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Dietary Reference Intakes for Japanese 2010: Macrominerals

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Summary Dietary Reference Intakes of five macrominerals (sodium, potassium, calcium, magnesium and phosphate) were determined for Japanese. The estimated average requirement (EAR) and the recommended dietary allowance (RDA) for adults ages 18 y and older were determined in calcium and magnesium. In sodium, the EAR was determined. The RDA was not determined because the values were much lower than normal intake levels. Furthermore the dietary goal for preventing lifestyle-related diseases (DG) was determined based on preventing hypertension. In potassium, the value that is considered appropriate to maintain in vivo potassium balance was used as the adequate intake, the DG was established from a standpoint of prevention of hypertension. In calcium, the EAR and RDA were determined by the factorial method. In phosphate, the AI was determined based on the intake level of the National Health and Nutrition Surveys. The tolerable upper intake level (UL) for adults was determined in calcium, phosphate and magnesium, but the UL of magnesium was applied from a source other than ordinary food.

Key Words sodium, potassium, calcium, magnesium, phosphate

Sodium

Background information

Sodium, the main cation contained in extracellular fluid, is necessary to maintain extracellular fluid volume, plasma osmolality, and acid-base balance. Sodium is mostly consumed in the form of sodium chloride (NaCl), commonly referred to as salt. The largest portion of ingested sodium is absorbed from the small intestine and the majority of absorbed sodium is excreted in the urine via the kidneys. If sodium intake increases, the amount of urinary excretion will increase, and if intake decreases, the amount of urinary excretion will decrease.

A NaCl equivalent is calculated as follows from the molecular weight of salt and sodium:

$$\text{NaCl equivalent} = \text{sodium (g)} \times 58.5/23 = \text{sodium (g)} \times 2.54.$$

If kidney functioning is normal, sodium balance will be maintained by the re-absorption of sodium in the kidneys, thereby preventing sodium deficiency. Endogenous loss of sodium is calculated as the sum of the sodium excreted in the urine, feces, dermal tissue, and other tissues when sodium intake is 0 mg/d.

Determining the Dietary Reference Intakes (DRIs)

Based on the belief that the amount of endogenous sodium loss is equal to the amount of sodium required, the estimated average requirement (EAR) was established with the goal of compensating for endogenous loss. However, the values are less than 1% of the value of intake distribution, determined by the National Health and Nutrition Survey (*1*, *2*). Therefore, the meaning in practical use does not presume to provide the average required quantity. Since it has no meaning when utilizing the amount recommended, it was not calculated.

For infants aged 0 to 5 mo, the adequate intake (AI) was calculated using the average concentration of sodium in breast milk (135 mg/L) (*3*, *4*) and average volume of breast milk secreted per day (0.78 L/d) (*5*, *6*). For infants aged 6 to 11 mo, the AI was calculated using the average consumption of sodium from breast milk (*3*, *4*, *7*, *8*) and complementary food (*9*). The dietary goal for preventing lifestyle-related diseases (DG) for sodium was established by epidemiology research that considered the relationship between high blood pressure (*10*, *11*) and cancer (*12*) and sodium ingestion, changes in sodium intake in the Japanese (*1*, *2*), and the desirable level of sodium established in many Western countries. In adults, the target to attain over 5 y was calculated to be less than 9 mg/d for men and less than 7.5 mg/d for women. In children aged 1 to 11 y, the value was calculated by extrapolation from the value for adults aged 18 to 29 y by the 0.75th power of the weight ratio. The

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Table 1. DRIs for sodium (mg/d, the value in parentheses is equivalent to table salt [g/d]).

Sex	Males			Females		
Age	EAR	AI	DG	EAR	AI	DG
0–5 mo	—	100 (0.3)	—	—	100 (0.3)	—
6–11 mo	—	600 (1.5)	—	—	600 (1.5)	—
1–2 y	—	—	(<4.0)	—	—	(<4.0)
3–5 y	—	—	(<5.0)	—	—	(<5.0)
6–7 y	—	—	(<6.0)	—	—	(<6.0)
8–9 y	—	—	(<7.0)	—	—	(<7.0)
10–11 y	—	—	(<8.0)	—	—	(<7.5)
12–14 y	—	—	(<9.0)	—	—	(<7.5)
15–17 y	—	—	(<9.0)	—	—	(<7.5)
18–29 y	600 (1.5)	—	(<9.0)	600 (1.5)	—	(<7.5)
30–49 y	600 (1.5)	—	(<9.0)	600 (1.5)	—	(<7.5)
50–69 y	600 (1.5)	—	(<9.0)	600 (1.5)	—	(<7.5)
≥70 y	600 (1.5)	—	(<9.0)	600 (1.5)	—	(<7.5)
Pregnant women (amount to be added)				—	—	—
Lactating women (amount to be added)				—	—	—

DRIs, Dietary Reference Intakes; EAR, estimated average requirement; AI, adequate intake; DG, tentative dietary goal for preventing lifestyle-related diseases.

value for adults aged 18 to 29 y was applied to adolescents aged 12 to 17 y.

DRIs for sodium are summarized in Table 1.

Potassium

Background information

As the main cation contained in intracellular fluid, potassium is an important factor in determining the osmotic pressure of aqueous humors and maintaining acid-base balance, and participates in nerve transmission, muscle contraction, and vascular tone. In healthy individuals, potassium deficiency is rarely observed, typically afflicting only those experiencing diarrhea or heavy perspiration or taking diuretics. Average sodium intake in Japan is high compared with that of many countries (*1*, *2*). As the urinary excretion of sodium is related to potassium intake, it is believed that increasing ingestion of potassium is important for the Japanese.

Determining DRIs

Based on the National Health and Nutrition Survey data, the AI was determined to compensate for endogenous potassium loss and maintenance of potassium balance at the present intake level (*1*, *2*). In research conducted in other countries, an intake of 1,600 mg was found adequate to maintain potassium balance (*13*). The current intake of the Japanese was found to exceed this value (*1*, *2*), reaching an AI of 2,500 mg for men, which is not an unrealizable value, nor is 2,000 mg for women in consideration of the difference in energy intake.

Based on the AI of adults aged 18 to 29 y, it was extrapolated by the 0.75th power of the weight ratio in consideration of the growth factor. The AI for infants aged 0 to 5 mo infants was calculated using the average concentration of potassium in breast milk (*3*, *4*) and the average volume of breast milk secreted per day (*5*, *6*). The AI for infants aged 6 to 11 mo was calculated using the average consumption of potassium from breast milk (*7*, *8*) and complementary food (*8*). Since it is supplied with normal meals, the additional amount required for pregnant women was not determined. The additional amount required for lactating women was calculated as follows:

Additional amount of potassium required for lactating women
=average amount of potassium in breast milk (*3*, *4*)×the amount of milk (*5*, *6*).

If renal functioning is normal, the potassium intake from normal meals will not lead to excessive potassium levels, which can cause metabolic disorder. Therefore, the tolerable upper intake level (UL) was not determined.

The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (*14*) reported that an intake of 3,500 mg potassium/d is desirable to prevent high blood pressure. This value is supported from the viewpoint of primary prevention of lifestyle-related diseases, centering on prevention of high blood pressure. However, considering that the current median intake of adult Japanese is 2,384 mg for men and 2,215 mg for women (*1*, *2*), this intake may be difficult to realize. Aiming for its realization 5 y from now, it was considered appropriate to aim at the mean value of the current median intake and the value reported in *the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (*14*), and to calculate the DG

Table 2. DRIs for potassium (mg/d).

Sex	Males		Females	
Age	AI[1]	UL[2]	AI[1]	UL[2]
0–5 mo	400	—	400	—
6–11 mo	700	—	700	—
1–2 y	900	—	800	—
3–5 y	1,000	—	1,000	—
6–7 y	1,300	—	1,200	—
8–9 y	1,500	—	1,400	—
10–11 y	1,900	—	1,700	—
12–14 y	2,300	—	2,100	—
15–17 y	2,700	—	2,000	—
18–29 y	2,500	2,800	2,000	2,700
30–49 y	2,500	2,900	2,000	2,800
50–69 y	2,500	3,000	2,000	3,000
≥70 y	2,500	3,000	2,000	2,900
Pregnant women (amount to be added)			+0	—
Lactating women (amount to be added)			+400	—

UL, tolerable upper intake level.

[1] The value that is considered appropriate to maintain in vivo potassium balance was used as the adequate intake.

[2] The value was established from a standpoint of prevention of hypertension.

Table 3. EAR and RDA of calcium determined using the factorial method.

Sex	Age (y)	Reference body weight (kg)	Accumulation (A) (mg/d)	Urinary excretion (B) (mg/d)	Percutaneous loss (C) (mg/d)	A+B+C (mg/d)	Apparent absorption rate (D) (%)	EAR (E=(A+B+C)/D) (mg/d)	RDA (E×1.2) (mg/d)
Males	1–2	11.7	99	38	6	143	40	358	430
	3–5	16.2	114	48	8	171	35	487	585
	6–7	22.0	99	61	10	170	35	486	583
	8–9	27.5	103	72	12	187	35	534	641
	10–11	35.5	134	87	15	236	40	590	707
	12–14	48.0	242	109	18	370	45	821	986
	15–17	58.4	151	127	21	299	45	664	797
	18–29	63.0	38	134	22	195	30	648	778
	30–49	68.5	0	143	24	167	30	556	667
	50–69	65.0	0	137	23	160	27	593	712
	≥70	59.7	0	129	21	150	25	601	722
Females	1–2	11.0	95	36	6	137	40	343	412
	3–5	16.2	99	48	8	156	35	444	533
	6–7	22.0	86	61	10	157	35	449	539
	8–9	27.2	135	71	12	218	35	624	749
	10–11	34.5	171	85	14	271	45	601	722
	12–14	46.0	178	106	18	302	45	670	804
	15–17	50.6	89	114	19	222	40	555	665
	18–29	50.6	33	114	19	166	30	553	663
	30–49	53.0	0	118	20	138	25	550	660
	50–69	53.6	0	119	20	139	25	555	666
	≥70	49.0	0	111	19	130	25	519	622

RDA, recommended dietary allowance.

Table 4. DRIs for calcium (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	200	—	—	—	200	—
6–11 mo	—	—	250	—	—	—	250	—
1–2 y	350	400	—	—	350	400	—	—
3–5 y	500	600	—	—	450	550	—	—
6–7 y	500	600	—	—	450	550	—	—
8–9 y	550	650	—	—	600	750	—	—
10–11 y	600	700	—	—	600	700	—	—
12–14 y	800	1,000	—	—	650	800	—	—
15–17 y	650	800	—	—	550	650	—	—
18–29 y	650	800	—	2,300	550	650	—	2,300
30–49 y	550	650	—	2,300	550	650	—	2,300
50–69 y	600	700	—	2,300	550	650	—	2,300
≥70 y	600	700	—	2,300	500	600	—	2,300
Pregnant women (amount to be added)					+0	+0	—	—
Lactating women (amount to be added)					+0	+0	—	—

based on this view.

DRIs for potassium are summarized in Table 2.

Calcium

Background information

Calcium accounts for 1% to 2% of body weight, with more than 99% of total body calcium contained in the bones and teeth and the remaining 1% contained in blood, tissue fluid, and cells, where it plays a role in various bodily functions. The calcium concentration in the blood is controlled within a very narrow range. If the concentration decreases, parathyroid hormone will stimulate the absorption of calcium from bone, which undergoes repeated bone resorption (resorption of calcium from the bones) and bone formation (accumulation of the calcium in the bones). Bone mass increases during growth and begins to decrease in menopause or later and then continues to do so during the aging process (*15, 16*). Since the primary means of prevention of bone fracture is increasing bone mass, the calcium requirement has the character of a DG.

Determining DRIs

The EAR was calculated using the factorial method, which considers the amount of calcium accumulated in the body (*17–27*), excreted by urine (*28–30*), lost via dermal tissue (*31*), and the apparent rate (*32–50*) (Table 3).

Assuming that infants aged 0 to 5 mo can obtain the required calcium from their mother's milk, the AI was calculated using the average concentration of calcium in breast milk (*3, 4, 8*) and the average volume of breast milk secreted per day (*5, 6*). For infants aged 6 to 11 mo, the AI was calculated using the average consumption of calcium from breast milk (*3, 4, 7, 8*), and complementary food (*9*).

It was assumed that determining the additional amount required for pregnant and lactating women was unnecessary. Although the metabolism of calcium changes during pregnancy and lactation, during which more calcium is taken into the body, the calcium accumulated in an embryo and in the mother's milk originates from the bones of the mother's body, and even if they supply calcium, they cannot prevent bone mass reduction in the mother's body. Furthermore, since calcium intake is excreted in the mother's urine, the bone mass reduction that occurs during pregnancy and lactation is recovered within 6 mo after breast feeding is terminated if the quantity required before pregnancy is being consumed, and thus ingesting any additional amount is unnecessary.

Because milk alkali syndrome, a type of hypercalcemia that occurs with excessive ingestion of calcium and alkaline chemicals, has been reported (*51–59*), the UL was calculated with high reliability based on case reports of the obstacles encountered by superfluous ingestion of calcium. The UL was determined using the lowest observed adverse effect level (LOAEL) of calcium that causes milk alkali syndrome, which is 2.8 g, and dividing it by an uncertainty factor of 1.2, which yields a UL of 2.3 g.

DRIs for calcium are summarized in Table 4.

Magnesium

Background information

Magnesium contributes to the maintenance of bone health and various enzyme reactions. Approximately 25 g of magnesium exists in the adult body, and it exists in bone at levels of 50% to 60% (*60*). If magnesium is deficient, re-absorption of magnesium occurs from the kidneys, for which magnesium absorption increase from

Table 5. DRIs for magnesium (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL[1]	EAR	RDA	AI	UL[1]
0–5 mo	—	—	20	—	—	—	20	—
6–11 mo	—	—	60	—	—	—	60	—
1–2 y	60	70	—	—	60	70	—	—
3–5 y	80	100	—	—	80	100	—	—
6–7 y	110	130	—	—	110	130	—	—
8–9 y	140	170	—	—	140	160	—	—
10–11 y	180	210	—	—	170	210	—	—
12–14 y	240	290	—	—	230	280	—	—
15–17 y	290	350	—	—	250	300	—	—
18–29 y	280	340	—	—	230	270	—	—
30–49 y	310	370	—	—	240	290	—	—
50–69 y	290	350	—	—	240	290	—	—
≥70 y	270	320	—	—	220	260	—	—
Pregnant women (amount to be added)					+30	+40	—	—
Lactating women (amount to be added)					+0	+0	—	—

[1] When the nutrient is obtained from ordinary food, no upper threshold is set. When the nutrient is obtained from a source other than ordinary food, the upper threshold is set at 350 mg/d for adults and 5 mg/kg weight/d for children.

the bone will be used. At an average intake of approximately 300 to 350 mg, magnesium is absorbed from the intestinal tract at a rate of approximately 30% to 50% (*61*), with the rate increasing with lower intake.

Magnesium deficiency causes hypercalcemia, muscular convulsions, and coronary-artery spasms (*62*). Moreover, no fixed view exists, although it is suggested that insufficient magnesium over a long period raises the risk of lifestyle-related diseases, such as osteoporosis, cardiac disease, and diabetes (*60*). Although adverse effects are not caused by ingestion from meals, diarrhea may be caused by superfluous ingestion from supplements.

Determining DRIs

The EAR was calculated on the basis of results obtained by a previous study of magnesium balance (*63*). The research for Japanese was thought to be important, and 4.5 mg was made into the EAR per an adult's body weight. The EAR value of 4.5 mg was adopted as the recommended dietary allowance (RDA) after multiplying it by the reference body weight, applying a factor of 1.2, and assuming a coefficient of variation of 10%.

The results of an American balance test examining 12 boys and 13 girls aged 9 to 14 y using a stable magnesium isotope determined the EAR to be 5 mg (*33*). This value was subsequently adopted as the RDA after multiplying it by the reference body weight and applying a factor of 1.2, as had been applied to the adult EAR. The AI for infants aged 0 to 5 mo was calculated using the average concentration of magnesium in breast milk (*3, 4*) and the average volume of breast milk secreted per day (*5, 6*). The AI for infants aged 6 to 11 mo was calculated using the average consumption of magnesium from breast milk (*3, 4, 7, 8*) and complementary food (*9*). The additional amount required for pregnant women was calculated using the results of a magnesium balance study of pregnant woman (*64*). Because neither calcium balance nor the amount of magnesium excreted in urine changes during lactation (*65, 66*), it was assumed that determining the additional amount required during lactation was unnecessary.

The first-stage undesirable effect of superfluous ingestion of magnesium from sources other than food is diarrhea. Many individuals may experience mild transient diarrhea even without increased magnesium intake. Therefore, it is thought that it becomes the clearest index for the existence of development of symptoms of diarrhea to determine the UL. In addition, the report supposes that undesirable health effects of superfluous ingestion of magnesium from typical food sources were not found. Therefore, the UL from intake of typical foods was not determined.

DRIs for magnesium are summarized in Table 5.

Phosphorus

Background information

Phosphorus is indispensable to energy metabolism, which depends on phosphorylation in the cell. Even when phosphorus loss due to cooking is taken into consideration, the quantity of phosphorus ingested from food every day is always sufficient. The possibility of excessive ingestion of phosphorus is regarded as questionable, particularly as various orthophosphates are widely used as food additives.

Determining DRIs

Due to the lack of evidence in determining the pre-

Table 6. DRIs for phosphorus (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	120	—	—	—	120	—
6–11 mo	—	—	260	—	—	—	260	—
1–2 y	—	—	600	—	—	—	600	—
3–5 y	—	—	800	—	—	—	700	—
6–7 y	—	—	900	—	—	—	900	—
8–9 y	—	—	1,100	—	—	—	1,000	—
10–11 y	—	—	1,200	—	—	—	1,100	—
12–14 y	—	—	1,200	—	—	—	1,100	—
15–17 y	—	—	1,200	—	—	—	1,000	—
18–29 y	—	—	1,000	3,000	—	—	900	3,000
30–49 y	—	—	1,000	3,000	—	—	900	3,000
50–69 y	—	—	1,000	3,000	—	—	900	3,000
≥70 y	—	—	1,000	3,000	—	—	900	3,000
Pregnant women (amount to be added)					—	—	+0	—
Lactating women (amount to be added)					—	—	+0	—

sumed EAR and RDA, the AI for phosphorus was determined using the median intake reported in the National Health and Nutrition Survey (*1*, *2*) and the DRIs for the United States and Canada (*67*). The AI for infants aged 0 to 5 mo was calculated using the average concentration of phosphorus in breast milk (*3*, *4*) and the average volume of breast milk secreted per day (*5*, *6*). The AI for infants aged 6 to 11 mo was calculated using average consumption of phosphorus from breast milk (*3*, *4*, *7*, *8*) and complementary food (*9*). The additional amount for pregnant and lactating women was not calculated. It is known that serum inorganic phosphorus level increases in accordance with increases in phosphorus intake. The no observable adverse effect level (NOAEL) is considered to be an intake in the case where serum inorganic phosphorus serves as a normal upper limit. We set the uncertainty factor to 1.2, and calculated UL.

DRIs for phosphorus are summarized in Table 6.

Dr. Takatoshi Esashi who is one of the authors passed away on March 26, 2012. He was a leader of the working group for minerals in the decision of DRIs for Japanese, 2010. We would like to offer our respectful condolences on his death.

REFERENCES

1) Ministry of Health, Labour and Welfare, Japan. 2007. National Health and Nutrition Survey Japan (2005). Tokyo.

2) Ministry of Health, Labour and Welfare, Japan. 2008. National Health and Nutrition Survey Japan (2006). Tokyo.

3) Yamawaki N, Yamada M, Kan-no T, Kojima T, Kaneko T, Yonekubo A. 2005. Macronutrient, mineral and trace element composition of breast milk from Japanese women. *J Trace Elem Med Biol* **19**: 171–181.

4) Idota T. 2007. The components of Japanese mother's milk. The survey for the composition of human milk obtained from Japanese mothers—the goal of infant formula—. *Obstet Gynecol Pract* **56**: 315–325.

5) Suzuki K, Sasaki S, Shinzawa K, Totani M. 2004. Milk intake by breast-fed infants before weaning. *Jpn J Nutr Diet* **62**: 369–372 (in Japanese).

6) Hirose J, Endo M, Nagao S, Mizushima K, Narita H, Shibata K. 2008. Amount of breast milk sucked by Japanese breast feeding infants. *J Jpn Soc Breastfeeding Res* **2**: 23–28 (in Japanese).

7) Yoneyama K. 1998. Growth of breast-fed infants and intake of nutrients from breast-milk. *Journal of Child Health* **57**: 49–57 (in Japanese).

8) Yoneyama K, Goto I, Nagata H. 1995. Changes in the concentrations of nutrient components of human milk during lactation. *Jpn J Public Health* **42**: 472–481 (in Japanese).

9) Nakao T, Idota T, Nakajima I. 2003. The survey of nutrient intake from weaning foods in Japan. *J Child Health* **62**: 630–639 (in Japanese).

10) Intersalt Cooperative Research Group. 1988. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *BMJ* **297**: 319–328.

11) He FJ, Macgregor GA. 2009. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. *J Hum Hypertens* **23**: 363–384.

12) World Cancer Research Fund/American Institute for Cancer Research. 2007. Food, Nutrition, Physical Activity and the Prevention of Cancer, a Global Perspective. AICR, Washington DC.

13) Sebastian A, McSherry E, Morris RC Jr. 1971. Renal potassium wasting in renal tubular acidosis (RTA): its occurrence in type 1 and 2 RTA despite sustained correction of systemic acidosis. *J Clin Invest* **50**: 667–678.

14) Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

1997. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). *Arch Inetrn Med* **157**: 2413–2446.

15) Weaver CM. 2006. Calcium. *In*: Present Knowledge in Nutrition, 9th ed (Bowman BA, Russell RM, eds), Vol I, p 373–382. ILSI Press, Washington DC.

16) Dawson-Hughes B. 2006. Osteoporosis. *In*: Present Knowledge in Nutrition, 9th ed (Bowman BA, Russel RM, eds), Vol II, p 687–697. ILSI Press, Washington DC.

17) van der Sluis IM, de Ridder MA, Boot AM, Krenning EP, de Muinck Keizer-Schrama SM. 2002. Reference data for bone density and body composition measured with dual energy x-ray absorptiometry in white children and young adults. *Arch Dis Child* **87**: 341–347.

18) Bachrach LK, Hastie T, Wang MC, Narasimhan B, Marcus R. 1999. Bone mineral acquisition in healthy Asia, Hispanic, Black, and Caucasian youth: a longitudinal study. *J Clin Endocrinol Metab* **84**: 4702–4712.

19) Maynard LM, Guo SS, Chumlea WC, Roche AF, Wisemandle WA, Zeller CM, Towne B, Siervogel RM. 1998. Total-body and regional bone mineral content and areal bone mineral density in children aged 8–18 y: the Fels longitudinal study. *Am J Clin Nutr* **68**: 1111–1117.

20) Kalkwarf HJ, Zemel BS, Gilsanz V, Lappe JM, Horlick M, Oberfield S, Mahboubi S, Fan B, Frederick MM, Winer K, Shepherd JA. 2007. The bone mineral density in childhood study: bone mineral content and density according to age, sex, and race. *J Clin Endocrinol Metab* **92**: 2087–2099.

21) Molgaad C, Thomasen BL, Michaelsen KF. 1999. Whole body bone mineral accretion in healthy children and adolescents. *Arch Dis Child* **81**: 10–15.

22) Zhu K, Zhang Q, Foo LH, Trube A, Ma G, Hu X, Du X, Cowell CT, Fraser DR, Greenfield H. 2006. Growth, bone mass, and vitamin D status of Chinese adolescent girls 3 y after withdrawal of milk supplementation. *Am J Clin Nutr* **83**: 714–721.

23) Abrams SA, Copeland KC, Gunn SK, Gundberg CM, Klein KO, Ellis KJ. 2000. Calcium absorption, bone mass accumulation, and kinetics increase during early pubertal development in girls. *J Clin Endocrinol Metab* **85**: 1805–1809.

24) Martin AD, Bailey DA, McKay HA, Whiting S. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* **66**: 611–615.

25) Whiting SJ, Vatanparast H, Baxter-Jones A, Faulkner RA, Mirwald R, Bailey DA. 2004. Factors that affect bone mineral accrual in the adolescent growth spurt. *J Nutr* **134**: 696–700S.

26) Nishiyama S, Kiwaki K, Inomoto T, Seino Y. 1999. Bone mineral density of the lumber spine and total body mass in Japanese children and adolescents. *Pediatrics International* **103**: 1131–1138 (in Japanese).

27) Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. 2000. Body composition during the first 2 years of life: an updated reference. *Pediatr Res* **47**: 578–585.

28) Schaafsma G. 1992. The scientific basis of recommended dietary allowance for calcium. *J Int Med* **231**: 187–194.

29) Uenishi K, Ishida H, Kamei A, Shiraki M, Ezawa I, Goto S, Fukuoka H, Hosoi T, Orimo H. 2000. Calcium requirement in young Japanese female. *Osteoporosis Jpn* **8**: 217–219 (in Japanese).

30) Uenishi K, Ishida H, Kamei A, Shiraki M, Ezawa I, Goto S, Fukuoka H, Hosoi T, Orimo H. 2001. Calcium requirement estimated by balance study in elderly Japanese people. *Osteoporosis Int* **12**: 858–863.

31) Charles P, Eriksen EF, Hasling C, Sondergard K, Mosekilde L. 1991. Dermal, intestinal, and renal obligatory losses of calcium: relation to skeletal calcium loss. *Am J Clin Nutr* **54** (Suppl): S266–273.

32) Abrame SA, Wen J, Stuff JE. 1997. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* **41**: 384–390.

33) Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997. Calcium and magnesium balance in 9–14-y-old children. *Am J Clin Nutr* **66**: 1172–1177.

34) Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* **47**: 262–264.

35) Abrams SA, Copeland KC, Gunn SK, Stuff JE, Clarke LL, Ellis KJ. 1999. Calcium absorption and kinetics are similar in 7- and 8-year-old Mexican-American and Caucasian girls despite hormonal differences. *J Nutr* **129**: 666–671.

36) Miller JZ, Smith DL, Flora L, Slemenda C, Jiang XY, Johnston CC Jr. 1998. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* **48**: 1291–1294.

37) Abrams SA, O'brien KO, Liang LK, Stuff JE. 1995. Differences in calcium absorption and kinetics between black and white girls aged 5–16 years. *J Bone Miner Res* **10**: 829–833.

38) Bryant RJ, Wastney ME, Martin BR, Wood O, McCabe GP, Morshidi M, Smith DL, Peacock M, Weaver CM. 2003. Racial differences in bone turnover and calcium metabolism in adolescent females. *J Clin Endocrinol Metab* **88**: 1043–1047.

39) Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* **61**: 577–581.

40) Uenishi K, Ishida H, Kamei A, Shiraki M, Ezawa I, Goto S, Fukuoka H, Hosoi T, Orimo H. 2003. Calcium balance in pregnant and lactating women. *Osteoporosis Jpn* **11**: 249–251 (in Japanese).

41) Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* **4**: 469–475.

42) Roughead ZK, Johnson LK, Lykken GI, Hunt JR. 2003. Controlled high meat diets do not affect calcium retention or indices of bone status in healthy postmenopausal women. *J Nutr* **133**: 1020–1026.

43) Tahiri M, Tressol JC, Arnaud J, Bornet FR, Bouteloup-Demange C, Feillet-Coudray C, Brandolini M, Ducros V, Pepin D, Brouns F, Roussel AM, Rayssiguier Y, Coudray C. 2003. Effect of short-chain fructooligosaccharides on intestinal calcium absorption and calcium status in postmenopausal women: a stable-isotope study. *Am J Clin Nutr* **77**: 449–457.

44) Cifuentes M, Riedt CS, Brolin RE, Field MP, Sherrell RM, Shapses SA. 2004. Weight loss and calcium intake influence calcium absorption in overweight postmenopausal women. *Am J Clin Nutr* **80**: 123–130.

45) Lynch MF, Griffin IJ, Hawthorne KM, Chen Z, Hamzo M, Abrams SA. 2007. Calcium balance in 1–4-y-old children. *Am J Clin Nutr* **85**: 750–754.

46) Kohlenberg-Mueller K, Raschka L. 2003. Calcium bal-

ance in young adults on a vegan and lactovegetarian diet. *J Bone Miner Metab* **21**: 28–33.

47) Abrams SA, Griffin IJ, Hawthorne KM, Liang L. 2005. Height and height z-score are related to calcium absorption in five-to fifteen-year-old girls. *J Clin Endocrinol Metab* **90**: 5077–5081.

48) O'Brien KO, Abrams SA, Liang LK, Ellis KJ, Gagel RF. 1996. Increased efficiency of calcium absorption during short periods of inadequate calcium intake in girls. *Am J Clin Nutr* **63**: 579–583.

49) Weaver CM, McCabe LD, McCabe GP, Braun M, Martin BR, Dimeglio LA, Peacock M. 2008. Vitamin D status and calcium metabolism in adolescent black and white girls on range of controlled calcium intakes. *J Clin Endocrinol Metab* **93**: 3907–3914.

50) Moser-Veillon PB, Mangels AR, Vieira NE, Yergey AL, Patterson KY, Hill AD, Veillon C. 2001. Calcium fractional absorption and metabolism assessed using stable isotope differ between postpartum and never pregnant women. *J Nutr* **131**: 2295–2299.

51) Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yergey AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* **123**: 326–331.

52) Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk alkali syndrome: an appropriate response? *Postgrad Med J* **63**: 789–792.

53) Campbell SB, Macfarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m methylene diphosphonate in milk-alkali syndrome. *Clin Nucl Med* **19**: 207–211.

54) Carroll PR, Clark OH. 1983. Milk alkali syndrome. Does it exist and can it be differentiated from primary hyperparathyroidism? *Ann Surg* **197**: 427–433.

55) Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: a case report. *Nebr Med J* **67**: 128–130.

56) Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome. A case report. *S Afr Med J* **64**: 287–288.

57) Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* **146**: 1965–1968.

58) Kleinman GE, Rodriquez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): successful treatment with hemodialysis. *Obstet Gynecol* **78**: 496–499.

59) Schuman CA, Jones HW 3rd. 1985. The 'milk-alkali' syndrome: two case reports with discussion of pathogenesis. *Q J Med* **55**: 119–126.

60) Fleet JC, Cashman KD. 2001. Magnesium. *In*: Present Knowledge in Nutrition (Bowman BA, Russell RM, eds), 8th ed, p 292–301. ILSI Press, Washington DC.

61) Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable 26Mg. *Am J Clin Nutr* **39**: 571–576.

62) Food and Nutrition Board, Institute of Medicine. 1997. Magnesium. *In*: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (Institute of Medicine, ed), p 190–249. National Academies Press, Washington DC.

63) Nishimuta M, Kodama N, Morikuni E. 2004. Balances of calcium, magnesium and phosphorus in Japanese young adults. *J Nutr Sci Vitaminol* **50**: 19–25.

64) Seeling MS. 1980. Magnesium balance in pregnancy. *In*: Magnesium Deficiency in the Pathogenesis of Disease. Plenum Medical, New York.

65) Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* **28**: 1099–1104.

66) Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. Longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* **61**: 779–786.

67) Food and Nutrition Board, Institute of Medicine. 1997. Phosphorus. *In*: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (Institute of Medicine, ed), p 146–189. National Academies Press, Washington DC.

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Dietary Reference Intakes for Japanese 2010: Microminerals

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Summary The Dietary Reference Intakes (DRIs) of 8 microminerals (iron, zinc, copper, manganese, iodine, selenium, chromium and molybdenum) were determined for Japanese. The estimated average requirement (EAR) and the recommended dietary allowance (RDA) for adults ages 18 y and older were determined in seven microminerals other than for manganese. Due to lack of data with which to set the EAR for manganese, determination of the adequate intake (AI) of manganese was based on the average manganese intake of the Japanese population. Data with which to determine the EARs were obtained using the following methods: iron and zinc, use of a factorial modeling method; copper and selenium, determination of the relationship between biomarkers and intake; iodine, determination of thyroid iodine accumulation and turnover; and chromium and molybdenum, performance of a balance test. The EARs and RDAs of iron, zinc, copper, iodine and selenium for children and adolescents aged 1 to 17 y were also determined. Based on the average micromineral concentration in the milk of Japanese women and the average intake of breast milk in Japanese infants, the AI for infants was determined for 8 microminerals. The tolerable upper intake level (ULs) of adults were determined for all microminerals except chromium, for which there are insufficient data. The ULs for iron, iodine and selenium for children and adolescents were also determined.

Key Words chromium, copper, iodine, iron, manganese, molybdenum, selenium, zinc

Iron

Background information

Iron functions as a component of a number of proteins, including hemoglobin and several enzymes. Iron deficiency induces anemia and decreases physical performance and cognitive functions. Women's iron status is highly influenced by menstrual iron loss. In Japan, approximately 25% of women aged 30 through 39 y have been diagnosed with anemia, defined as a hemoglobin level lower than 12.0 g/dL (*1*).

Determining the Dietary Reference Intakes (DRIs)

The estimated average requirement (EAR) for iron was determined using a factorial modeling method in which the factors were basal iron loss (mostly via fecal loss), menstrual iron loss, iron storage with growth (mostly via increase in hemoglobin mass), increased iron requirement with pregnancy or lactation, and extent of dietary iron absorption. The average basal iron loss was estimated to be 0.96 mg/d, as determined by a study of 41 persons in 4 groups of a mean body weight of 68.6 kg (*2*), and this value extrapolated to each sex and age group using the 0.75th power of a weight ratio. The average menstrual iron loss was estimated to be 0.46 mg/d for girls aged 10 to 17 y and 0.55 mg/d for women aged 18 y and older based on the average menstrual blood loss of Japanese women (*3*, *4*). The iron storage with growth for each sex and age group (0.09 to 0.46 mg/d) was estimated based on blood volume and hemoglobin concentration by age group (*5*, *6*), iron content in hemoglobin (3.39 mg/g) (*7*), increase in tissue iron (non-storage iron), and increase in storage iron (*8*). The average of increased iron requirements due to pregnancy (0.32, 2.68, and 3.64 mg/d for the early, mid, and late stages of pregnancy, respectively) were calculated based on fetal and placental iron storage (*9*) and increase in hemoglobin mass caused by erythrocyte

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Table 1. Dietary Reference Intakes for iron (mg/d).[1]

Sex	Males				Females					
Age	EAR	RDA	AI	UL	Non-menstruating women		Menstruating women		AI	UL
					EAR	RDA	EAR	RDA		
0–5 mo	—	—	0.5	—	—	—	—	—	0.5	—
6–11 mo	3.5	5.0	—	—	3.5	4.5	—	—	—	—
1–2 y	3.0	4.0	—	25	3.0	4.5	—	—	—	20
3–5 y	4.0	5.5	—	25	4.0	5.5	—	—	—	25
6–7 y	4.5	6.5	—	30	4.5	6.5	—	—	—	30
8–9 y	6.0	8.5	—	35	5.5	8.0	—	—	—	35
10–11 y	7.0	10.0	—	35	6.5	9.5	9.5	13.5	—	35
12–14 y	8.0	11.0	—	50	7.0	10.0	10.0	14.0	—	45
15–17 y	8.0	9.5	—	45	5.5	7.0	8.5	10.5	—	40
18–29 y	6.0	7.0	—	50	5.0	6.0	8.5	10.5	—	40
30–49 y	6.5	7.5	—	55	5.5	6.5	9.0	11.0	—	40
50–69 y	6.0	7.5	—	50	5.5	6.5	9.0	11.0	—	45
≥70 y	6.0	7.0	—	50	5.0	6.0	—	—	—	40
Pregnant women (amount to be added)										
Early-stage					+2.0	+2.5	—	—	—	—
Mid and late-stage					+12.5	+15.0	—	—	—	—
Lactating women (amount to be added)					+2.0	+2.5	—	—	—	—

EAR, estimated average requirement; RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level.

[1] The values were set excluding those with menorrhagia (blood loss exceeding 80 mL/period).

mass expansion. The average iron requirement due to by lactation (0.33 mg/d) was calculated from the average iron concentration (0.426 mg/L) (*10*) and volume of secretion (0.78 L/d) (*11*, *12*) of breast milk in Japanese women.

In accordance with a value adopted by the World Health Organization (WHO) and the Food and Agricultural Organization (FAO) (*13*), the average percentage of dietary iron absorption by all ages is estimated to be 15% except for women during the mid and late stages of pregnancy, for whom it is estimated to be 25% (*14*). The EARs were calculated as follows: men and non-menstruating women aged 18 y and older, EAR=basal loss/absorption; menstruating women aged 18 y and older, EAR=(basal loss+menstrual loss)/absorption; boys and non-menstruating girls aged 6 mo to 17 y, EAR=(basal loss+accumulation with growth)/absorption; menstruating girls aged 10 to 17 y, EAR=(basal loss+menstrual loss+accumulation with growth)/absorption; pregnant and lactating women, additional EAR=increased demand induced by pregnancy or lactation/absorption. The recommended dietary allowances (RDAs) were determined as follows: children aged 6 mo to 14 y, EAR×1.4; aged 15 or older, EAR×1.2.

The adequate intake (AI) for infants aged 0 to 5 mo was calculated based on mean iron intake of infants fed breast milk as follows: AI=average iron concentration in breast milk in Japanese women (0.426 mg/L) (*10*)×average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*). The tolerable upper intake levels (ULs) for individuals aged 15 y or older was set at 0.8 mg/kg/d according to the provisional maximal tolerable intake reported by the WHO and FAO (*15*). The UL for toddlers aged 1 to 2 y was set at 2.0 mg/kg/d based on the lowest observed adverse effect level (LOAEL) for toddlers, which is 60 mg/kg/d (*16*), and an uncertainty factor of 30. The ULs for children aged 3 to 5 y, 6 to 7 y, 8 to 9 y, and 10 to 14 y were set at 1.6, 1.4, 1.2, and 1.0 mg/kg/d, respectively.

Table 1 summarizes the DRIs for iron. The EARs and RDAs in this table do not apply to women with hypermenorrhea, defined as menstrual blood loss over 80 mL per month.

Zinc

Background information

Zinc is an essential component of almost 100 specific enzymes, including alcohol dehydrogenase and RNA polymerases. Zinc deficiency may occur in patients receiving prolonged total parenteral nutrition (TPN) without zinc supplementation (*17*) or in infants fed breast milk with low zinc content (*18*), and manifests as several specific symptoms, including acrodermatitis enteropathica, hypogeusia, and chronic diarrhea.

Table 2. Dietary Reference Intakes for zinc (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	2	—	—	—	2	—
6–11 mo	—	—	3	—	—	—	3	—
1–2 y	4	5	—	—	4	5	—	—
3–5 y	5	6	—	—	5	6	—	—
6–7 y	6	7	—	—	6	7	—	—
8–9 y	7	8	—	—	7	8	—	—
10–11 y	8	10	—	—	8	10	—	—
12–14 y	9	11	—	—	8	9	—	—
15–17 y	11	13	—	—	7	9	—	—
18–29 y	10	12	—	40	7	9	—	35
30–49 y	10	12	—	45	8	9	—	35
50–69 y	10	12	—	45	8	9	—	35
≥70 y	9	11	—	40	7	9	—	30
Pregnant women (amount to be added)					+1	+2	—	—
Lactating women (amount to be added)					+3	+3	—	—

Determining DRIs

The EAR for zinc was determined using a factorial modeling method in which the factors were urinary zinc excretion, the sum of integumental and sweat zinc loss, zinc loss in semen or menstrual blood, endogenous zinc excretion via the intestine, and the extent of absorption of dietary zinc. The RDA for zinc was set equal to 120% of the EAR. As estimated according to the US/Canadian DRIs (*19*), urinary zinc excretion, the sum of integumental and sweat zinc loss, and zinc loss in semen or menstrual blood for adults of a reference body weight (men, 76 kg; women, 61 kg) were found to be the following: urinary zinc loss, 0.63 (men) and 0.44 mg/d (women); sum of integumental and sweat zinc loss, 0.54 (men) and 0.46 mg/d (women); zinc loss in semen, 0.10 mg/d; and zinc losses in menstrual blood, 0.10 mg/d. As a result, endogenous zinc losses via routes other than the intestine for men and women were determined to be 1.27 (0.63+0.54+0.10) mg/d and 1.00 (0.44+0.46+0.10) mg/d, respectively.

The results of several studies using a stable isotope (*20–26*) have shown that the relationship between endogenous zinc excretion via the intestine and the quantity of zinc absorbed in adults with a body weight of 76 kg can be calculated using the following equation: endogenous excretion via the intestine$=0.628\times$(quantity absorbed$+0.2784$). Because total endogenous zinc excretion is the sum of endogenous excretion via the intestine and other routes, the relationship between total endogenous zinc excretion and quantity of zinc absorbed in adults with a body weight of 76 kg can be calculated using the following equations: men, total endogenous excretion$=0.628\times$(quantity absorbed$+0.2784+1.27$); women, total endogenous excretion$=0.628\times$(quantity absorbed$+0.2784+1.00\times(76/61)^{0.75}$). The quantity of zinc intake necessary to achieve zinc balance, the state in which zinc absorption is equal to total endogenous excretion, has been calculated to be 4.16 mg/d for men and 3.92 mg/d for women. The relationship between zinc absorption and zinc intake is expressed by the following equation (*20–26*): quantity of absorbed zinc $=1.113\times(\text{zinc intake})^{0.5462}$. The EAR for zinc, defined as the minimal intake necessary to maintain zinc balance, for adults with a body weight of 76 kg was determined to be 11.18 mg/d for men and 10.03 mg/d for women. These values were extrapolated to the EAR for each age group of adults aged 18 y or older using the 0.75th power of a weight ratio. The EAR for adolescents aged 12 to 17 y was determined by extrapolation of the EAR for adults using the 0.75th power of a weight ratio and a growth factor.

In a study of Japanese children (mean body weight, 16.34 kg), the minimal intake necessary to maintain zinc balance was estimated to be 3.87 mg/d (*27*). Thus, the EAR for children with a body weight of 16.34 kg was calculated to be 4.06 mg/d, which is obtained by addition of 3.87 mg/d to the sum of integumental and sweat zinc loss (0.19 mg/d). The EAR for children aged 1 to 11 y was determined by extrapolation of 4.06 mg/d to each age group using the 0.75th power of a weight ratio and a growth factor. The additional EAR for pregnant women, which was determined by measurement of zinc storage during pregnancy (0.40 mg/d) (*28*) and extent of zinc absorption (27%) (*19*), was set at 1 mg/d. The additional EAR for lactating women, which was determined by measurement of average zinc content in Japanese breast milk (1.83 mg/L) (*29, 30*), average intake of breast milk in Japanese infants (0.78 L/d) (*11,*

Table 3. Dietary Reference Intakes for copper (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	0.3	—	—	—	0.3	—
6–11 mo	—	—	0.3	—	—	—	0.3	—
1–2 y	0.2	0.3	—	—	0.2	0.3	—	—
3–5 y	0.3	0.3	—	—	0.3	0.3	—	—
6–7 y	0.3	0.4	—	—	0.3	0.4	—	—
8–9 y	0.4	0.5	—	—	0.4	0.5	—	—
10–11 y	0.5	0.6	—	—	0.5	0.6	—	—
12–14 y	0.6	0.8	—	—	0.6	0.8	—	—
15–17 y	0.7	0.9	—	—	0.6	0.7	—	—
18–29 y	0.7	0.9	—	10	0.6	0.7	—	10
30–49 y	0.7	0.9	—	10	0.6	0.7	—	10
50–69 y	0.7	0.9	—	10	0.6	0.7	—	10
≥70 y	0.6	0.8	—	10	0.5	0.7	—	10
Pregnant women (amount to be added)					+0.1	+0.1	—	—
Lactating women (amount to be added)					+0.5	+0.6	—	—

12), and extent of zinc absorption by lactating women (53%) (*31*), was set at 3 mg/d.

Because there is no remarkable difference between the zinc intake from breast milk of US and Japanese infants, the AI for Japanese infants aged 0 to 5 mo was set at 2 mg/d in accordance with the US/Canadian DRIs (*19*). The AI for infants aged 6 to 11 mo was mean of the extrapolation of 2 mg/d using the 0.75th power of a weight ratio (2.6 mg/d) and the sum of zinc intake from complementary food and formula milk (3.1 mg/d) (*32*).

Based on the results of a study in which subjects were administered 50 mg/d of zinc supplements (*33*), the LOAEL of zinc was estimated to be 60 mg/d in women with a body weight of 61 kg. Based on this value and an uncertainty factor of 1.5, the UL for adults was set at 0.66 mg/kg/d. Since there are no available data, no ULs for infants, children, pregnancy and lactating women have been set.

Table 2 summarizes the DRIs for zinc. The values are expressed as integral values in consideration of limitations in the accuracy of EAR calculation.

Copper

Background information

Copper functions as a component of several metalloenzymes, including monoamine oxidase, ferroxidase (ceruloplasmin), cytochrome *c* oxidase, and superoxide dismutase (CuSOD). Since ferroxidase is an essential enzyme in heme synthesis, copper deficiency induces normocytic, hypochromic anemia. Simple copper deficiency in human is rare, but has been observed in infants with a low copper intake (*34*) or patients receiving prolonged TPN (*35*).

Determining DRIs

The EAR for copper in adults was determined using biomarkers of copper status. Biomarkers used were plasma copper, urinary copper, and salivary copper levels and plasma CuSOD activity. According to 2 reliable studies using a stable isotope (*36*, *37*), the minimal intake to achieve saturation of these biomarkers is estimated to be 0.72 mg/d. Because the mean body weight of the subjects in these studies was 74.7 kg, the 0.72 mg/d was set as the EAR for adults with a body weight of 74.7 kg. Thus, the EAR for each sex and age group of adults aged 18 y and older was determined by extrapolation of 0.72 mg/d using the 0.75th power of a weight ratio, and the EAR for children and adolescents aged 1 to 17 y by extrapolation of 0.72 mg/d using the 0.75th power of a weight ratio and a growth factor. Based on copper storage (13.7 mg) (*38*) and the extent of dietary copper absorption (60%) (*39*) in a full-term fetus, the additional EAR for pregnant women was determined to be 0.08 (13.7÷280 d÷0.6) mg/d. Based on the average copper concentration (0.35 mg/L) (*40*) and average volume of secretion (0.78 L/d) (*11*, *12*) of breast milk in Japanese women and an estimated copper absorption rate of 60%, (*39*) the additional EAR for lactating women was determined to be 0.455 (0.35×0.78÷0.6) mg/d, and the RDA set equal to 130% of the EAR.

Based on the average copper concentration in breast milk in Japanese women (0.35 mg/L) (*40*) and the average intake of breast milk by Japanese infants (0.78 L/d) (*11*, *12*), the AI for infants aged 0 to 5 mo was determined to be 0.273 (0.35×0.78) mg/d. Based on the average copper concentration in breast milk in Japanese women more than 6 mo after a delivery (0.16 mg/L) (*40*), the average intake of breast milk (0.525 L/d) (*41*, *42*), and the average copper intake from complementary foods (0.195 mg/d) (*32*), the AI for infants aged 6 to 11 mo was determined to be 0.279

Table 4. Dietary Reference Intakes for manganese (mg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	0.01	—	—	—	0.01	—
6–11 mo	—	—	0.5	—	—	—	0.5	—
1–2 y	—	—	1.5	—	—	—	1.5	—
3–5 y	—	—	1.5	—	—	—	1.5	—
6–7 y	—	—	2.0	—	—	—	2.0	—
8–9 y	—	—	2.5	—	—	—	2.5	—
10–11 y	—	—	3.0	—	—	—	3.0	—
12–14 y	—	—	4.0	—	—	—	3.5	—
15–17 y	—	—	4.5	—	—	—	3.5	—
18–29 y	—	—	4.0	11	—	—	3.5	11
30–49 y	—	—	4.0	11	—	—	3.5	11
50–69 y	—	—	4.0	11	—	—	3.5	11
≥70 y	—	—	4.0	11	—	—	3.5	11
Pregnant women (amount to be added)					—	—	+0	—
Lactating women (amount to be added)					—	—	+0	—

(0.16×0.525+0.195) mg/d. Based on estimation of the no observed adverse effect level (NOAEL) of copper (10 mg/d) by a case report from an ingestion study of copper supplements (*43*) and an uncertainty factor of 1.0, the UL for adults was set at 10 mg/d. Since there are no data available, ULs for children and adolescents have not been set.

Table 3 summarizes the DRIs for copper.

Manganese

Background information

Since there are several manganese metalloenzymes, including arginase, pyruvate carboxylase and manganese superoxide dismutase, manganese is considered an essential nutrient. In a human study, 5 of 7 young men fed a low manganese diet (≤0.11 mg/d) for 39 d manifested a skin abnormality diagnosed as miliaria crystallina that was successfully treated by manganese repletion (1.53 to 2.55 mg/d) (*44*). However, the possibility of dietary manganese deficiency is nearly 0% because plant foods, including cereals and beans, contain high levels of manganese.

Determining DRIs

Several manganese balance studies have been performed to estimate manganese requirements (*45, 46*). However, the USA/Canada DRIs concluded that a minimal requirement to maintain manganese balance could not be estimated from a short-term balance study (*47*). Accordingly, as there is insufficient information with which to set the EAR, the AI was set based on the average manganese intake of the Japanese population, which far exceeds the minimal requirement to maintain manganese balance. Based on a review of the manganese intake of the Japanese population, the average manganese intake of adults is estimated to be 3.7 mg/d (*48*). To account for the differences in male and female energy intake, the AI for adults aged 18 y and older was set at 4.0 mg/d for men and 3.5 mg/d for women. The AI for children and adolescents aged 1 to 17 y was determined by extrapolation of the AI using the 0.75th power of a weight ratio and a growth factor. Based on the average manganese concentration in breast milk in Japanese women (0.011 mg/L) (*40*) and the average intake of breast milk in Japanese infants (0.78 L/d) (*11, 12*), the AI for infants aged 0 to 5 mo was set at 0.086 (0.011×0.78) mg/d. Based on the average manganese concentration in breast milk in Japanese women, the average intake of breast milk (0.525 L/d) (*41, 42*), and the average manganese intake from complementary foods (0.44 mg/d) (*32*), the AI for infants aged 6 to 11 mo was set at 0.45 (0.011×0.525+0.44) mg/d.

The AI for women who are not pregnant/lactating (3.5 mg/d) far exceeds the AI for pregnant women in the USA/Canada DRIs (2.0 mg/d) (*47*). Accordingly, the AI for pregnant women was set at the same value as the AI for women who are not pregnant (3.5 mg/d). Based on the average manganese concentration in breast milk in Japanese women (0.011 mg/L) (*40*), the average intake of breast milk in Japanese infants (0.78 L/d) (*11, 12*), and the average extent of absorption of dietary manganese (about 5%) (*49*), manganese loss by lactation is estimated to be less than 0.3 (0.011×0.78÷0.05) mg/d, which is much lower than the AI for women who are not pregnant/lactating (3.5 mg/d). Therefore, the AI for lactating women was set at the same value of the AI for women who are not pregnant/lactating.

Based on the manganese intake of vegetarians (*47, 50*), the USA/Canada DRIs estimated the NOAEL of manganese to be 11 mg/d. Based on this value and an uncertainty factor of 1.0, the UL for manganese in

Table 5. Dietary Reference Intakes for iodine (μg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	100	250	—	—	100	250
6–11 mo	—	—	130	250	—	—	130	250
1–2 y	35	50	—	250	35	50	—	250
3–5 y	45	60	—	350	45	60	—	350
6–7 y	55	75	—	500	55	75	—	500
8–9 y	65	90	—	500	65	90	—	500
10–11 y	75	110	—	500	75	110	—	500
12–14 y	95	130	—	1,300	95	130	—	1,300
15–17 y	100	140	—	2,100	100	140	—	2,100
18–29 y	95	130	—	2,200	95	130	—	2,200
30–49 y	95	130	—	2,200	95	130	—	2,200
50–69 y	95	130	—	2,200	95	130	—	2,200
≥70 y	95	130	—	2,200	95	130	—	2,200
Pregnant women (amount to be added)					+75	+110	—	—
Lactating women (amount to be added)					+100	+140	—	—

adults was set at 11 mg/d. Since there are no data available, ULs for children and adolescents have not been set.

Table 4 summarizes the DRIs for manganese.

Iodine

Background information

Iodine is an essential component of thyroid hormone. As such, iodine deficiency induces mental retardation, hypothyroidism, goiter, cretinism, and varying degrees of other growth and development abnormalities.

Marine products contain iodine at high levels, in particular, *kombu* (a type of kelp) contains it at more than 2 mg/g dry weight. Since the Japanese routinely eat *kombu*, their average iodine intake is very much higher than that of other populations. Based on measurement of urinary iodine excretion (*51, 52*), annual consumption of *kombu* (*53*), and chemical iodine analysis of duplicate diets (*54, 55*), the average iodine intake of the Japanese, which has been found to be intermittently high, is estimated to be 1.5 mg/d.

Determining DRIs

Similar to the USA/Canada DRIs (*56*), the EAR for iodine was determined by measurement of thyroid iodine accumulation and turnover. Based on the results of 2 USA studies (*57, 58*), the average accumulation of radioiodine by the thyroid gland is estimated to be 93.9 μg/d in adults. Thus, the EAR for adults aged 18 y and older was set at 95 μg/d, and the RDA set equal to 140% of the EAR. The EAR for children and adolescents aged 1 to 17 y was determined by extrapolation of the EAR for adults aged 18 to 29 y using the 0.75th power of a weight ratio and a growth factor.

The iodine content of Japanese breast milk varies markedly with iodine intake (*59*). When a woman's iodine intake is less than 1.5 mg/d or her *kombu* ingestion is restricted, the average iodine content in her breast milk is estimated to be 133 μg/L (*59, 60*). Based on this average iodine concentration of breast milk and the average intake of breast milk in Japanese infants (0.78 L/d) (*11, 12*), the AI for infants aged 0 to 5 mo was set at 100 (133×0.78) μg/d. The AI for infants aged 6 to 11 mo (130 μg/d) was determined by extrapolation of this value using the 0.75th power of a weight ratio.

Based on the median value of iodine turnover in newborn infants (75 μg/d) (*61*), the additional EAR for pregnant women was set at 75 μg/d. Based on the average iodine content in breast milk in Japanese women (133 μg/L) (*59, 60*), the average intake of breast milk in Japanese infants (0.78 L/d) (*11, 12*), and the extent of absorption of dietary iodine (100%), the additional EAR for lactating women was determined to be 100 (133×0.78) μg/d, and the RDA set equal to 140% of the EAR.

Initially, excessive iodine intake also induces hypothyroidism and goiter, a phenomenon referred to as the Wolff-Chaikoff effect. However, the Wolff-Chaikoff effect does not occur with continuous excessive iodine intake, a phenomenon referred to as "escape." Based on the results of an epidemiological study of subjects living in a coastal area of Hokkaido (*62, 63*), which estimated the NOAEL of iodine for Japanese adults to be 3.3 mg/d, and an uncertainty factor of 1.5, the UL for iodine in adults was set at 2.2 mg/d. As this UL applies to continuous daily iodine intake, it is not necessary to restrict intermittent high iodine (up to about 5 mg/d) intake.

In a study of children aged 6 to 12 y, a significant increase in thyroid size was observed in subjects whose estimated iodine intake was more than 500 μg/d (*64*). Based on this observation, the UL for children aged 6

Table 6. Dietary Reference Intakes for selenium (μg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	15	—	—	—	15	—
6–11 mo	—	—	15	—	—	—	15	—
1–2 y	10	10	—	50	10	10	—	50
3–5 y	10	15	—	70	10	15	—	70
6–7 y	15	15	—	100	15	15	—	100
8–9 y	15	20	—	120	15	20	—	120
10–11 y	20	25	—	160	20	20	—	150
12–14 y	25	30	—	210	20	25	—	200
15–17 y	25	35	—	260	20	25	—	220
18–29 y	25	30	—	280	20	25	—	220
30–49 y	25	30	—	300	20	25	—	230
50–69 y	25	30	—	280	20	25	—	230
≥70 y	25	30	—	260	20	25	—	210
Pregnant women (amount to be added)					+5	+5	—	—
Lactating women (amount to be added)					+15	+20	—	—

to 11 y was set at 500 μg/d. The UL for children aged 1 to 5 y was determined by extrapolation of the UL for children aged 6 to 7 y using a weight ratio. The UL for adolescents aged 12 to 14 y was set as the mean of 2 values: the value of the extrapolation of the UL for children aged 10 to 11 y using a weight ratio and the value of the extrapolation of the UL for adults aged 18 to 29 y using a weight ratio. The UL for adolescents aged 15 to 17 y was determined by extrapolation of the UL for adults aged 18 to 29 y using a weight ratio.

Based on a case report of hypothyroidism in infants fed breast milk (*60*), the NOAEL of iodine for infants ages 0 through 5 mo is estimated to be 254 μg/d. Based on this value and an uncertainty factor of 1.0, the UL for infants aged 0 to 5 mo was set at 250 μg/d. Since the UL is 250 μg/d for both infants aged 0 through 5 mo and children aged 1 to 2 y, the UL for infants aged 6 to 11 mo was also set at 250 μg/d.

Excessive ingestion of iodine by pregnant or lactating women can cause hypothyroidism in their infants. In a case report of hypothyroidism in infants fed breast milk (*60*), the mothers' iodine intake from *kombu* was estimated to be 2.28 to 3.18 mg/d. If the iodine intake from foods other than *kombu* is taken into consideration, their total iodine intake would exceed the UL for women who are not pregnant. Accordingly, the UL for women who are not pregnant can be applied to pregnant and lactating women.

Table 5 summarizes the DRIs for iodine.

Selenium

Background information

Selenium functions as a form of selenocysteine residue in protein. Genome analysis has identified 25 selenium-containing proteins in humans, including glutathione peroxidase (GPX), iodothyronine deiodinase, and thioredoxin reductase. Keshan disease, an endemic form of fatal cardiomyopathy that has been observed in children living in a low-selenium area of China, has been firmly linked to selenium deficiency, with administration of selenium having been found to prevent it (*65*). Several clinical selenium-responsive syndromes have been observed in patients receiving prolonged TPN, among whom one patient with an extremely low plasma selenium concentration (9 ng/mL) developed muscle pain and tenderness in the thighs, resulting in an inability to walk (*66*), while another developed a cardiomyopathy and died after a cardiac arrest secondary to septic shock (*67*).

Determining DRIs

Synthesis of selenium-containing protein is strongly associated with selenium intake. The relationship between selenium intake and plasma GPX activity has been particularly well established. In the USA/Canada DRIs, the EAR for selenium was set based on determination of the minimal intake resulting in saturation in plasma GPX activity (45 μg/d for adults with a body weight of 76 kg) (*68*). However, the WHO concluded that selenium deficiency is prevented when 2/3 of the value of saturated plasma GPX activity is maintained (*69*). Based on the results of a Chinese study (*70*), the selenium intake necessary to maintain 2/3 of the value of saturated plasma GPX activity is estimated to be 24.2 μg/d for adults with a body weight of 60 kg. Accordingly, the EAR for selenium in adults aged 18 y and older was calculated by extrapolation of this value using the 0.75th power of a weight ratio. The EAR for children and adolescents aged 1 to 17 y was calculated by extrapolation of this value using the 0.75th power of a weight ratio and a growth factor.

Table 7. Dietary Reference Intakes for chromium (μg/d).[1]

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	0.8	—	—	—	0.8	—
6–11 mo	—	—	1.0	—	—	—	1.0	—
1–2 y	—	—	—	—	—	—	—	—
3–5 y	—	—	—	—	—	—	—	—
6–7 y	—	—	—	—	—	—	—	—
8–9 y	—	—	—	—	—	—	—	—
10–11 y	—	—	—	—	—	—	—	—
12–14 y	—	—	—	—	—	—	—	—
15–17 y	—	—	—	—	—	—	—	—
18–29 y	35	40	—	—	25	30	—	—
30–49 y	35	40	—	—	25	30	—	—
50–69 y	30	40	—	—	25	30	—	—
≥70 y	30	35	—	—	20	25	—	—
Pregnant women					—	—	—	—
Lactating women					—	—	—	—

[1] Computed using the estimated energy requirement for physical activity level II.

Based on average body selenium concentration (250 μg/kg) (*71*) and the sum of placenta and birth weight (3.5 kg), fetal and placental selenium storage is estimated to be approximately 900 μg (250×3.5) during pregnancy. Based on average blood selenium concentration (184 μg/L), the increased selenium requirement due to increase in blood volume (1.5 L) during pregnancy is estimated to be approximately 300 μg (*72*). Because absorption of dietary selenium is estimated to be about 90% (*73*), the additional EAR for pregnancy is estimated to be 4.8 ((900+300)÷280 d÷0.9) μg/d, and the RDA set equal to 120% of the EAR. Based on the average selenium content in the breast milk of Japanese women (17 μg/L) (*40*), the average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*), and the extent of absorption of dietary selenium (90%) (*73*), the additional EAR for lactating women was set at 15 (17×0.78÷0.9) μg/d, and the RDA set equal to 120% of the EAR.

Based on the average selenium concentration in the milk of Japanese women (17 μg/L) (*40*) and the average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*), the AI for infants aged 0 to 5 mo was set at 13.3 (17×0.78) μg/d. The AI for infants aged 6 to 11 mo was determined by extrapolation of 13.3 μg/d using the 0.75th power of a weight ratio.

Based on a Chinese report of chronic selenium intoxication, the NOAEL of selenium is estimated to be 13.3 μg/kg/d (*74*). However, an epidemiological study found that long-term supplementation of 200 μg/d of selenium increased the incidence of Type 2 diabetes in subjects with sufficient selenium intake (*75*), indicating that supplementation at this level causes adverse effects if intake through other sources is adequate. The average selenium intake of the Japanese population is estimated to be approximately 100 μg/d (*76*), which far exceeds the RDA of selenium. Thus, the UL of selenium was set at 300 (100+200) μg/d for men aged 30 to 49 y, whose mean body weight (68.5 kg) is the highest among the sex and age groups. The ULs for other sex and age groups, including children and adolescents, were determined by extrapolation of 300 μg/d using a weight ratio.

Table 6 summarizes the DRIs for selenium.

Chromium

Background information

Trivalent chromium is believed to enhance the action of insulin in the form of a chromium-binding oligopeptide. Patients receiving prolonged TPN without chromium supplementation have been observed to experience glucose intolerance together with several symptoms and disorders, including weight loss, peripheral neuropathy, and low respiratory quotient (*77*). Since these symptoms disappear with administration of trivalent chromium, their origin has been attributed to chromium deficiency.

Determining DRIs

As there is currently no means of determining the metabolic balance of chromium in adults, the USA/Canada DRIs set the AI for chromium based on a chromium intake study (*78*). Because no study has investigated chromium intake in Japan, the EAR was tentatively based on the results of a balance test of chromium in the elderly (*79*), in which a positive balance was observed in subjects whose average chromium intake was 12.8 μg/1,000 kcal. Accordingly, the EAR for adults aged 18 y and older was determined based on the an average chromium intake of 12.8 μg/1,000 kcal and the estimated energy requirement for physical activity level II, and the RDA for chromium set equal to 120% of the EAR. The EAR for children and adolescents aged 1 to 17 y has not been set due to the tentative nature of the

Table 8. Dietary Reference Intakes for molybdenum (μg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	2	—	—	—	2	—
6–11 mo	—	—	3	—	—	—	3	—
1–2 y	—	—	—	—	—	—	—	—
3–5 y	—	—	—	—	—	—	—	—
6–7 y	—	—	—	—	—	—	—	—
8–9 y	—	—	—	—	—	—	—	—
10–11 y	—	—	—	—	—	—	—	—
12–14 y	—	—	—	—	—	—	—	—
15–17 y	—	—	—	—	—	—	—	—
18–29 y	20	25	—	550	20	20	—	450
30–49 y	25	30	—	600	20	25	—	500
50–69 y	20	25	—	600	20	25	—	500
≥70 y	20	25	—	550	20	20	—	450
Pregnant women					—	—	—	—
Lactating women (amount to be added)					+3	+3	—	—

adult EAR, nor has the EAR for either pregnant women or lactating women, the former due to lack of data and the latter due to an inability to measure absorption of dietary chromium.

Based on the median chromium concentration in milk in Japanese women (1.0 μg/L) (*80*) and the average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*), the AI for infants aged 0 to 5 mo was set at 0.78 μg/d. The AI for infants aged 6 to 11 mo was determined by extrapolation of 0.78 μg/d using the 0.75th power of a weight ratio.

The UL for chromium has not been set because the quantitative relationship between trivalent chromium intake and the possible adverse effects of excessive trivalent chromium intake has been insufficiently established.

Table 7 summarizes the DRIs for chromium.

Molybdenum

Background information

Molybdenum functions as a cofactor for a limited number of enzymes, including xanthine oxidase, aldehyde oxidase, and sulfite oxidase in mammals, and is believed to be an essential trace element in animal nutrition. Human nutritional deficiency of molybdenum was observed in a patient subjected to prolonged TPN (*81*), who manifested clinical symptoms suggestive of sulfite oxidase deficiency. Other symptoms, including irritability, leading to coma, tachycardia, tachypnea, and night blindness, have been reported.

Determining DRIs

The EAR for molybdenum was based on the results of a human balance test of 4 American male subjects (mean body weight, 76.4 kg), all of whom showed a positive balance and no manifestation of any disorder when they ingested 22 μg/d of molybdenum for 102 d (*82*). Based on estimation of integumental and sweat molybdenum loss (3 μg/d) (*83*), the EAR for adults with a body weight of 76.4 kg was calculated to be 25 μg/d. The EAR for adults aged 18 y and older was calculated by extrapolation of 25 μg/d using the 0.75th power of a weight ratio. Since the EAR for adults is based on 1 study of only 4 subjects, the EAR for children and adolescents aged 1 to 17 y has not been set, nor has the additional EAR for pregnant women due to lack of data. Based on the average molybdenum content of the milk of Japanese women (3 μg/L) (*80*, *84*), the average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*), and the extent of absorption of dietary molybdenum (93%) (*85*), the additional EAR for lactating women was set at 3 μg/d (3×0.78÷0.93), and the RDA for molybdenum set equal to 120% of the EAR.

Based on the average molybdenum content of the milk of Japanese women (3 μg/L) (*80*, *84*) and the average intake of breast milk in Japanese infants (0.78 L/d) (*11*, *12*), the AI for infants aged 0 to 5 mo was set at 3 (3×0.78) μg/d. The AI for infants aged 6 to 11 mo was determined by extrapolation of 2.34 μg/d using the 0.75th power of a weight ratio.

Due to the lack of data regarding the dose-dependent adverse effects of excessive molybdenum intake in humans, the UL for molybdenum is based on the NOAEL of molybdenum for rats (900 μg/kg/d) (*86*). Based on the NOAEL and an uncertainty factor of 100, the UL for adults aged 18 y and older was set at 9 μg/kg/d. Due to lack of data, ULs for children and adolescents have not been set.

Table 8 summarizes the DRIs for molybdenum.

Dr. Takatoshi Esashi, who is one of the authors, passed away on March 26, 2012. He was a leader of the working group for minerals in the decision of DRIs for Japanese, 2010. We would like to offer our respectful condolences on his death.

REFERENCES

1) Ministry of Health, Labour and Welfare, Japan. 2011. Outline of the National Health and Nutritional Survey of Japan in 2008, p 195. Dai-ichi Shuppan, Tokyo (in Japanese).

2) Green R, Charlton R, Seftel H, Bothwell T, Mayet F, Adams B, Finch C, Layrisse M. 1968. Body iron excretion in man: a collaborative study. *Am J Med* **45**: 336–353.

3) Yokoi K. 2003. Numerical methods for estimating iron requirements from population data. *Biol Trace Elem Res* **95**: 155–172.

4) Nogami Y. 1966. Studies on the amount of menstruation. *Nippon Funin Gakkai Zasshi (Jap J Fert Ster)* **11**: 189–203 (in Japanese).

5) Hawkins WW. 1964. Iron, copper and cobalt. *In*: Nutrition: A Comprehensive Treatise (Beaton GH, McHenry EW, eds), p 309–372. Academic Press, New York.

6) Beaton GH, Corey PN, Steele C. 1989. Conceptual and methodological issues regarding the epidemiology of iron deficiency and their implications for studies of the functional consequences of iron deficiency. *Am J Clin Nutr* **50**: 575–585.

7) Smith NJ, Rios E. 1974. Iron metabolism and iron deficiency in infancy and childhood. *Adv Pediatr* **21**: 239–280.

8) Dallman PR. 1986. Iron deficiency in the weanling: a nutritional problem on the way to resolution. *Acta Paediatr Scand* **323**: 59–67.

9) Bothwell TH, Charlton RW. 1981. Iron Deficiency in Women, p 7–9. The Nutrition Foundation, Washington DC.

10) Hirai Y, Kawakata N, Satoh K, Ikeda Y, Hisayasu S, Orimo H, Yoshino Y. 1990. Concentrations of lactoferrin and iron in human milk at different stages of lactation. *J Nutr Sci Vitaminol* **36**: 531–544.

11) Suzuki K, Sasaki S, Shinzawa K, Totani M. 2004. Milk intake by breast-fed infants before weaning. *Eiyo-gaku Zasshi (Jpn J Nutr Diet)* **62**: 369–372 (in Japanese).

12) Hirose J, Endo M, Nagao S, Mizushima K, Narita H. 2008. Amount of breast milk sucked by Japanese breast feeding infants. *J Jpn Soc Breastfeeding Res* **2**: 23–28 (in Japanese).

13) FAO/WHO Expert Consultation. 1988. Requirements of Vitamin A, Iron, Folate and Vitamin B12. FAO Food and Nutrition Series No. 23, p 33–50. Food and Agriculture Organization of the United Nations, Rome.

14) Barrett JF, Whittaker PG, Williams JG, Lind T. 1994. Absorption of non-haem iron from food during normal pregnancy. *BMJ* **309**: 79–82.

15) FAO/WHO. 1983. Evaluation of certain food additives and contaminants (27th report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696.

16) Food and Drug Administration. 1997. Federal Register 62. 2217–2250, January 15, 1997. Iron-containing supplements and drugs: label warning statements and unit-dose packaging requirements. Downloaded from http://vm.cfsan.fda.gov/~lrd/fr970115.html.

17) Okada A, Takagi Y, Itakura T, Satani M, Manabe H. 1976. Skin lesions during intravenous hyperalimentation: zinc deficiency. *Surgery* **80**: 629–635.

18) Iwata H, Fujisawa S, Takeuchi M, Morishima T, Kubota A. 1990. Two brother cases of acquired acrodermatitis enteropathica caused by mother's milk with low levels of zinc. *Hifuka no Rinsho* **32**: 951–955 (in Japanese).

19) Food and Nutrition Board, Institute of Medicine. 2001. Zinc. *In*: Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (Institute of Medicine, ed), p 442–501. National Academies Press, Washington DC.

20) Jackson MJ, Jones DA, Edwards RH, Swainbank IG, Coleman ML. 1984. Zinc homeostasis in man: Studies using a new stable-dilution technique. *Br J Nutr* **51**: 199–208.

21) Hunt JR, Mullen LK, Lykken GI. 1992. Zinc retention from an experimental diet based on the U.S. F.D.A. total diet study. *Nutr Res* **112**: 1335–1344.

22) Lee DY, Prasad AS, Hydrick-Adair C, Brewer G, Johnson PE. 1993. Homeostasis of zinc in marginal human zinc deficiency: Role of absorption and endogenous excretion of zinc. *J Lab Clin Med* **122**: 549–556.

23) Taylor CM, Bacon JR, Aggett PJ, Bremner I. 1991. Homeostatic regulation of zinc absorption and endogenous losses in zinc-deprived men. *Am J Clin Nutr* **53**: 755–763.

24) Turnlund JR, King JC, Keyes WR, Gong B, Michel MC. 1984. A stable isotope study of zinc absorption in young men: Effects of phytate and alpha-cellulose. *Am J Clin Nutr* **40**: 1071–1077.

25) Wada L, Turnlund JR, King JC. 1985. Zinc utilization in young men fed adequate and low zinc intakes. *J Nutr* **115**: 1345–1354.

26) Turnlund JR, Durkin N, Costa F, Margen S. 1986. Stable isotope studies of zinc absorption and retention in young and elderly men. *J Nutr* **116**: 1239–1247.

27) Suzuki K, Goto S, Kanke Y, Kitano T, Koishi H. 1983. The zinc and copper balance of the preadolescent children. *Nippon Eiyô Shokuryô Gakkaishi (J Jpn Soc Nutr Food Sci)* **36**: 231–237 (in Japanese).

28) Swanson CA, King JC. 1987. Zinc and pregnancy outcome. *Am J Clin Nutr* **46**: 763–771.

29) Higashi A, Ikeda T, Uehara I, Matsuda I. 1982. Zinc and copper contents in breast milk of Japanese women. *Tohoku J Exp Med* **137**: 41–47.

30) Ohtake M, Tamura T. 1993. Changes in zinc and copper concentrations in breast milk and blood of Japanese women during lactation. *J Nutr Sci Vitaminol* **39**: 189–200.

31) Sian L, Krebs NF, Westcott JE, Fengliang L, Tong L, Miller LV, Sonko B, Hambidge M. 2002. Zinc homeostasis during lactation in a population with a low zinc intake. *Am J Clin Nutr* **75**: 99–103.

32) Nakano T, Kato K, Kobayashi N, Shimatani M, Ishii K, Takimoto H, Totani M. 2003. Nutrient intake from baby foods, infant formula and cow's milk. Results from a nation-wide infant's dietary survey. *Shoni Hoken Kenkyu (J Jpn Soc Child Health)* **62**: 630–639 (in Japanese).

33) Black MR, Medeiros DM, Brunett E, Welke R. 1988. Zinc supplements and serum lipids in young adult white males. *Am J Clin Nutr* **47**: 970–975.

34) Shaw JCL. 1992. Copper deficiency in term and preterm infants. *In*: Nutritional Anemias (Fomon SJ, Zlotkin S, eds), p 105–117. Vevey/Raven Press, New York.

35) Fujita M, Itakura T, Takagi Y, Okada M. 1989. Copper

deficiency during total parenteral nutrition: Clinical analysis of three cases. *J Parent Enter Nutr* **13**: 421–425.

36) Turnlund JR, Keen CL, Smith RG. 1990. Copper status and urinary and salivary copper in young men at three levels of dietary copper. *Am J Clin Nutr* **51**: 658–664.

37) Turnlund JR, Scott KC, Peiffer GL, Jang AM, Keyes WR, Keen CL, Sakanashi TM. 1997. Copper status of young men consuming a low-copper diet. *Am J Clin Nutr* **65**: 72–78.

38) Widdowson EM, Dickerson JWT. 1964. Chemical composition of the body. *In*: Mineral Metabolism: An Advanced Treatise (Comar CL, Bronner F, eds), Vol II, Part A, p 1–248. Academic Press, New York.

39) Turnlund JR, Keyes WR, Peiffer GL, Scott KC. 1998. Copper absorption, excretion, and retention by young men consuming low dietary copper determined by using the stable isotope 65Cu. *Am J Clin Nutr* **67**: 1219–1225.

40) Yamawaki N, Yamada M, Kan-no T, Kojima T, Kaneko T, Yonekubo A. 2005. Macronutrient, mineral and trace element composition of breast milk from Japanese women. *J Trace Elem Med Biol* **19**: 171–181.

41) Yoneyama K. 1998. Growth of breast-fed infants and intake of nutrients from breast-milk. *Shoni Hoken Kenkyu (J Jpn Soc Child Health)* **57**: 49–57 (in Japanese).

42) Yoneyama K, Goto I, Nagata H. 1995. Changes in the concentrations of nutrient components of human milk during lactation. *Nippon Koshu Eisei Zasshi (Jpn J Public Health)* **42**: 472–481 (in Japanese).

43) Pratt WB, Omdahl JL, Sorenson JR. 1985. Lack of effects of copper gluconate supplementation. *Am J Clin Nutr* **42**: 681–682.

44) Friedman BJ, Freeland-Graves JH, Bales CW, Behmardi F, Shorey-Kutschke RL, Willis RA, Crosby JB, Trickett PC, Houston SD. 1987. Manganese balance and clinical observation in young men fed manganese-deficient diet. *J Nutr* **117**: 133–143.

45) Freeland-Graves JH, Behmardi F, Bales CW, Dougherty V, Lin PH, Crosby JB, Trickett PC. 1988. Metabolic balance of manganese in young men consuming diets containing five levels of dietary manganese. *J Nutr* **118**: 764–773.

46) Nishimuta M, Inoue N, Kodama N, Morikuni E, Yoshioka YH, Matsuzaki N, Shimada M, Sato N, Iwamoto T, Ohki K, Takeyama H, Nishimuta H. 2006. Moisture and mineral content of human feces-high fecal moisture is associated with increased sodium and decreased potassium content. *J Nutr Sci Vitaminol* **52**: 121–126.

47) Food and Nutrition Board, Institute of Medicine. 2001. Manganese. *In*: Dietary Reference Intake for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (Institute of Medicine, ed), p 394–419. National Academies Press, Washington DC.

48) Shiraishi K. 1994. Intake of trace elements. *Rinsho Eiyo (Jpn J Clin Nutr)* **84**: 381–389 (in Japanese).

49) Johnson PE, Lykken GI, Korynta ED. 1991. Absorption and biological half-life in humans of intrinsic and extrinsic 54Mn tracers from foods of plant origin. *J Nutr* **121**: 711–717.

50) Schroeder HA, Balassa JJ, Tripton IH. 1966. Essential trace metals in man: Manganese. A studying homeostasis. *J Chron Dis* **19**: 545–571.

51) 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.

52) 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.

53) Nagataki S. 2008. The average of dietary iodine intake due to the ingestion of seaweed is 1.2 mg/day in Japan. *Thyroid* **18**: 667–668.

54) Suzuki M, Tamura T. 1985. Iodine intake of Japanese male university students: Urinary iodine excretion of sedentary and physically active students and sweat iodine excretion during exercise. *J Nutr Sci Vitaminol* **31**: 409–415.

55) Katamine S, Mamiya Y, Sekimoto K, Hoshino N, Totsuka K, Naruse U, Watabe A, Sugiyama R, Suzuki M. 1986. Iodine content of various meals currently consumed by urban Japanese. *J Nutr Sci Vitaminol* **32**: 487–495.

56) Food and Nutrition Board, Institute of Medicine. 2001. Iodine. *In*: Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (Institute of Medicine, ed), p 258–289. National Academies Press, Washington DC.

57) Fisher DA, Oddie TH. 1969. Thyroidal radioiodine clearance and thyroid iodine accumulation: contrast between random daily variation and population data. *J Clin Endocrinol Metab* **29**: 111–115.

58) Fisher DA, Oddie TH. 1969. Thyroid iodine content and turnover in euthyroid subjects: validity of estimation of thyroid iodine accumulation from short-term clearance studies. *J Clin Endocrinol Metab* **29**: 721–727.

59) Muramatsu Y, Sumiya M, Ohmomo Y. 1983. Stable iodine contents in human milk related to dietary algae consumption. *Hoken Butsuri* **18**: 113–117.

60) Nishiyama S, Mikeda T, Okada T, Nakamura K, Kotani T, Hishinuma A. 2004. Transient hypothyroidism or persistent hyperthyrotropinemia in neonates born to mothers with excessive iodine intake. *Thyroid* **14**: 1077–1083.

61) Delange F. 1989. Iodine nutrition and congenital hypothyroidism. *In*: Research in Congenital Hypothyroidism (Delange F, Fisher DA, Glinoer D, eds), p 173–185. Plenum press, New York.

62) Konno N, Makita H, Yuri K, Iizuka N, Kawasaki K. 1994. Association between dietary iodine intake and prevalence of subclinical hypothyroidism in the coastal regions of Japan. *J Clin Endocrinol Metab* **78**: 393–397.

63) Konno N, Iizuka N, Kawasaki K, Taguchi H, Miura K, Taguchi S, Murakami K, Hagiwara K, Noda Y, Ukawa S. 1994. Screening for thyroid dysfunction in adults residing in Hokkaido Japan, in relation to urinary iodine concentration and thyroid autoantibodies. *Hokkaido Igaku Zasshi* **69**: 614–626 (in Japanese).

64) Zimmermann MB, Ito Y, Hess SY, Fujieda K, Molinari L. 2005. High thyroid volume in children with excess dietary iodine intake. *Am J Clin Nutr* **81**: 840–844.

65) Chen X, Yang G, Chen J, Chen X, Wen Z, Ge K. 1980. Studies on the relations of selenium and Keshan disease. *Biol Trace Elem Res* **2**: 91–107.

66) van Rij AM, Thomson CD, McKenzie JM, Robinson MF.

1979. Selenium deficiency in total parenteral nutrition. *Am J Clin Nutr* **32**: 2076–2085.

67) Lockitch G, Taylor GP, Wong LT, Davidson AG, Dison PJ, Riddell D, Massing B. 1990. Cardiomyopathy associated with nonendemic selenium deficiency in a Caucasian adolescent. *Am J Clin Nutr* **52**: 572–577.

68) Food and Nutrition Board, Institute of Medicine. 2000. Selenium. *In*: Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (Institute of Medicine, ed), p 284–324. National Academies Press, Washington DC.

69) WHO/FAO/IAEA. 1996. Selenium. *In*: Trace Elements in Human Nutrition and Health, p 105–122. WHO, Geneva.

70) Yang GQ, Ge KY, Chen JS, Chen XS. 1988. Selenium-related endemic diseases and the daily selenium requirement of humans. *World Rev Nutr Diet* **55**: 98–152.

71) Schroeder HA, Frost DV, Balassa JJ. 1970. Essential trace metals in man: selenium. *J Chronic Dis* **23**: 227–243.

72) Himeno S. 2010. Selenium. *Nippon Rinsho* **68** (Suppl 1): 329–332 (in Japanese).

73) Sunde RA. 2006. Selenium. *In*: Present Knowledge in Nutrition (Bowman BA, Russell RM, eds), 9th ed, p 480–497. ILSI Press, Washington DC.

74) Yang GQ, Zhou RH. 1994. Further observations on the human maximum safe dietary selenium intake in a seleniferous area of China. *J Trace Elem Electrolytes Health Dis* **8**: 159–165.

75) Stranges S, Marshall JR, Natarajan R, Donahue RP, Trevisan M, Combs GF, Cappuccio FP, Ceriello A, Reid ME. 2007. Effects of long-term selenium supplementation on the incidence of type 2 diabetes: a randomized trial. *Ann Intern Med* **147**: 217–223.

76) Yoshida M. 1992. Selenium intake and blood selenium level in Japanese. *Nippon Eiyô Shokuryô Gakkaishi (J Jpn Soc Nutr Food Sci)* **45**: 485–494 (in Japanese).

77) Jeejeebhoy KN, Chu RC, Marliss EB, Greenberg GR, Bruce-Robertson A. 1977. Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition. *Am J Clin Nutr* **30**: 531–538.

78) Food and Nutrition Board, Institute of Medicine. 2001. Chromium. *In*: Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc (Institute of Medicine, ed), p 197–223. National Academies Press, Washington DC.

79) Bunker VW, Lawson MS, Delves HT, Clayton BE. 1984. The uptake and excretion of chromium by the elderly. *Am J Clin Nutr* **39**: 797–802.

80) Yoshida M, Takada A, Hirose J, Endo M, Fukuwatari T, Shibata K. 2008. Molybdenum and chromium concentrations in breast milk from Japanese women. *Biosci Biotechnol Biochem* **72**: 2247–2250.

81) Abumrad NN, Schneider AJ, Steel D, Rogers LS. 1981. Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdate therapy. *Am J Clin Nutr* **34**: 2551–2559.

82) Turnlund JR, Keyes WR, Peiffer GL. 1995. Molybdenum absorption, excretion, and retention studied with stable isotopes in young men at five intakes of dietary molybdenum. *Am J Clin Nutr* **62**: 790–796.

83) Food and Nutrition Board, Institute of Medicine. 2001. Molybdenum. *In*: Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (Institute of Medicine, ed), p 420–441. National Academies Press, Washington DC.

84) Yoshida M, Itô C, Hattori H, Tsuchita H, Yonekubo A, Nishimuta M. 2004. Molybdenum contents in human milk and formula milk, and estimation of molybdenum intake of infants in Japan. *Trace Nutr Res* **21**: 59–64 (in Japanese).

85) Yoshida M, Hattori H, Ota S, Yoshihara K, Kodama N, Yoshitake Y, Nishimuta M. 2006. Molybdenum balance in healthy young Japanese women. *J Trace Elem Med Biol* **20**: 245–252.

86) Fungwe TV, Buddingh F, Demick DS, Lox CD, Yang MT, Yang SP. 1990. The role of dietary molybdenum on estrous activity, fertility, reproduction and molybdenum and copper enzyme activities of female rats. *Nutr Res* **10**: 515–524.