

Japan's iodine status – too high or just right?

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Unlike in most other countries, where dietary iodine comes from bread, dairy products, fish, and iodized salt, in Japan the primary source of iodine is seaweed. Nori (*Porphyra*), Wakame (*Undaria*) and Kombu (*Laminaria*) are the most popular seaweed products in the country. The highest iodine content (approximately 2,400 µg/g) is found in Kombu, edible kelp, which is consumed widely throughout East Asia. Kombu extract is often an ingredient of pre-packaged processed foods; however, the iodine it provides is often not listed on the label.

Japan is a country of long-standing iodine sufficiency, and the issue of iodine nutrition has not been on the forefront of the public health agenda. Prior to 1999 iodine was not even included in the government's dietary reference intake tables (1), and it took until 2010 for iodine content in foods to be reported in the standard composition tables (2). Because there is no national surveillance system to monitor iodine intakes, recent data on the population's iodine status is lacking.

'Endemic coast goiter' and iodine nutrition

The misconception that most Japanese consume too much iodine may have its roots in several early studies in the coastal area of Hokkaido. In 1933, Jesse F McClendon of the University of Minnesota reported that Japan was the only non-goitrous country in the world, with one case of goiter per million people (3). The northern island of Hokkaido was an apparent exception, where cases of endemic goiter could be traced back to 1899 (4). But when later surveys, conducted between 1948 and 1952, reported goiter throughout Japan (with goiter rates in children ranging from 0.9% to 20.6% across 11 of 46 prefectures), they went largely unnoticed by the international scientific community.

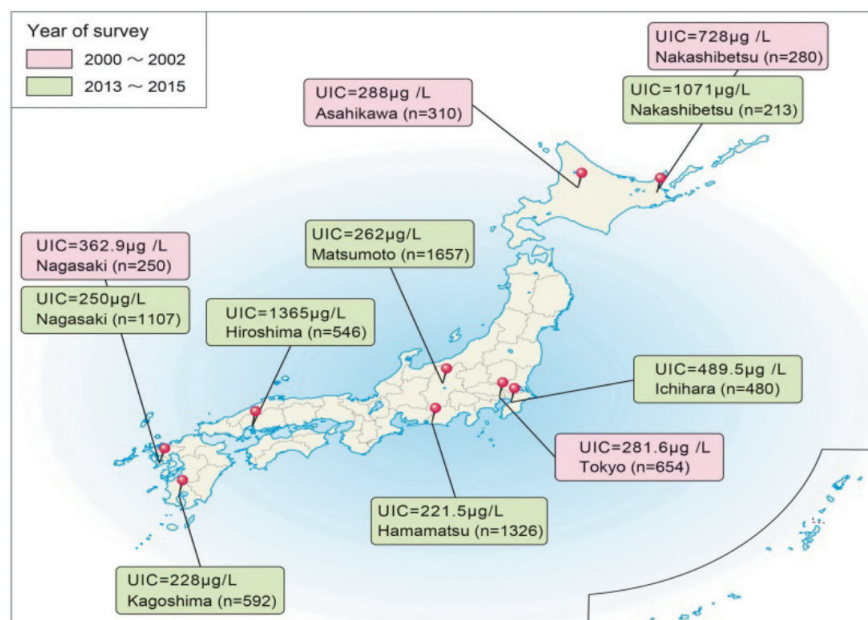


Kombu (edible kelp) is consumed widely throughout South-East Asia and provides almost 2.5 mg of iodine per gram.

The first large epidemiological study in Japan was conducted in 1960–1964 in three goitrous regions on the coast of Hokkaido (Hidaka District, and Rebun and Rishiri Islands), and it was published in English (5). A total of 8,074 children aged 6–17 were enrolled, and 3,400 children in Sapporo city were recruited as control. The prevalence of obvious goiter was 6.6% in Hidaka, 9.0% in Rebun, and 2.6% in Rishiri, all of which were significantly higher than in the Sapporo children (1.3%). The highest prevalence (24.2%) was observed in a seaweed fishing village on Rishiri Island, in the absence of any well-known goitrogens. Other features observed in the study included a lack of clinical hyper- or hypothyroidism among the children with goiter, and a high daily consumption of Kombu (10–20 g/day) combined with very high urinary iodine excretion (mean UIE = 23.3 mg/day). Based on their findings, the authors concluded that longstanding excessive intake of dietary iodine was the most

likely cause of goiter in Japan. The name "endemic coast goiter" was coined, even though it was generally accepted that the biggest factor in the development of endemic goiter around the world was iodine deficiency. After repeating the survey five years later in a larger area of Hokkaido, the authors found the same close relationship between goiter rates and seaweed. Their reports had a major impact on the international goiter research community.

It wasn't until another large study was conducted in 1972–1975 that the concept of seaweed-induced goiter could be called into question. A comparison of 10,220 school-children from urban (Kanazawa City) and seaside (Wajima City) areas found no significant difference in the prevalence of goiter (2.7 vs. 3.0%). But this was the last reported goiter survey in Japan, and its findings cannot be compared with more recent data.

FIGURE 2 Median UIC values in school-age children in Japan.

Current data on iodine intake in Japan

According to the latest Iodine Global Scorecard, the median UIC in Japan is 287 µg/L, which has been derived from subnational studies conducted in 2002 in 6–12 year-old schoolchildren from Tokyo, Asahikawa, and Nakashibetsu, Hokkaido (7, 8). Although the distance between Tokyo and Asahikawa is around 580 miles, their median UICs were very similar (281.6 and 288.0 µg/L, respectively). And despite this fairly high urinary iodine excretion, the thyroid volume in Tokyo was found to be lower than in other iodine-sufficient areas around the world. In Nakashibetsu, the median UIC was clearly in the excessive range (728 µg/L), and the mean thyroid volume was approximately twice that reported in other countries (9). Nakashibetsu is a dairy farming town with a population of 24,000 in an inland area, and the reason for the high median UIC and large thyroid volume is unclear.

Did excessive iodine intake contribute to thyroid dysfunction?

Since 1978 there have been several case reports linking thyroid dysfunction with dietary iodine. They included cases of Hashimoto's thyroiditis induced by ingesting large amounts of seaweed, reversible hypothyroidism after restriction of iodine-rich foods, hypothyroidism in anorexic patients consuming 50–100 g of Kombu daily, and transient hypothyroidism or persistent hyperthyrotropinemia in infants due to a high maternal intake of iodine-rich foods during pregnancy.

In 1992 a survey in 1,061 adults from five coastal areas of Hokkaido measured serum TSH and urinary iodine concentrations (UICs) (6). The mean urinary iodine measured by an iodide-selective electrode was 3,300 µg/L (27.1 µmol/L) in 4,138 healthy adults in Sapporo. In addition, kelp-induced goiter had disappeared, but high UI concentrations correlated with non-autoimmune hypothyroidism. On balance, the authors concluded that, in addition to chronic thyroiditis, excessive iodine was a possible cause of hypothyroidism in this iodine-sufficient area. Interestingly, subsequent UI studies in adults reported concentrations in the range of 213–241 µg/L, and the reason for the extremely high urinary iodine in the Sapporo study is not clear.

Recent epidemiological studies

More epidemiological studies of iodine nutrition were conducted between 2002 and 2011 in approximately 3,000 individuals from different age groups in metropolitan areas including Tokyo, Chiba, and Kanagawa prefectures (Table 1). The median UIC ranged from 109 to 282 µg/L indicating that iodine intake was not excessive according to the WHO criteria. At the same time, the median UIC in breastfeeding women was relatively low (116 and 136 µg/L), although still sufficient.

TABLE 1 Urinary iodine concentrations in a metropolitan area of Japan (2002-2011)

Population	Age	Median UIC (µg/L)	Median daily iodine intake (µg/day)
Term newborns (days)	0	109	
	4	225	Not available
Infants (days)	29	256	
Schoolchildren (yrs)	9.6	282	
Junior High School students (yrs)	13.3	230	272.3
Adults (yrs)	47.7	213	257.7
Pregnant Women (21 wks)	30.9	219	290.0
Pregnant Women (32 wks)	32.1	164	316.8
Lactating Women (34 days)	30.9	135	164.0
Lactating Women (29 days)	32.1	116	276.3

TABLE 2 Tolerable upper limits of iodine ($\mu\text{g/day}$)

Population	Japan (2010)	US *	Europe *
1–3 yr olds	250 – 350	200	200
4–6 yr olds	350 – 500	300	250
7–10 yr olds	500	300	300
11–14 yr olds	500 – 1200	300	450
15–17 yr olds	2000	900	500
Adults	3000	1100	600
Pregnancy	2000	1100	600

*Zimmermann 2009 (See Ref. 10)

In 2013 began the first nationwide school-based survey of iodine nutrition. It will measure UICs in 6–12 year-old children and iodine intake in their guardians using an iodine-specific food frequency questionnaire. So far approximately 6,000 children and 7,500 guardians from 12 schools in 7 prefectures have been enrolled. At present, the overall median UIC is 290 $\mu\text{g/L}$ suggesting iodine sufficiency. But across the prefectures, the median UICs vary from 221 to more than 1000 $\mu\text{g/L}$ in Hiroshima and Nakashibetsu, Hokkaido (Figure 2). Moreover, 26% of the 12 year-olds and 31% of the 6–11 year-olds have urinary iodine concentrations exceeding the national age-specific tolerable upper limit of iodine (Table 2).

On balance, it is not clear at present that the iodine intake in Japan is excessive, although the daily consumption of iodine is higher than in most other countries. Future epidemiological studies in Japan should continue investigating the role of iodine in thyroid dysfunction.

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The first national survey of iodine status will determine whether children in Japan are at risk of iodine-related thyroid problems.