metab* **24**, 107–115.
8. Zhao JK, Wang PH, Shang L *et al.* (2000) Endemic goiter associated with high iodine intake. *Am J Public Health* **90**, 1633–1635.
9. Yv ZH, Zhu HM, Chen CY *et al.* (1999) Proceedings of the study on endemic goiter caused by iodine excess. *Chin J Endemiol* **18**, 301–304 (in Chinese).
10. World Health Organization/UNICEF/International Council for Control of Iodine Deficiency Disorders (2008) *Elimination of Iodine Deficiency Disorders: A Manual for Health Workers*. Cairo: WHO Regional Office for the Eastern Mediterranean.
11. Brunn J, Block U, Ruf G *et al.* (1981) Volumetric analysis of thyroid lobes by real-time ultrasound. *Dtsch Med Wochenschr* **106**, 1338–1340 (in German).
12. Ministry of Health (2007) *Diagnostic Criterion for Endemic Goiter*. Beijing: MOH (in Chinese).
13. Ministry of Health (2006) *Method for Determination of Iodine in Urine by As³⁺–Ce⁴⁺ Catalytic Spectrophotometry*. Beijing: MOH (in Chinese).
14. World Health Organization (1994) *Indicators for Assessing Iodine Deficiency Disorders and their Control through Salt Iodization*. Geneva: WHO/UNICEF/ICCIDD.
15. State Bureau of Quality and Technical Supervision (1999) *General Test Method in Salt Industry – Determination of Iodide Ion*. Beijing: SBQTS (in Chinese).
16. Ministry of Health (2006) *The Standard Test Method for Drinking Water*. Beijing: MOH.
17. Guo XW, Qin QL & Chen ZP (2007) Iodine nutrition status of population in the areas with different iodine concentrations of drinking water. *Acta Nutrimenta Sinica* **29**, 526–534 (in Chinese).
18. Zhang XD, Jia QZ, Wang ZH *et al.* (2007) Epidemiological survey of inland water-borne high iodine in drinking water in Shanxi Province. *Chin Trop Med* **17**, 679–681 (in Chinese).
19. Guo XW, Qin QL, Liu CJ *et al.* (2007) Study on iodine nutritional status of target population due to different iodine concentrations in drinking water after stopped iodized salt. *J Hyg Res* **36**, 427–431 (in Chinese).
20. Xu TC, Wang ZF, Hu P *et al.* (2009) Existing problems and their solutions of diet structure in China. *Food Nutr Chin* **4**, 57–59.
21. Jia QZ, Zhang XD, Wang ZH *et al.* (2006) An epidemiological study on the distributive characters and the harm of high water iodine in Shanxi Province. *Chin J Endemiol* **25**, 294–296 (in Chinese).
22. Zhang ZZ, Fan J, Guo HY *et al.* (2007) Distribution and goiter status of areas with high iodine in Inner Mongolia. *J Baotou Med Col* **23**, 466–468 (in Chinese).
23. Zimmermann MB, Ito Y, Hess SY *et al.* (2005) High thyroid volume in children with excess dietary iodine intakes. *Am J Clin Nutr* **81**, 840–844.
24. Yu ZH, Chen CY & Tan FZ (2001) Identification process and distribution profile of endemic goiter induced by high iodine in China. *Chin J Prev Med* **35**, 351–352 (in Chinese).
25. World Health Organization/International Council for Control of Iodine Deficiency Disorders (1997) Recommended normative values for thyroid volume in children aged 6–15 y. *Bull World Health Organ* **75**, 95–97.
26. Zimmermann MB, Hess SY, Molinari L *et al.* (2004) New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. *Am J Clin Nutr* **79**, 231–237.