

16 Iodine

16.1 Introduction

Most of the iodine in nature is found in marine sediment in the form of iodine salts. Iodine is an essential trace element required for the synthesis of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). The human body contains 15-20 mg of iodine with 70-80% being located in the thyroid gland. Iodine that is taken up in the thyroid gland is oxidized by hydrogen peroxide and thyroid peroxidase. The oxidized (active) iodine is attached to a glycoprotein called thyroglobulin. The active iodine reacts with the tyrosine components of thyroglobulin to form 3-monoiodotyrosine (MITs) and 3,5-diiodotyrosine (DITs). The MITs and DITs are coupled to form triiodothyronine (T_3) and thyroxine (T_4) residues on the thyroglobulin. The MITs and DITs couple to form the active thyroid hormones, T_3 and T_4 . These thyroid hormones are attached to thyroglobulin and stored as the main component of the thyroid colloid. Proteolytic enzymes subsequently release T_3 and T_4 from thyroglobulin into the blood. When these hormones are utilized in various body cells, they are replaced by T_3 and T_4 from the bound pool. The liberated iodine may be reutilized by the thyroid gland, while the remainder iodine is excreted in the urine. Typically, urine contains more than 90% of all ingested iodine. Most of the remainder is excreted in feces and a small amount may be lost in sweat (IOM, 2001).

Thyroid hormones are essential for life as they regulate key biochemical reactions, especially protein synthesis and enzymatic activities, in target organs such as are the developing brain, muscle, heart, pituitary and kidney.

16.2 Food sources

The iodine content of foods depends on the iodine content of the soil in which it is grown. Seawater is a rich source of iodine. Seaweeds and fish, which thrive on seaweeds, are also rich in iodine. Thus, populations living near the sea and consuming seaweeds and reef fish such as the Japanese have a high intake of iodine. A wide variety of food contains iodine including eggs, meat, milk and milk products, cereal grains, dried legumes, dried vegetables and dried fruits, but the good sources are limited to marine fishes and shellfish. The iodine content of foods varies with geographic location, ranging widely from 30 $\mu\text{g}/100\text{ g}$ to 800 $\mu\text{g}/100\text{ g}$ (FAO/WHO, 2002). Hence, the average iodine content of foods from one country cannot be universally used for estimating the iodine intake for another population. Examples of iodine content in foods are shown in Table 16.1.

Table 16.1 Iodine content of selected foods ($\mu\text{g}/100\text{ g}$)

Food	Fresh basis		Dry basis	
	Mean	Range	Mean	Range
Fish (freshwater)	30	17-40	116	68-194
Fish (marine)	832	163-3,180	3,715	471-4,591
Shellfish	798	308-1,300	3,866	1,292-4,987
Meat	50	27-97	-	-
Milk	47	35-56	-	-
Eggs	93	-	-	-
Cereal grains	47	22-72	65	34-92
Fruits	18	10-29	154	62-277
Legumes	30	23-36	234	223-245
Vegetables	29	12-201	385	204-1,636
Iodized salt*	25 mg/kg	20 – 30 mg/kg	-	-

Source: FAO/WHO (2002)

*Malaysian Food Regulations 1985 (Regulation 285)

16.3 Deficiencies

Iodine insufficiency induces an increase in thyroid-stimulating hormone (TSH) in response to decreased production of thyroid hormone. Goitre develops as a consequence of the stimulation action of TSH. Serious iodine deficiency also leads to functional and developmental abnormalities such as hypothyroidism. Hypothyroidism causes physical and mental retardation in infants and children. In neonate, iodine deficiency causes perinatal mortality, infant mortality and low birth weight. Severe iodine deficiency in the fetal and neonatal period may lead to cretinism, which is characterized by stunted growth, mental and other neurological retardation, and delay in development of secondary sex characteristics. In adults, it causes reduction in mental function and lethargy (FAO/WHO, 2002). This diverse array of iodine deficiency problems in different age groups is described as Iodine Deficiency Disorder (IDD). IDD thus includes mental retardation, hypothyroidism, goitre, cretinism and varying degrees of other growth and developmental abnormalities as a result of iodine insufficiency (IOM, 2001).

Worldwide, IDD remains a significant public health problem in 130 countries, although it has been eliminated in 61 countries (ICCIDD/UNICEF/WHO, 2001). It is estimated that approximately 740 million people (13% of total population) are affected by goitre while 2,225 million people (38%) are at risk of IDD. Eastern Mediterranean (32% of its population), Africa (20%), Europe (15%) and Southeast Asia (12%) have high prevalence of goitre. In Asia, IDD is widespread with prevalence of total goitre rate (TGR) among school children ranging from 4% to 50%. IDD is particularly severe in India near the Himalayas, Indonesia, Myanmar, Maldives and Sri Lanka.

Several studies have been undertaken on IDD in Malaysia, many of which focused on different population groups in various parts of Sarawak. During the 1970s and 1980s, the prevalence of endemic goitre in remote and rural areas in Malaysia was reported as ranging from 20% to over 90% (Chen & Lim, 1982; Kiyu, Zainab & Yahaya, 1998). In 1993, a Sarawak state-wide survey of neonatal iodine deficiency was done by measuring thyroid-stimulating hormone (TSH) levels in the umbilical cord blood of 3,014 newborns (Kiyu *et al.*, 1995). Findings revealed that the overall prevalence of neonatal iodine deficiency in Sarawak was 7.5%.

In 1994-96, the Ministry of Health conducted a National IDD survey that involved almost 12,000 school children aged 8-10 years. Based on the WHO/ICCIDD reference, the survey found a goitre prevalence of 0.7% in Sarawak, 2.2% in Peninsular Malaysia and 18% in Sabah (MOH, 2003). The median urinary iodine level was 66.0 µg/l in Sabah, 82.2 µg/l in the Peninsula and 126.0 mg/l in Sarawak. The overall improved iodine status in Sarawak could be attributed to the distribution of iodized salt and installation of iodicators in the water supply of schools and longhouses in IDD endemic areas a few years prior to the survey (Foo *et al.*, 1990). Based on the survey results for Sabah, a state-level programme for salt iodization was launched and fully implemented by June 2000. The situation in Sabah has improved as monitoring of school children aged 8-10 years in 2002 found the median urinary iodine level at 240 µg/l.

Among adults, a survey of IDD amongst long house inhabitants in Sarawak reported a goitre prevalence of 27% at Hilir Lemanak (1993), 37% at Batang Ai (1993) and 52% at Ulu Lemanak (1998). The corresponding median urinary iodine concentrations were 72 µg/l, 22 µg/l and 37 µg/l for the 3 populations. Osman *et al.* (1993) reported that in Pahang rural areas, prevalence of goitre was 20 and 70% depending on village, ethnic group, age and gender. The Aborigines in Pahang had a goitre prevalence of more than 20% and urinary iodine content of 2.0-5.0 µg/dl (Osman *et al.*, 1993).

Some of the causes for iodine deficiency in Malaysia include low iodine content of soil and water, inadequate iodine content in local foods and low consumption of marine seafood. The consumption of cassava, known to contain goitrogens, was an additional contributory factor (Kiyu *et al.*, 1998). Currently, IDD prevention and control programs in Malaysia include the following strategies:

- Mandatory universal salt iodization in Sabah
- Mandatory salt iodization in 16 endemic districts and 3 sub-districts in Sarawak
- Iodization of the water supply in remote schools and villages
- Distribution of iodized salt to pregnant women living in endemic areas
- Health education on food choices and preparation

16.4 Factors affecting iodine requirements

Iodine is ingested in a variety of chemical form in food. Most ingested iodine is reduced in the gut and absorbed almost completely. Some iodine containing compounds are absorbed intact. The thyroid selectively concentrates iodide in the amounts required for adequate thyroid hormone synthesis. The thyroid gland traps approximately 60 µg per day iodine to maintain an adequate supply of thyroxine (IOM, 2001). Several other tissues also concentrate iodine, including salivary glands, breast, choroids plexus and gastric mucosa.

Under normal circumstances, the absorption of dietary iodine is greater than 90%. When thyroxine is given orally, the bioavailability is approximately 75%. Certain micronutrients are necessary for the utilization of iodine for thyroid hormone synthesis. Selenium deficiency for example, inhibits the conversion of T₄ to T₃ in liver. Iron deficiency impairs thyroid metabolism leading to an inability to control body temperature. Protein malnutrition affects iodine absorption and metabolism by decreasing thyroidal iodine clearance (Pennington, 1988). Soy flour has been shown to inhibit iodine absorption, and when iodine was added to this formula, goitre did not appear (IOM, 2001).

Some foods contain goitrogens that are substances that interfere with thyroid hormone production or utilization. Examples include cassava, crucifera vegetables (cabbage, broccoli, cauliflower), bamboo shoots, maize, lima beans and millet. Most of these substances are not of major clinical importance unless there is co-existing iodine deficiency (IOM, 2001).

Currently there is no available data on the intake of iodine in Malaysia. Lack of iodine content in the Malaysian food composition database may be one plausible explanation. The US Department of Agriculture Continuing Survey of Food Intakes by Individuals (1994-1996) showed that the median intake of iodine from food in the United States is approximately 240-300 µg/day for men and 190-210 µg/day for women (IOM, 2001). In the UK, the intake of iodine was 243 and 176 µg/day for men and women respectively (DOH-UK, 1995).

16.5 Setting requirements and recommended intakes of iodine

Indicators for estimating requirements for iodine includes using the daily uptake and release (turnover) of iodine in the body, urinary iodine excretion, thyroid size and iodine balance. Urinary iodine excretion and thyroid size using ultrasonography is recommended by the WHO/UNICEF/ICCIDD (1996) for assessing iodine nutrition worldwide. Balance studies have several limitations but data from them were used for estimating requirements in children (IOM, 2001).

The FAO/WHO (2002) report of an expert consultation several years ago and the IOM (2001) report were the main references used by the Technical Sub-Committee (TSC) on Minerals. The rationale and approaches used by these reports were considered. Several local reports on the magnitude of IDD and the intervention measures taken were also useful references.

Since there is lack of scientific data on iodine requirements in Malaysia, the TSC has recommended to following the approach used by the FAO/WHO (2002). The actual RNIs for Malaysia are based on the body weights of the local population. The recommended intakes for iodine for Malaysians of various age groups are given in bold in the following paragraphs according to age groups and summarised in Appendix 16.1.

Infants

No functional criteria of iodine status have been demonstrated that reflect response to dietary intake of iodine in infants. The DRI committee of IOM (2001) therefore based the recommended intake of iodine on an adequate intake that reflects the observed mean iodine intake of infants fed exclusively on human milk. The FAO/WHO Consultation also used a similar approach to estimating recommended intakes for this age group.

Iodine requirements in infancy are derived from the iodine content in human milk in infants growing at a satisfactory rate. The iodine content in human milk is a function of the iodine intake of the population. It has been reported to range from 20-330 µg/l in Europe and from 30-490 µg/l in the United States. Among population groups with severe iodine deficiency, it could be as low as 12 µg/l. An average human-milk intake of 750 ml/day would give an iodine intake of about 60 µg/day in Europe and 120 µg/day in USA. Positive iodine balance, which is required for the increasing stores of the thyroid, in the infant is achieved only when the iodine intake is at least 15 µg/kg/day in full-term infants and 30 µg/kg/day in pre-term infants (FAO/WHO, 2002). Using the reference weights of 6 kg and 8 kg for 0-5 months and 6-12 months infants, respectively, the values correspond approximately to iodine intakes of 90 µg/day and 120 µg/day.

RNI for infants

0 - 5 months (full term)	9 µg/day
6 - 11 months	120 µg/day

Children

The DRI Committee (IOM, 2001) had based the estimated requirement for iodine in children 1-9 years on two balance studies. RDAs were then calculated based on 140% of the requirement.

The daily iodine needs on a body weight basis decreases with age. The iodine recommendation by FAO/WHO (2002) for children is 6 µg/kg/day for ages 1-6 years and 4 µg/kg/day for ages 7-12 years. Using the mean body weight as that is deemed appropriate for Malaysian children, the TSC for Minerals had recommended the intake for iodine for children to be as follows.

RNI for children

1 - 3 years	72 µg/day
4 - 6 years	108 µg/day
7 - 9 years	104 µg/day

Adolescents and adults

In adolescents and adults, most dietary iodine eventually appears in the urine, so the urinary iodine concentration is a useful measure for assessing iodine intake. A urinary iodine concentration of above 100 µg/l corresponds to a dietary iodine intake of 150 µg/day. Urinary iodine values below 100 µg/l are associated with increases in thyroid size and serum TSH. WHO/UNICEF/ICCIDD (1996) proposed that 150 µg/day iodine in adolescents and adults (12 years and above) provides the necessary intake to maintain plasma iodide level above the critical limit of 0.10 µg/dL and maintain iodine stores of the thyroid. Similar to FAO/WHO (2002), the Malaysian RNI for iodine for adolescents and adults is calculated based on 2 µg/kg/day, making use of the mean body weights of the local population.

RNI for adolescent boys

10 – 12 years	144 µg/day
13 – 15 years	106 µg/day
16 – 18 years	118 µg/day

RNI for adolescent girls

10 – 12 years	148 µg/day
13 – 15 years	98 µg/day
16 – 18 years	104 µg/day

RNI for adults

Men	19 – 65 years	124 µg RE/day
Women	19 – 65 years	110 µg RE/day

RNI for elderly

Men	> 65 years	114 µg RE/day
Women	> 65 years	98 µg RE/day

Pregnancy & lactation

The iodine requirement during pregnancy is increased to provide the needs of the foetus and to compensate for the increased loss of iodine in the urine resulting from an increased renal clearance of iodine during pregnancy. These requirements have been derived from studies of thyroid function during pregnancy and in the neonate under conditions of moderate iodine deficiency. These data indicated that the iodine intake required to prevent the onset of subclinical hypothyroidism of mother and foetus during pregnancy, and thus to prevent the possible risk of brain damage of the foetus, is approximately 3.5 µg/kg/day or 200 µg/day (FAO/WHO, 2002). The TSC on Minerals decided to adopt the same recommendations for the Malaysian RNI.

RNI for

Pregnancy	200 µg/day
Lactation	200 µg/day

Discussion on revised RNI for Malaysia

Compared to the iodine intake recommendations by FAO/WHO (2002), IOM (2001) had recommended higher intakes for all age groups except for infants (7-11 months) and children (1-13 years). The RDA for pregnancy and lactation, particularly the latter, were also higher in the latter recommendation. The latter had also made the same recommendations for adults of all ages and also for both sexes as it was felt that there is no evidence to suggest that the average iodine requirement is altered with aging, or to have differences based on gender in adults.

The TSC on Minerals had taken on the approach of the FAO/WHO (2002) in deriving at RNI for iodine. However, as previously mentioned, the TSC had set the RNI based on the mean body weight of Malaysians as in Table 1.1. Hence, due to the lower reference body weights of Malaysians, the daily recommended iodine intakes are slightly lower than the values proposed by FAO/WHO (2002) (Appendix 16.1).

16.6 Toxicity and tolerable upper intake levels

Most people are very tolerant to excess iodine intake from food with the exception of certain subgroups with autoimmune thyroid disease and iodine deficiency. High intakes of iodine from food, water and supplements have been associated with thyroiditis, goitre (due to increased thyroid stimulating hormones [TSH] stimulation), hypothyroidism, hyper-thyroidism, sensitivity reactions, thyroid papillary cancer and acute responses in some individuals. Symptoms of acute iodine poisoning include burning of the mouth, throat, and stomach, abdominal pain, fever, nausea, vomiting, diarrhea, weak pulse, cardiac irritability, coma and cyanosis (IOM, 2001).

The recommendation of IOM (2001) for the upper limits of intakes for iodine are given in Table 16.2.

Table 16.2: Tolerable upper intake levels (UL) for iodine for various age groups

Group	µg/day iodine
Infants	Not possible to establish
Children	
1-3 years	200
4-8 years	300
9-13 years	600
Adolescents, 14-18 years	900
Adults, ≥ 19 years	1,100
Pregnant women	
14 – 18 years	900
> 19 years	1,100
Lactating women	
14 – 18 years	900
> 19 years	1,100

16.7 Research recommendations

The following priority areas of research are recommended:

- Determine iodine intake and food sources among communities of various ages.
- Periodic studies to determine goitre prevalence and urinary iodine excretion across age groups
- Evaluation of iodized salt programmes
- Relationship between iodine deficiency and mental performance and immune status in children

16.8 References

Chen PCY & Lim PPE (1982). The prevalence of endemic goitre in the Tinjar Area, Sarawak. *Med J Mal* 37(3):265-269.

DOH-UK (1995). Dietary reference value for food energy and nutrients for the United Kingdom. Report on Health and Social Subjects No. 41. Department of Health, London, United Kingdom.

FAO/WHO (2002). Iodine. *In: Human vitamin and mineral requirements*. Report of a Joint FAO/WHO Expert Consultation. FAO, Rome; pp 181-194.

- Foo LC, Zainab T, Goh SY, Letchumanan GR, Nafikudin M, Doraisingam P & Khalid BAK (1990). Iodization of village water supply in the control of endemic iodine deficiency in rural Sarawak, Malaysia. *Biomed Environ Sci* 9:236-241.
- ICCIDD/UNICEF/WHO (2001). Assessment of Iodine Deficiency Disorders and Monitoring their Elimination. A Guide for Programme Managers. 2nd Edition. World Health Organization, Geneva.
- IOM (2001). Iodine. In: *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Food and Nutrition Board, Institute of Medicine. National Academy Press, Washington DC; pp 258-289.
- Kiyu A, Lau KB, Wong HY, Jamilah H (1995). Neonatal iodine deficiency in Sarawak. Sarawak Health Department, Kuching.
- Kiyu A, Zainab T & Yahaya A (1998). Iodine deficiency disorders in Sarawak. *Asia Pacific J Clin Nutr* (7): 256-261.
- MOH (2003). Annual Report 2002. Division of Family Health Development, Ministry of Health Malaysia, Kuala Lumpur.
- Osman A, Muda Khalida, Abu Bakar Azman, R.Jamil, TT Tan, LL Wu, SO Sakinah & BAK Khalid (1993). Iodine content in drinking water not an important determinant of endemic goitre. *Asia Pacific J Clin Nutr* 2:115-118.
- Pennington JT (1988). Iodine. In: *Trace minerals in Foods*. Smith KT (ed). 1st ed. Marcel Dekker, Inc. New York. Pg 249-289.
- WHO/UNICEF/ICCDD (1996). Recommended Iodine Levels in Salt and Guidelines for Monitoring their Adequacy and Effectiveness. Report of a Joint WHO/UNICEF/ICCDD Consultant. World Health Organization, Geneva.

Appendix 16.1 Comparison of recommended intake for iodine: RNI Malaysia (2005), RNI of FAO/WHO (2002), and RDA of IOM (2001)

Malaysia (2005)		FAO/WHO (2002)		IOM (2001)	
Age groups	RNI (µg/day)	Age groups	RNI (µg/day)	Age group	AI (µg/day)
Infants		Infants		Infants	
0 – 5 months	90	0 – 6 months	90	0 – 6 months	110
6 – 11 months	120	7 – 11 months	135	7 – 12 months	130
					RDA (µg/day)
Children		Children		Children	
1 – 3 years	72	1 – 3 years	75	1 – 3 years	90
4 – 6 years	108	4 – 6 years	110	4 – 8 years	90
7 – 9 years	104	7 – 9 years	100		
Boys		Boys		Boys	
10 – 12 years	144	10 – 11 years	135	9 – 13 years	120
13 – 15 years	106	> 12 years	110	14 – 18 years	150
16 – 19 years	118				
Girls		Girls		Girls	
10 – 12 years	148	10 – 11 years	140	9 – 13 years	120
13 – 15 years	98	> 12 years	100	14 – 18 years	150
16 – 19 years	104				
Men		Men		Men	
19 – 65 years	124	19 – 65 years	130	19 – 30 years	150
> 65 years	114	> 65 years	130	31 – 50 years	150
				51 – 70 years	150
				> 70 years	150
Women		Women		Women	
19 – 65 years	110	19 – 65 years	110	19 – 30 years	150
> 65 years	98	> 65 years	110	31 – 50 years	150
				51 – 70 years	150
				> 70 years	150
Pregnancy		Pregnancy		Pregnancy	
1 st trimester	200	1 st trimester	200	14 – 18 years	220
2 nd trimester	200	2 nd trimester	200	19 – 30 years	220
3 rd trimester	200	3 rd trimester	200	31 – 50 years	220
Lactation		Lactation		Lactation	
0 – 3 months	200	0 – 3 months	200	14 – 18 years	290
4 – 6 months	200	4 – 6 months	200	19 – 30 years	290
7 – 12 months	200	7 – 12 months	200	31 – 50 years	290