Evaluation of the Prevalence of Iodine Intakes above the Tolerable Upper Intake Level from Four 3-Day Dietary Records in a Japanese Population

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Summary The Japanese population routinely consumes iodine-rich seaweed, thereby probably making Japan the nation with the highest iodine intake worldwide. The present study aimed to estimate the duration of dietary records (DRs) needed to calculate the usual iodine intake and to ascertain the frequency of iodine intakes above the tolerable upper intake level (UL) in the Dietary Reference Intakes for Japanese. Four 3-d DRs for the 4 seasons within a year were collected for 55 men and 58 women. On the basis of analysis of variance, the total variance in iodine intake was classified into inter-individual and intra-individual components. The frequency of appearance for high iodine intakes was estimated. The most commonly consumed types of iodine-containing food items were seaweed, milk and milk products, fish and shellfish, and *tofu*. The percentage contribution of intra-individual variance was markedly greater than that of inter-individual variance, and the excessive iodine intake was intermittent rather than continuous. The duration for which dietary records were required to assess the usual intake of iodine within 10% of their true mean was 6,276 d for men and 4,953 d for women. The period that transpired until a value was exceeded once was 6.3 d/occurrence for values above UL (2,200 μg), 8.5 d/occurrence for values above 3,000 μg , 9.8 d/occurrence for values above 4,000 μg , 11.2 d/occurrence for values above 5,000 μg , and 16.7 d/occurrence for values above 10,000 μg . To avoid errors in interpretation, it is inappropriate to assess the habitual nutrient intake of a nutrient that is intermittently consumed at maximal levels. It is important to assess the iodine intake in consideration of the range of the nutrient intake and of the time period in which the upper limit is exceeded.

Key Words Japanese, iodine intake, dietary records, the tolerable upper intake level, Dietary Reference Intakes for Japanese

Iodine deficiency is considered to be one of the most common nutritional disorders worldwide (1) and the most common cause of goiter. However, the Japanese population routinely consumes iodine-rich seaweed products; this might result in disorders related to excess intake of iodine through the consumption of meals and between-meal snacks prepared using seaweed. It has been reported that iodine intakes by the Japanese are typically in the range of 1,000–3,000 $\mu\text{g}/\text{d}$ (2–5). However, these studies were reported for a given day and not as a mean of several days.

Moreover, high iodine intakes can cause disturbances in thyroid function (6, 7). Because of the assumption that most Japanese individuals have experienced iodine escape (8, 9), the tolerable upper intake levels (UL) of the Dietary Reference Intakes for Japanese (DRIs-J 2010) of 2,200 $\mu\text{g}/\text{d}$ is relatively high compared with that of other countries (500–1,100 $\mu\text{g}/\text{d}$), as presented

in Appendix 1 (10–16).

Iodine status has traditionally been assessed using urinary iodide excretion or goiter rate, which is calculated on the basis of thyroid gland size (17). Although measurement of urinary iodine excretion is usually sufficient when conducting population-based studies, such data are scarce. Estimating the distribution of the normal dietary intake in the population using dietary record(s) (DRs) and 24-h dietary recall is generally used in surveys (18).

The aims of this study were to provide an estimate of the number of days needed to accurately calculate the usual iodine intake and to ascertain the frequency of iodine intakes above UL provided in DRIs-J 2010.

MATERIALS AND METHODS

Study design and subjects. The data set for this study was obtained from data originally collected to assess the validity and reproducibility of a food frequency questionnaire used in 3 large-scale cohort studies on cancer

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(19). The subjects of the present study were the residents of two rural towns in Miyagi Prefecture in the northern part of Japan. A total of 59 male and 60 female participants (mean age 62.5 and 61.2 y, respectively) were selected on a voluntary basis. In the present study, only those participants who provided information for intake data for all 12 d of data collection were included. Thus, data from 113 participants (55 men and 58 women) were analyzed.

DRs. Standardized methodology was used to calculate energy and nutrient intakes. DRs were collected using 3-d DRs as a reference method during each of the 4 seasons over a period of 1 y: in the month of November (autumn) 1996 and in February (winter), May (spring), and August (summer) 1997 (20, 21).

The participants were instructed to record all food items and beverages consumed in a standardized booklet. They were asked to provide detailed descriptions of each food item (open ended), including the weights prepared and proportions consumed. Research dietitians assessed the records in a standardized manner after completion by the participants. Iodine intake was calculated from these records using the Japanese Standard Food Composition Table 2010 (22) published by the Ministry of Education, Culture, Sports, Science and Technology. To avoid arbitrariness, we presented the results based on items from the Food Composition Table 2010. The iodine intake values were reported only for 34.1% (642/1,878 items) of the total food items in the Food Composition Table 2010. Moreover, we did not complement the missing values by using other resources to avoid introducing variability in the measurement method used in this study.

Data analyses. All the analyses were performed using SAS software (version 9.3 SAS Institute Inc., Cary, NC, USA).

(1) Estimation of the duration needed to record accurate iodine intake: The total iodine intake was classified on the basis of analysis of variance into the following 2 classes: (1) inter-individual variance in the subjects' usual intake and (2) residual variance, which represents the intra-individual variability in daily intake.

Estimates of within-person (σ_w^2) and between-person variances (σ_b^2) were calculated by setting mean squares (MS) equal to their expected values. The values for (σ_w^2) and σ_b^2 were estimated from the following equations:

$$\begin{aligned} MS_w &= \sigma_w^2 \\ \sigma_b^2 &= (MS_b - \sigma_w^2)/c \\ c &= (N - \sum_{i=1}^a n_i^2/N)/(a-1) \end{aligned}$$

Here "a" is the number of subjects, n_i is the number of days for which DRs provided by the i -th subject were available, and $N = \sum_{i=1}^a n_i^2$ is the total number of days for which DRs were available from all the subjects. All the calculations were performed using the SAS variance component procedure in the PROC VARCOMP application. This was used to calculate the ratios of within-person and between-person variance (σ_w^2/σ_b^2).

In addition, the number of days required to estimate an individual's true iodine intake with 95% confidence intervals within 10% and 20% of their true mean was

Table 1. The top 30 items which contribute to the high iodine intake in the present subjects.

Top	Food item number ¹	Food and description	$\mu\text{g/d} \cdot \text{person}$
1	9017	Ma-konbu dried	1,102.7
2	9020	Kizami-konbu	559.9
3	9015	Naga-konbu dried	302.8
4	9031	Hijiki boiled and dried	159.3
5	9023	Konbu Tsukudani	93
6	9045	Wakame blanched and desalted	50
7	13003	Ordinary liquid milk	17
8	10205	Pacific cod raw	10.6
9	2004	Konjac block	8
10	9004	Purple laver toasted	7.8
11	9039	Wakame dried	7.8
12	9026	Tengusa Tokoroten	3.6
13	13026	Yogurt skimmed and sweetened	2
14	10087	Skipjack caught in autumn, raw	2
15	10292	Oysters cultured and raw	1.9
16	10202	Tarako: walleye pollack, raw	1.4
17	4032	Tofu: momen-tofu	1.2
18	10253	Bluefin tuna lean meat and raw	1.1
19	10070	Japanese eel Kabayaki	1.1
20	6134	Daikon root without skin and raw	1
21	10173	Pacific saury, raw	0.9
22	18001	Curry beef and retort-pouched dishes	0.8
23	16006	Beer pale	0.8
24	9047	Wakame fruit-bearing leaves and raw	0.8
25	10100	Brown sole, raw	0.7
26	10281	Short-necked clams, raw	0.7
27	10174	Pacific saury baked	0.6
28	15060	Rice crackers Shio-senbei	0.6
29	13025	Yogurt whole milk and unsweetened	0.5
30	9002	Green laver dried	0.5

¹ Item numbers were addressed under the Food Composition Table 2010.

calculated, using the following formula (23):

$$n = (Z_\alpha CV_w / D_0)^2$$

Here n = the number of days required per person, $Z_\alpha = 1.96$, CV_w = the within-person coefficient of variation (%), and D_0 = the specific degree of error expressing a percentage of long-term true iodine intake (10% or 20%). All the analyses were performed separately for male and female subjects.

(2) Estimation of the frequency of appearance above UL: The frequency of occurrence of high iodine intake was estimated for the following 5 different values: (a) above UL, i.e., 2,200 $\mu\text{g/d}$ provided in the current DRIs-J 2010; (b) above 3,000 $\mu\text{g/d}$; (c) above 4,000 $\mu\text{g/d}$; (d) above 5,000 $\mu\text{g/d}$; and (e) above 10,000 $\mu\text{g/d}$, from the data of all 12 assessment days throughout a 1-y period. Among the 1,356 person-days of the subjects, the frequencies at which the each intake exceeded five different values were tabulated and converted to the occurrence period. For example, there were 216 occurrences of iodine level above 2,200 $\mu\text{g/d}$ which is equivalent to $1,356/216 = 6.3$ d per occurrence. Given the considerable difference between intra-individual and inter-individual variance for iodine, the frequency of peak

Table 2-1. Ratios of intra- and inter-individual variance and the number of repeated dietary records per individual needed to assure that the efficiency of estimation of the true iodine intake is within 10% and 20% of the true mean in men.

	Mean intake	Percentage contribution of variance components		Intra-/Inter-individual	Coefficient of variation		10% ¹ (d)	20% ² (d)
		Intra-individual	Inter-individual		Intra- (%)	Inter- (%)		
Energy (kcal)	2,545	48.1	51.9	0.9	17.5	18.2	12	3
Protein (g)	94	68.1	31.9	2.1	22.6	15.5	20	5
Fat (g)	56	76.8	23.2	3.3	317.8	20.8	55	14
Carbohydrates (g)	362	45.3	54.7	0.8	18	19.8	12	3
Vitamin								
Vitamin A ($\mu\text{g RE}$)*	361	98.3	1.7	56.9	254.7	33.8	2,491	623
Vitamin D (μg)	13.9	89.4	10.6	8.4	82.9	28.5	264	66
Vitamin E (mg)	8.1	77.8	22.2	3.5	36.6	19.6	52	13
Vitamin K (μg)	337	74.2	25.8	2.9	54.4	32	114	28
Vitamin B ₁ (mg)	1	85.4	14.6	5.9	39.6	16.4	60	15
Vitamin B ₂ (mg)	1.6	75.4	24.6	3.1	31.3	17.9	38	9
Niacin (mg)	21	76.3	23.7	3.2	41.2	23	65	16
Vitamin B ₆ (mg)	2	71.5	28.5	2.5	31.2	19.7	37	9
Vitamin B ₁₂ (μg)	13	88	12	7.3	79.6	29.4	244	61
Folate (μg)	424	73	27	2.7	32.7	19.9	41	10
Pantothenic acid (mg)	8	60.3	39.7	1.5	23.2	18.8	21	5
Biotin (μg)	37	84.6	15.4	5.5	44.6	19	76	19
Vitamin C (mg)	120	78.3	21.7	3.6	49	25.8	92	23
Mineral								
Sodium (mg)	5,648	73.7	26.3	2.8	28	16.7	30	8
Potassium (mg)	3,218	69.5	30.5	2.3	26.5	17.5	27	7
Calcium (mg)	679	63.7	36.3	1.8	35.5	26.8	48	12
Magnesium (mg)	369	71	29	2.4	25.7	16.4	25	6
Phosphorus (mg)	1,392	65	35	1.9	22.5	16.5	19	5
Iron (mg)	11.2	75.7	24.3	3.1	28.6	16.2	31	8
Zinc (mg)	11	70.9	29.1	2.4	26.7	17.1	27	7
Copper (mg)	1.8	82.2	17.8	4.6	37.2	17.3	53	13
Manganese (mg)	5.2	53.7	46.3	1.2	24.2	22.5	22	6
Iodine (μg)	2,550	98.6	1.4	70.2	404.2	48.2	6,276	1,569
Selenium (μg)	74	89	11	8.1	69.5	24.4	185	46
Chromium (μg)	7	85.5	14.5	5.9	50	20.6	96	24
Molybdenum (μg)	289	54.1	45.9	1.2	28.7	26.4	32	8

* Vitamin A ($\mu\text{g RE}$) = retinol (μg) + β -carotene (μg) $\times$ 1/12 + α -carotene (μg) $\times$ 1/24 + β -cryptoxanthin (μg) $\times$ 1/24 + other provitamin A carotenoids (μg) $\times$ 1/24.

¹ The number of the days of collecting food record which would be required to estimate the true intake within 10% of their true mean with 95% confidence.

² The number of the days of collecting food record which would be required to estimate the true intake within 20% of their true mean with 95% confidence.

iodine intake among the subjects was estimated as the frequency of peak iodine intake by individuals. The data for both genders were combined for this analysis.

RESULTS

In this study, 113 participants (55 men and 58 women) provided information regarding intake data for all 12 d of data collection; only these data were analyzed in the study.

The male subjects were aged 45–77 y [mean $\pm$ standard deviation (SD): 62 $\pm$ 9 y] and the female subjects were aged 47–76 y (mean $\pm$ SD: 61 $\pm$ 9 y). By occupation, most participants were farmers, self-employed, or housewives. The percentage of current smokers in

men was 49.1% (27 subjects); no current smokers were present among the women. The mean/median iodine intake data for 3 consecutive days in each season were 2,659/140 $\mu\text{g/d}$ in spring, 1,616/107 $\mu\text{g/d}$ in summer, 2,125/116 $\mu\text{g/d}$ in autumn, and 2,999/163 $\mu\text{g/d}$ in winter.

Dietary sources and intake

Table 1 presents the top 30 food sources that contributed to high iodine intake in the study subjects. In this study, the most commonly consumed iodine-containing food was seaweed (*konbu*, *hijiki*, *wakame*, and *nori*), followed by milk and milk products, fish and shellfish (codfish, bonito, tuna, giant pacific oyster, and eel) and *tofu*. However, the iodine content of other food items was

Table 2-2. Ratios of intra- and inter-individual variance and the number of repeated dietary records per individual needed to assure that the efficiency of estimation of the true iodine intake is within 10% and 20% of the true mean in women.

	Mean intake	Percentage contribution of variance components		Intra-/Inter-individual	Coefficient of variation		10% ¹ (d)	20% ² (d)
		Intra-individual	Inter-individual		Intra- (%)	Inter- (%)		
Energy (kcal)	1,977	66.3	33.7	2	17.3	12.4	12	3
Protein (g)	80	72.5	27.5	2.6	23.4	14.4	21	5
Fat (g)	53	79.8	20.2	3.9	33.9	17.1	44	11
Carbohydrates (g)	290	59.3	40.7	1.5	17.4	14.4	12	3
Vitamin								
Vitamin A ($\mu\text{g RE}$)*	304	100	0	∞	307.5	0	3,633	908
Vitamin D (μg)	11	91.8	8.2	11.1	80.6	24.1	249	62
Vitamin E (mg)	8.3	75.5	24.5	3.1	33.8	19.3	44	11
Vitamin K (μg)	315	81.2	18.8	4.3	52.3	25.2	105	26
Vitamin B ₁ (mg)	0.9	82.3	17.7	4.6	31.7	14.7	39	10
Vitamin B ₂ (mg)	1.6	71.6	28.4	2.5	28	17.6	30	8
Niacin (mg)	18	78.2	21.8	3.6	40.8	21.6	64	16
Vitamin B ₆ (mg)	1	76.3	23.7	3.2	29.7	16.5	34	8
Vitamin B ₁₂ (μg)	11	89	11	8.1	87	30.6	291	73
Folate (μg)	435	67.8	32.2	2.1	31.9	22	39	10
Pantothenic acid (mg)	7	68.1	31.9	2.1	23.3	15.9	21	5
Biotin (μg)	33	87.9	12.1	7.2	44.8	16.7	77	19
Vitamin C (mg)	141	71.8	28.2	2.6	42	26.3	68	17
Mineral								
Sodium (mg)	5,079	73.6	26.4	2.8	28.2	16.9	31	8
Potassium (mg)	3,131	67.8	32.2	2.1	24.2	16.7	23	6
Calcium (mg)	665	66.9	33.1	2	32.7	23	41	10
Magnesium (mg)	328	71.6	28.4	2.5	25	15.7	24	6
Phosphorus (mg)	1,215	70.9	29.1	2.4	22.8	14.6	20	5
Iron (mg)	10.6	71.2	28.8	2.5	28.7	18.2	32	8
Zinc (mg)	9	78.8	21.2	3.7	29.2	15.1	33	8
Copper (mg)	1.5	75.6	24.4	3.1	25.3	14.3	25	6
Manganese (mg)	4.8	63.1	36.9	1.7	26.6	20.3	27	7
Iodine (μg)	2,160	96.7	3.3	29.8	359.1	65.8	4,953	1,238
Selenium (μg)	63	87.1	12.9	6.7	69.1	26.6	183	46
Chromium (μg)	7	88.5	11.5	7.7	47.4	17.1	86	22
Molybdenum (μg)	215	77.4	22.6	3.4	31.5	17	38	10

* Vitamin A ($\mu\text{g RE}$) = retinol (μg) + β -carotene (μg) $\times$ 1/12 + α -carotene (μg) $\times$ 1/24 + β -cryptoxanthin (μg) $\times$ 1/24 + other provitamin A carotenoids (μg) $\times$ 1/24.

¹ The number of the days of collecting food record which would be required to estimate the true intake within 10% of their true mean with 95% confidence.

² The number of the days of collecting food record which would be required to estimate the true intake within 20% of their true mean with 95% confidence.

low. None of the subjects reported an iodine intake of 0 $\mu\text{g/d}$, whereas higher iodine intakes occurred at intervals depending on which food items the subject had consumed on a particular day. For example, the three subjects who presented the highest iodine intake, exceeding 120,000 $\mu\text{g/d}$ over all the observation days, consumed *konbu* on the third assessment day in autumn, whereas on other days, they did not consume high iodine-containing food items (data not shown).

Time period required to assess usual iodine intake

Table 2-1 (males) and Table 2-2 (females) present the ratio of intra-individual and inter-individual coefficients of variation and the number of days with the available DR data required to assess the usual intake, with

an error margin within the specified limits (10% and 20%). The percentage contribution of intra-individual variance was markedly larger compared with that of inter-individual variance. Therefore, the ratio of intra-individual and inter-individual coefficients of variation was large. Compared with other nutrients, the time period for which DRs were required to assess the usual intake of iodine within 10% of their true mean was extensive (within 10%: 6,276 d for males and 4,953 d for females).

Estimation of the frequency at which UL is exceeded

The frequency at which the selected values were exceeded decreased as the value increased. The period that transpired until a value was exceeded once was

6.3 d/occurrence for values above UL, 8.5 d/occurrence for values above 3,000 μg , 9.8 d/occurrence for values above 4,000 μg , 11.2 d/occurrence for values above 5,000 μg , and 16.7 d/occurrence for values above 10,000 μg .

DISCUSSION

The current study indicates that the number of days for which DRs are required to assess the mean iodine intake is not feasible in standard study time frames. The percentage contribution of intra-individual variance was markedly greater than that of inter-individual variance, and excessive iodine intake was intermittent rather than continuous. The UL (2,200 μg) was exceeded approximately once a week in this study group. *Are there Japanese individuals who consume iodine in excess of the UL?*

DRIs-J states that the UL presents the highest level of habitual iodine intake that is considered to pose no risk of adverse health effects to virtually any healthy individuals. As long as the daily intake is obtained from food items and beverages, rather than from supplements, this intake value is unlikely to be exceeded (15, 24). However, long-term intakes above the UL increase the risk of health problems.

In the present study, we observed that Japanese individuals habitually but intermittently consumed high quantities of iodine from food, and iodine intake among the subjects was estimated to exceed the UL once a week. The frequency at which the UL was exceeded decreased in association with an increase in the value; however, even individuals with iodine intake of more than 10,000 mg once every 2 wk were reported.

It is important to note that during nutritional surveys or other activities aimed at diet improvement or food services management, the nutrient intake values are usually computed from the raw weight of food items before cooking and processing and not from the actual quantity consumed. Furthermore, most food items with high iodine levels are usually used for preparing soup stock and are not consumed directly in their raw forms (25, 26) such as *konbu*, which has the highest levels of iodine. Because it is usually used for preparing soup stock or is consumed as a *tsukudani* (*konbu* boiled in soy sauce), most of the iodine strains out from the soup and little iodine is actually consumed from this source. Consequently, true iodine intake in traditional Japanese dishes is estimated to be approximately 10–50% of the usual iodine intake calculated by DRs (25, 26).

In recent years, there has been a growing concern regarding disorders caused by excessive iodine intake through the consumption of between-meal snacks prepared using seaweed, particularly those prepared using *konbu*, which are popular in Japan (27). Thus, the excessive iodine intake from between-meal snacks, in parallel with high iodine intake from normal meals in the Japanese culture, needs to be carefully monitored. As long as the iodine intake is primarily obtained from food items and beverages, the proportion of individuals with an iodine intake above the UL is likely to be less than that

presumed at the present time. However, the possibility that there are individuals with iodine intake above these levels cannot be denied.

Special care needed for assessment and interpretation of iodine intake

In general, the fewer the number of observation days, the broader the intake distribution. We observed that DRs for an extended period of time were required to characterize the long term mean iodine intake in this population. Accordingly, estimation of deficient or excessive iodine intake from short term DRs leads to overestimation or underestimation, which thereby leads to increased risk of misperceptions. However, considering the burden placed on the participants, obtaining data over a longer period of time is not feasible in epidemiological settings or nutrition surveys. The present study results suggest that excessive consumption of iodine is dependent on particular food items and that high iodine intake is intermittent rather than continuous. For this reason, it is inappropriate to assess the habitual nutrient intake of a particular nutrient that is consumed at high levels only intermittently. For estimating or interpreting the intermittent intake of nutrients such as iodine in epidemiological settings or nutrition surveys, including NHNS-J, it is necessary to determine not only the mean or median intake but also the range of the nutrient intake, and the time period until the value (i.e., UL provided by DRIs-J) is exceeded. In addition, careful consideration should be given to the food items that are consumed and the frequency at which they are consumed. Further investigation and evidence with detailed long term data regarding foods, doses, and patterns of iodine intakes for a large number of participants are required to confirm the value of iodine intake for DRIs-J.

Study limitations

Several limitations of this study need to be discussed. First, as mentioned earlier, iodine intake was calculated from the data using the Japanese Standard Food Composition Table published in 2010 (22), but iodine values were reported for only 34.1% of the total food items in these tables. It is possible that the iodine intake values reported here could be underestimations of the true values. However, considering that DRs are the main source for the assessment of dietary intake, it is presumed that the present findings are useful to illustrate the difficulties involved in such a study.

Second, we also need to consider the possibility of a selection bias when generalizing the present findings because of the small sample size ($n=113$). Because marked differences exist in terms of food culture and dietary habits among different areas of Japan, it has been reported that the average intake of seaweeds differs greatly according to age, family structure, and region (3); thus, further research with a larger sample size from different regions and age groups is needed to confirm the generalizability of our findings in Japan.

Finally, the present study estimated information of the food and nutrient intake on the basis of dietary recall for elderly subjects in 1996–1997. It is possible that the dietary intakes measured did not accurately reflect the

current situation. Iodine status has traditionally been assessed using the urinary iodide excretion or the goiter rate. Further studies using such measurements over a longer duration are required to assess the frequency of individuals at risk for above UL iodine intake.

In conclusion, the present results indicate that the amount of time for which DRs are required to assess the usual iodine intake would be a year, which was not feasible in this survey and the frequency of iodine intake above UL was approximately once per week. To avoid misperceptions in assessing or interpreting the intermittent intake of nutrients such as iodine, it is necessary to display not only the mean or median iodine intake but also the range of the nutrient intake and the time period in which the upper limit is exceeded.

REFERENCES

- 1) WHO. 2007. Assessment of iodine deficiency disorders and monitoring their elimination: A guide for programme managers, p 20. World Health Organization, UNICEF, ICCIDD.
- 2) Zava TT, Zava DT. 2011. Assessment of Japanese iodine intake based on seaweed consumption in Japan: A literature-based analysis. *Thyroid Res* **4**: 14.
- 3) Nagataki S. 2008. The average of dietary iodine intake due to the ingestion of seaweeds is 1.2 mg/day in Japan. *Thyroid* **18**: 667–668.
- 4) Fuse Y, Saito N, Tsuchiya T, Shishiba Y, Irie M. 2007. Smaller thyroid gland volume with high urinary iodine excretion in Japanese schoolchildren: normative reference values in an iodine-sufficient area and comparison with the WHO/ICCIDD reference. *Thyroid* **17**: 145–155.
- 5) Zimmermann MB, Hess SY, Molinari L, De Benoist B, Delange F, Braverman LE, Fujieda K, Ito Y, Jooste PL, Moosa K, Pearce EN, Pretell EA, Shishiba Y. 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.
- 6) Wolff J. 1969. Iodide goiter and the pharmacologic effects of excess iodide. *Am J Med* **47**: 101–124.
- 7) Skare S, Frey HM. 1980. Iodine induced thyrotoxicosis in apparently normal thyroid glands. *Acta Endocrinol (Copenh)* **94**: 332–336.
- 8) Wolff J, Chaikoff IL. 1948. Plasma inorganic iodide as a homeostatic regulator of thyroid function. *J Biol Chem* **174**: 555–564.
- 9) Sherwin JR. 1982. Development of regulatory mechanisms in the thyroid: failure of iodide to suppress iodide transport activity. *Proc Soc Exp Biol Med* **169**: 458–462.
- 10) Food and Nutrition Board, Institute of Medicine. 2001. 8 Iodine, Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academy Press, Washington DC.
- 11) DGE, ÖGE, SGE/SVE. 2008. Referenzwerte für die Nährstoffzufuhr. Frankfurt.
- 12) Department of Health. 1991. 41 Dietary Reference Values for Food Energy and Nutrients for the United Kingdom: Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy. Report on Health and Social Subjects 41. The Stationery Office (TSO), London.
- 13) Martin A. 2000. Apports nutritionnels conseillés pour la population française 3 édition. Tec et Doc Lavoisier, Paris.
- 14) Nordic Council of Ministers. 2001. Nordic Nutrition Recommendations. Køb Publikation, Copenhagen.
- 15) Ministry of Health Law, Japan. 2009. Dietary Reference Intakes for Japanese 2010. Ministry of Health, Labour and Welfare, Japan, Tokyo (in Japanese).
- 16) Yoshida M, Kikunaga S, Yamauchi J, Tsubota-Utsugi M, Kodama H, Morita A, Esashi T. 2013. Dietary Reference Intakes for Japanese 2010: Microminerals. *J Nutr Sci Vitaminol* **59** (Suppl): S91–S102.
- 17) Nath SK, Moinier B, Thuillier F, Rongier M, Desjeux JF. 1992. Urinary excretion of iodide and fluoride from supplemented food grade salt. *Int J Vitam Nutr Res* **62**: 66–72.
- 18) Ministry of Health, Labour and Welfare, Japan. The National Health and Nutrition Survey of Japan. Ministry of Health, Labour and Welfare, Japan, Tokyo. [Online] Available: http://www.mhlw.go.jp/bunya/kenkou/kenkou_eiyou_chousa.html [accessed September 10, 2012]
- 19) Tsuji I, Nishino Y, Ohkubo T, Kuwahara A, Ogawa K, Watanabe Y, Tsubono Y, Bando T, Kanemura S, Izumi Y, Sasaki A, Fukao A, Nishikori M, Hisamichi S. 1998. A prospective cohort study on National Health Insurance beneficiaries in Ohsaki, Miyagi Prefecture, Japan: study design, profiles of the subjects and medical cost during the first year. *J Epidemiol* **8**: 258–263.
- 20) Ogawa K, Tsubono Y, Nishino Y, Watanabe Y, Ohkubo T, Watanabe T, Nakatsuka H, Takahashi N, Kawamura M, Tsuji I, Hisamichi S. 2003. Validation of a food-frequency questionnaire for cohort studies in rural Japan. *Public Health Nutr* **6**: 147–157.
- 21) Tsubono Y, Ogawa K, Watanabe Y, Nishino Y, Tsuji I, Watanabe T, Nakatsuka H, Takahashi N, Kawamura M, Hisamichi S. 2001. Food frequency questionnaire and a screening test. *Nutr Cancer* **39**: 78–84.
- 22) Ministry of Education, Culture, Sports, Science and Technology. 2010. Standard Tables of Food Composition in Japan 2010. Tokyo (in Japanese).
- 23) Beaton GH, Milner J, Corey P, McGuire V, Cousins M, Stewart E, de Ramos M, Hewitt D, Grambsch PV, Kassim N, Little JA. 1979. Sources of variance in 24-hour dietary recall data: implications for nutrition study design and interpretation. *Am J Clin Nutr* **32**: 2546–2559.
- 24) Sasaki S. 2013. Dietary Reference Intakes for Japanese 2010: Basic Theories for the Development. *J Nutr Sci Vitaminol* **59** (Suppl): S9–S17.
- 25) Katsura E, Nakadou R. 1960. The amount of iodine in a Japanese meal. *Eiyo to Shokuryo (J Jpn Soc Food Nutr)* **12**: 342–344 (in Japanese).
- 26) Yoshida M. 2013. Excess intake of microminerals: Is the iodine intake of Japanese people excessive. *FFI J (Foods and Food Ingredients Journal of Japan)* **218**: 12–19 (in Japanese).
- 27) Matsubayashi S, Mukuta T, Watanabe H, Fuchigami H, Taniguchi J, Chinen M, Ninomiya H, Sasaki H. 1998. Iodine-induced hypothyroidism as a result of excessive intake of confectionery made with tangle weed, Kombu, used as a low calorie food during a bulimic period in a patient with anorexia nervosa. *Eat Weight Disord* **3**: 50–52.

Appendix 1. Iodine reference values ($\mu\text{g}/\text{d}$) for the elderly in selected countries.

	Age group (y)	Mean – 2SD	Mean	Mean + 2SD	UL
Corresponding to DRIs-J			EAR	RDA	
Japan (15)	18+	NS	95	130	2,200
United States of America and Canada (10)	51–70	NS	95	150	1,100
Germany and Austria (11)	51+	NS	NS	180	500
United Kingdom (12)	50+	70	NS	140	NS
France (13)	55+	NS	NS	150	NS
The Nordic countries (14)	18+	70	100	150	NS (600)

SD, standard deviation; DRIs-J, Dietary Reference Intakes for Japanese; EAR, estimated average requirement; RDA, recommended dietary allowance; UL, tolerable upper intake level; NS, not stated.