fatty acids leads to an increase in blood LDL-cholesterol and a decrease in HDL-cholesterol concentration, resulting in an increase in the LDL-cholesterol/HDL-cholesterol and total cholesterol/HDL-cholesterol ratios in a dose-dependent manner (*81*). High intake of trans fatty acids has also been associated with increased risk of CHD in a dose-dependent manner (*11*). However, it is unclear whether the incidence of CHD is significantly higher among average Japanese adults, who consume a low amount of trans fatty acids, than it is among Japanese adults who consume no trans fatty acids at all. Nevertheless, it is conceivable that in individuals with multiple risk factors for CHD, such as smoking, hypertension, diabetes mellitus, and dyslipidemia, increased intake of trans fatty acids may promote atherosclerosis to a greater degree than in individuals without these risk factors. Increased intake of trans fatty acids may increase the incidence of several diseases, such as CHD, obesity, and allergies and result in lower birth weight and increased risk of fetal loss, especially in individuals with other risk factors. Therefore, it is recommended that we eat less trans fatty acids at all ages.

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J Nutr Sci Vitaminol, 59, S53–S56, 2013

Dietary Reference Intakes for Japanese 2010: Carbohydrates

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(Received October 26, 2012)

Summary The Dietary Reference Intakes (DRIs) of carbohydrates and dietary fiber were determined for Japanese. The estimated average requirement (EAR) and recommended dietary allowance (RDA) for carbohydrates were not determined because of insufficient data. The tentative dietary goal for preventing lifestyle-related diseases (DG) for children aged 1 y and above was determined for carbohydrates (% energy). In addition, the DG for adults aged 18 y and above was determined for dietary fiber. Dietary fiber intake is associated with myocardial infarction; therefore, the DG was determined on the basis of the results of a meta-analysis and the median dietary fiber intake of Japanese. The DG for alcohol was not determined because of insufficient data.

Key Words carbohydrate, dietary fibers, alcohol, lifestyle-related diseases

Introduction

A carbohydrate comprises either a monosaccharide or its polymer (*1*). Carbohydrates play an important nutritional role as an energy source; digestible carbohydrates (i.e., sugars and starches) contain approximately 4 kcal of energy/g. Although there is no internationally standardized definition, dietary fiber is usually considered an indigestible component in the diet, many of which are carbohydrates. Indigestible carbohydrates are fermented by intestinal bacteria, theoretically providing 0–2 kcal/g (*2*). Dietary fiber is an important nutrient, not as an energy source, but because of its relationship with lifestyle-related diseases attributable to physiological functioning.

Alcohol was included in this chapter considering that it has several effects on health and affects nutritional status and energy production.

Carbohydrates

Basic concept

The primary role of carbohydrates is to supply glucose to tissues that can ordinarily only use glucose as an energy source, such as the brain, nervous tissue, red blood cells, renal tubules, the testes, and oxygen-deficient skeletal muscle. It is estimated that the daily glucose requirement of these tissues is at least 100 g/d (*3*); however, this value is not the true minimal glucose requirement, because gluconeogenesis occurs in the liver. According to the National Health and Nutrition Survey in Japan (*4*, *5*), almost all Japanese consume the minimum requirement.

The dietary goal for preventing lifestyle-related diseases (DG) for carbohydrates was determined as the difference between the energy derived from proteins and lipids and the estimated energy requirement (EER), provided that sufficient proteins and a suitable amount of lipids are being ingested. Thus, the DG of carbohydrates is expressed as a percentage of energy. Since the indigestible carbohydrates in ordinary diets have almost no energy, they are considered to be carbohydrates. Furthermore, the energy derived from carbohydrates is not strongly influenced if the energy derived from ordinary amounts of alcohol consumption is included (*6*). However, this does not mean that alcohol can be used as a substitute for carbohydrates.

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Table 1. Dietary Reference Intakes for carbohydrates (% energy).[1]

Sex	Males	Females
Age	DG (range)	DG (range)
0–5 mo	—	—
6–11 mo	—	—
1–2 y	50≤, <70	50≤, <70
3–5 y	50≤, <70	50≤, <70
6–7 y	50≤, <70	50≤, <70
8–9 y	50≤, <70	50≤, <70
10–11 y	50≤, <70	50≤, <70
12–14 y	50≤, <70	50≤, <70
15–17 y	50≤, <70	50≤, <70
18–29 y	50≤, <70	50≤, <70
30–49 y	50≤, <70	50≤, <70
50–69 y	50≤, <70	50≤, <70
≥70 y	50≤, <70	50≤, <70
Pregnant women (amount to be added)		—
Lactating women (amount to be added)		—

DG, tentative dietary goal for preventing lifestyle-related diseases.
[1] Including energy derived from alcohol.

Table 2. Dietary Reference Intakes for dietary fibers (g/d).

Sex	Males	Females
Age	DG	DG
0–5 mo	—	—
6–11 mo	—	—
1–2 y	—	—
3–5 y	—	—
6–7 y	—	—
8–9 y	—	—
10–11 y	—	—
12–14 y	—	—
15–17 y	—	—
18–29 y	≥19	≥17
30–49 y	≥19	≥17
50–69 y	≥19	≥17
≥70 y	≥19	≥17
Pregnant women (amount to be added)		—
Lactating women (amount to be added)		—

DG, tentative dietary goal for preventing lifestyle-related diseases.

Determining the Dietary Reference Intakes

DG (Tentative dietary goal for preventing lifestyle-related diseases)

Adults/children. The DG for carbohydrates was determined for children aged 1 y and above. The DG was determined according to the intake of carbohydrates (60–72% energy), assuming that the subject is consuming their EER (physical activity level II), lipids within the DG, and the recommended dietary allowance (RDA) of protein. Although a lack of sufficient evidence, considering cases in which a person's protein intake is greater than the RDA and that EER differs with respect to physical activity level, the DGs for adults and children were set at 50–70% of energy intake.

DRIs values for carbohydrates are listed in Table 1.

Dietary fiber

Basic concept

Dietary fiber intake is associated with various lifestyle-related diseases. Many studies report negative relationships between dietary fiber intake and the incidence of myocardial infarction, myocardial infarction-related deaths (*7*), the incidence of diabetes (*8*), blood pressure (*9*), and low-density lipoprotein cholesterol (*10*). There are also many reports showing a correlation between dietary fiber intake and obesity (*11*, *12*). However, the associations between dietary fiber intake and cancer and its effect on bowel habits (e.g., constipation) are not well identified (*13*, *14*).

The lifestyle-related disease with the clearest connection to dietary fiber intake is myocardial infarction (*7*). Therefore, the DG was determined on the basis of the results of a meta-analysis (*7*) as well as the current intake levels of dietary fiber in Japanese.

Determining the Dietary Reference Intakes

Tentative dietary goal for preventing lifestyle-related diseases

Adults. The results of a meta-analysis of the correlation between dietary fiber intake and myocardial infarction revealed that the mortality rate decreases with a daily intake level of at least 24 g/d and increases with a daily intake level less than 12 g/d (*7*). According to the National Health and Nutrition Surveys Japan in 2005 and 2006 (*4*, *5*), the median dietary fiber intakes of male and female adults are 12.3–16.3 and 11.8–16.1 g/d, respectively.

The DG for dietary fiber was determined on the basis of the intermediate value (i.e., 18 g/d) between the 2 values indicated in the meta-analysis (*7*) although a lack of scientific basis. Furthermore, taking into account the age and body weight of the research subjects and the difference in standard body weight between Japanese men and women, the DG was determined to be 19 and 17 g/d for men and women, respectively.

DRIs values for dietary fiber are listed in Table 2.

Alcohol

Basic concept

In Japan, 7.1 kcal/g is used as the amount of available energy from alcohol (ethanol) (*15*, *16*). However, the energy utilization efficiency of alcohol varies according

to a variety of conditions including alcohol consumption levels, the ability to metabolize alcohol, dietary intake levels, and physical condition.

The range of "moderate alcohol consumption" (*17*) is thought to be in the order of 20 g/d pure alcohol equivalent. In this range, there would be no problem using 7.1 kcal/g to calculate the amount of energy from the perspective of maintaining body weight.

Epidemiological studies show that alcohol intake is correlated with death and the incidence of cardiovascular disease, cancer, and other lifestyle-related diseases (*18–21*). Western and Japanese have very different genetic backgrounds with respect to the metabolic enzymes of alcohol (*22*). Thus, it is possible that the health effects of alcohol in Japanese are different from those in Western people. The exact level of alcoholic intake that affects the total mortality rate is still controversial among cohort studies in Japan. Some studies report that the risk of mortality is lowest among subjects who consume less than 21 g alcohol/d (*23*), while others report that the risk is only high with a consumption of more than 43 g/d (*24*). Furthermore, other reports indicate that the risk increases gradually with increasing alcohol consumption (*25*). However, in all cases, it is clear that heavy alcohol consumption increases the risk of mortality.

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J Nutr Sci Vitaminol, 59, S57–S66, 2013

Dietary Reference Intakes for Japanese 2010: Fat-Soluble Vitamins

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(Received October 26, 2012)

Summary We have determined the Dietary Reference Intakes for fat-soluble vitamins (vitamin A, vitamin D, vitamin E, and vitamin K) for the Japanese. Regarding vitamin A, the estimated average requirement (EAR) and the recommended dietary allowance (RDA) were defined for those aged 1 y old and over. For vitamin D, vitamin E, and vitamin K, the EAR or RDA was not adopted, because of the insufficient data available. Thus, the adequate intake (AI) was determined for those vitamins based on the food surveillance data and biomarkers for each vitamin. The AI for vitamin D was decided as the median intake of vitamin D in the population with a circulating 25-hydroxy vitamin D level which was high enough for bone health. The basis for the AI for vitamin E was the median intake of α-tocopherol in the healthy population considering the lack of unfavorable health consequences attributable to its deficiency. The AI for vitamin K was determined as the vitamin K intake, required to avoid blood coagulation abnormalities. The tolerable upper intake level (UL) was determined for vitamin A, vitamin D and vitamin E, but not for vitamin K, since no adverse effects have been reported even with its high dosage.

Key Words vitamin A, vitamin D, vitamin E, vitamin K

Vitamin A

Background information

Compounds with potent vitamin A activity in vivo after oral intake include retinol; retinal; carotenoids; and 50 different types of provitamin A carotenoids, including β-carotene, α-carotene, and β-cryptoxanthin. The retinol equivalent (RE) is the vitamin A unit used in Dietary Reference Intakes for Japanese (DRIs-J) 2010, the most current Dietary Reference Intakes (DRIs) for the Japanese. Retinoic acid, a hormone binding to the nuclear receptor, is responsible for the majority of vitamin A activity in vivo, but is not converted to retinal or retinol in vivo, and its content in food is relatively low. Retinylester provitamin A carotenoids are the main forms of vitamin A contained in animal and plant foods, respectively. Retinylester hydrolase in the intestinal brush border catalyzes the hydrolysis of retinylester to retinol, which is then absorbed at a rate that ranges from 70% to 90% (*1*, *2*). Cleavage of carotenoids yields 2 molecules of vitamin A (retinal) from β-carotene (*3*) and 1 molecule from other provitamin A carotenoids.

In the DRIs-J 2010, the absorption rate of β-carotene is 1/6 of its total value, which is in accordance with rate in the DRIs for the United States and Canada (*4*). Assuming that the conversion rate of β-carotene to retinol is 50%, the bioavailability of β-carotene as vitamin A is 1/12 (1/6×1/2), such that 12 μg of food-derived β-carotene would correspond to 1 μg in RE units. Thus, the following formula can be used to convert the value of food-derived vitamin A-related compounds into RE units:

Retinol equivalent (μg RE)
=retinol (μg)+β-carotene (μg)×1/12
+α-carotene (μg)×1/24+β-cryptoxantin (μg)
×1/24+other provitamin A carotenoids (μg)
×1/24.

A word of caution is indicated when calculating the value for oil-solubilized β-carotene, as its bioavailability as a form of vitamin A is 1/2 of its total value, such that 2 μg of fat-solubilized β-carotene would correspond to 1 μg of retinol.

Determining DRIs

Classical vitamin A deficiency leads to corneal xerosis in infants and possibly to blindness and to night blindness in adults. Other deficiency signs include growth retardation; skeletal and neurological development defects; disturbed growth and differentiation of epi-

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thelial cells; dryness, thickening, and keratinization of the skin; immunodeficiency; and susceptibility to infection (5). Due to the abundant storage of vitamin A in the liver, inadequate intake does not lead to decreased plasma retinol concentration unless hepatic vitamin A storage is below 20 μg/g (6, 7). Thus, plasma retinol concentration cannot be used as an index of vitamin A status. Theoretically, hepatic vitamin A storage is the best index, but its measurement is highly invasive and not applicable to humans. Thus, the vitamin A intake required to maintain minimal hepatic vitamin A storage has been used for estimating the Estimated Average Requirement (EAR) for vitamin A.

Compartment analysis assuming the existence of 3 compartments—serum, liver, and other tissues—has shown that the daily disposal rate of vitamin A is approximately 2% (8, 9). Using this percentage, the daily disposal amount (DDA), daily disposal rate (DDR), body storage (BS) according to body weight (BW), and hepatic storage (HS) of vitamin A can be calculated as follows:

DDA (μg/d)=BS (μg)×DDR (2%/d (10)).

BS/BW (μg/kg BW)

=HS (≥20 μg/g)×liver weight/BW (21 g/kg BW) ×10/9,

where 90% of the body storage of vitamin A is in the liver (10, 11).

DDA/BW (μg/[kg BW·d])

=BS (≥20 μg/g×21 g/kg×10/9)×DDR (2/100)

=9.3 μg/kg BW.

Thus, the amount of vitamin A intake required to compensate for its daily elimination, thereby ensuring that hepatic storage of vitamin A is maintained and vitamin A deficiency is avoided, is estimated to be 9.3 μg RE/kg BW/d.

EAR and Recommended Dietary Allowance (RDA) for adults

The EAR for vitamin A for those aged 18 y and above, as calculated by multiplication of the reference value of 9.3 μg RE/kg BW/d and the reference BW, is 550 to 600 μg RE/d for males and 450 to 500 μg RE/d for females. Assuming the inter-individual variability in vitamin A requirement to be 20% (4), multiplication of these EAR values by 1.4 yields an RDA of 800 to 850 μg RE/d for males and 650 to 700 μg RE/d for females.

EAR and RDA for children

The RDA for children aged 6 to 17 y was determined by extrapolation from the EAR for adults aged 18 to 29 y by the 0.75th power of the BW ratio, which represents the ratio of body surface area (4). Extrapolation of the adult EAR to preschool children based on BW ratio may yield values that maintain plasma retinol levels below 20 μg/100 mL, and thus render children susceptible to corneal xerosis (12). Therefore, the RDA for children aged less than 5 y must be at least 200 μg RE/d to avoid this unfavorable outcome; therefore, for children aged less than 5 y, the DDA was calculated as follows, assuming the ratio of liver weight/BW to be 42 g/kg BW (10):

DDA/BW (μg/kg BW/d)

=BS (≥20 μg/g×42 g/kg×10/9)×DDR (2/100)

=18.7 μg/kg BW.

Using the value obtained, the EAR for children aged 1 to 5 y was calculated as follows:

EAR=18.7 μg/kg BW/d×reference BW×(1+growth factor)

=EAR×1.4.

Adequate Intake of infants aged 0 to 5 mo

Vitamin A concentration in breast milk is highest during the first 10 d after delivery, after which it gradually decreases (13, 14). Based on the values for average vitamin A concentration (411 μg RE/L) (14) and daily milk intake (0.78 L/d) (15, 16), vitamin A intake in breast milk-fed infants aged 0 to 5 mo was estimated at 320 μg RE/d. Thus, adequate intake (AI) for this age group was determined to be 300 μg/d. The level of provitamin A carotenoids was not taken into account because its availability is unknown.

AI of infants 6 to 11 mo

Based on extrapolation from the AI for infants aged 0 to 5 mo, the AI for infants aged 6 to 11 mo was determined to be 400 μg RE/d. The level of provitamin A carotenoids was not taken into account because its availability is unknown.

Amount to be added during pregnancy

The amount of vitamin A transported to the fetus through the placenta must be taken into account when estimating the vitamin A requirement for pregnant women. At the late-stage of a fetus, the amount of vitamin A deposited in the fetal liver was 1,800 μg (17, 18) so that the total amount of vitamin A transported to the fetus during pregnancy is estimated at 3,600 μg. Using this value, the EAR value for the additional amount of vitamin A required during the late stage was determined to be 60 μg RE/d, which, assuming an inter-individual variability of 20% (4), yielded an RDA value of 80 μg RE/d during the late-stage. The additional amount required during the early- and mid-stage was not determined.

Amount to be added during lactation

Based on measurement of the amount of vitamin A secreted in breast milk, the EAR value for the additional amount of vitamin A required during lactation was estimated at 300 μg RE/d, which, assuming an inter-individual variability of 20%, yielded an RDA value of 450 μg RE/d (4).

Tolerable upper intake level

An elevated plasma level of retinoic acid is considered responsible for most clinical signs (19) and symptoms of vitamin A intoxication, such as headache. Based on reported fetal abnormalities due to excessive intake of vitamin A, (20, 21) the no observable adverse effect level (NOAEL) during pregnancy was estimated at 4,500 μg RE/d, which, assuming an uncertainty factor of 1.5 and taking the additional amount into account, yielded an upper level (UL) of 3,000 μg RE/d.

Based on research into hepatotoxicity caused by the excessive vitamin A deposition (22), the NOAEL in adults was estimated at 13,500 μg RE/d, which, assuming an uncertainty factor of 5, yielded a UL of 2,700 μg RE/d. Based on clinical observation of increased intracranial pressure in infants caused by excessive vitamin

Table 1. DRIs for vitamin A (μg RE/d).[1]

Sex	Males				Females			
Age	EAR[2]	RDA[2]	AI[3]	UL[3]	EAR[2]	RDA[2]	AI[3]	UL[3]
0–5 mo	—	—	300	600	—	—	300	600
6–11 mo	—	—	400	600	—	—	400	600
1–2 y	300	400	—	600	250	350	—	600
3–5 y	300	450	—	700	300	450	—	700
6–7 y	300	450	—	900	300	400	—	900
8–9 y	350	500	—	1,200	350	500	—	1,200
10–11 y	450	600	—	1,500	400	550	—	1,500
12–14 y	550	750	—	2,000	500	700	—	2,000
15–17 y	650	900	—	2,500	450	650	—	2,500
18–29 y	600	850	—	2,700	450	650	—	2,700
30–49 y	600	850	—	2,700	500	700	—	2,700
50–69 y	600	850	—	2,700	500	700	—	2,700
≥70 y	550	800	—	2,700	450	650	—	2,700
Pregnant women (amount to be added)								
Early-stage					+0	+0	—	—
Mid-stage					+0	+0	—	—
Late-stage					+60	+80	—	—
Lactating women (amount to be added)					+300	+450	—	—

DRIs, Dietary Reference Intakes; RE, retinol equivalents; EAR, estimated average requirement; RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level.

[1] Retinol equivalent (μg RE)=retinol (μg)+β-carotene (μg)×1/12+α-carotene (μg)×1/24+β-cryptoxanthin (μg)×1/24 +other provitamin A carotenoids (μg)×1/24.

[2] Including provitamin A carotenoids.

[3] Excluding provitamin A carotenoids.

A intake (*23*), the NOAEL in infants was estimated at 6,000 μg RE/d, which, assuming an uncertainty factor of 10, yielded a UL of 600 μg RE/d.

The UL for children aged 1 to 17 y was determined by extrapolation from the UL for adults based on the ratio of body surface area. For safety reasons, the values for men were applied to women. Extrapolation to infants aged 1 to 2 y old yielded a UL of 500 μg RE/d, which is lower than that for infants aged 6 to 11 mo (600 μg RE/d). Thus, the UL for infants aged 1 to 2 y old was revised to 600 μg RE/d. Although a recent study found that ingesting approximately 1,500 μg RE/d of retinol for 30 y doubled the fracture risk in the elderly (*24*), data from other studies contradicted this finding. Thus, determination of a separate UL for vitamin A for the elderly was not considered in developing the most recent DRIs. Moreover, as excessive intake of β-carotene has not been reported to be associated with the unfavorable consequences of vitamin A intoxication described above, the level of provitamin A carotenoids was also not included in the estimation of UL.

Remarks regarding carotenoids

Due to the strict regulation of their conversion into vitamin A, provitamin A carotenoids, when ingested orally, cannot cause vitamin A intoxication. Unconverted provitamin A carotenoids, as well as carotenoids that are not metabolized to vitamin A are stored in vivo as they are. Beneficial actions have been reported with ingestion of these carotenoids, including anti-oxidant activity and immune potentiation and photoprotection of skin by anti-oxidation. Regarding the benefits of specific carotenoids, prevention of prostate cancer by lycopene, improvement in age-related macular degeneration by lutein and zeaxanthin, and the maintenance of retinal pigment by lutein and zeaxanthin have also been reported. Although the results of cohort studies suggest that higher intake of carotenoids is associated with lower incidence of lung cancer (*25*), supplementary intervention has been reported to be ineffective or even harmful in the prevention of cancer, especially lung cancer (*26–29*). Thus, further research into the efficacy and safety of carotenoids is required. In developing the current DRIs, the carotenoids were not separately considered because their deficiency has not been reported.

DRI values for vitamin A are listed in Table 1.

Vitamin D

Background information

Vitamin D_2 and vitamin D_3 are naturally occurring compounds with potent vitamin D activity. The indices for the DRI of vitamin D is based on the summation of the values of these 2 compounds. The human body obtains vitamin D from 2 sources. One is exposure to ultraviolet irradiation, which converts pro-vitamin D_3

(7-dehydrocholesterol) in the skin to pre-vitamin D_3, which in turn is converted into vitamin D_3 by thermal isomerization. The other is dietary intake of vitamin D_2 and vitamin D_3 from such sources as mushrooms and fish; good sources for vitamin D_2 and vitamin D_3, respectively. The current DRIs do not discriminate between vitamin D_2 and D_3 intake because the compounds have similar characteristics and a similar molecular weight and exert an almost equal level of biological activity.

Vitamin D is first metabolized to 25-hydroxy vitamin D (25OHD) before being metabolized to 1α,25-dihydroxy vitamin D ($1\alpha,25(OH)_2D$), its active form. Major actions of vitamin D include enhancing the absorption of calcium and phosphate in the intestine and kidneys and stimulating bone formation and growth. Circulating 25OHD level is the best index of vitamin D status. As vitamin D deficiency and resultant hypocalcemia cause elevated levels of serum parathyroid hormone (PTH), serum concentration of PTH can also be a good index of vitamin D deficiency (*30*).

Adequate intake

Evidence for determining AI

Vitamin D deficiency impairs calcium absorption from the intestine and kidney, thus decreases calcium availability, resulting in rickets in children and osteomalacia in adults. In adults, especially the elderly, even so-called "vitamin D insufficiency," which is milder than vitamin D deficiency, can result in increased secretion of PTH, increased bone resorption, and decreased bone mineral density. Therefore, the basis for determining the vitamin D requirement is maintenance of a serum 25OHD level sufficiently high to maintain normal calcium availability and avoid elevation of serum PTH level. Due to limitations on the data available, AI was determined as the median intake of vitamin D in a population in which the required circulating 25OHD level is maintained.

AI for adults

In a study conducted in the northern United States, an area in which residents receive limited sunshine exposure, serum PTH level after vitamin D administration decreased in those with a serum 25OHD level below 50 nmol/L but not in those with a level above 50 nmol/L (*31*). In a study in Niigata, those with a 25OHD level less than 50 nmol/L had higher serum PTH levels and a higher prevalence of low bone mineral density (*32*). Based on consideration of these results, maintenance of a circulating 25OHD level of at least 50 nmol/L is considered necessary to avoid elevation of serum PTH level and decrease in bone mineral density. In the study conducted in the northern United States, serum PTH level exhibited seasonal variation, reaching a nadir between August and October and a peak between March and May. However, this variation was not observed in those taking 5.5 μg/d or more of vitamin D (*33*), leading to the conclusion that taking at least 5.5 μg/d of vitamin D can prevent elevation of PTH in those living in areas in which they have limited sunshine exposure.

In 7 studies that examined Japanese women (*34–39*) aged 50 to 69 y, the average 25OHD level was found to exceed 50 nmol/L. In contrast, in several studies that examined women aged 18 to 29 y (*32, 34*) and women aged 30 to 49 y (*34*), the average level was found to be below 50 nmol/L. Based on these findings and the findings from US studies, the median vitamin D intake of adults aged 50 to 69 y was determined to be an appropriate basis for determining the adult AI. As the 2005 and 2006 National Health and Nutritional Survey (NHNS) (*40, 41*) found that the median intake of vitamin D in adults aged 50 to 69 y was 5.5 μg/d, the AI was set as 5.5 μg/d. Due to lack of data for those aged 18 to 29 y, 30 to 49 y, and above 70 y, as well as lack of data for males, AI for both males and females in these age groups was also set at 5.5 μg/d.

AI for children

As the findings regarding the relationship between vitamin D intake and plasma 25OHD concentration in children have been inconsistent, they were considered unsuitable as the basis for determining the vitamin D AI for children. Thus, the median vitamin D intake, as reported in the 2005 and 2006 NHNS (*40, 41*), was used as the basis for determining the AI.

AI for infants

In an epidemiological study conducted in Kyoto, 22% of neonates were found to have craniotabes, a mineralization defect of bone, likely due to vitamin D deficiency (*42*). The incidence of craniotabes exhibited seasonal variation, with a peak and nadir between January and May and between July and November, respectively. Circulating 25OHD level was found to be below 25 nmol/L in 37% of all neonates diagnosed with craniotabes at 1 mo after birth. In breast milk-fed neonates, serum concentration of 25OHD was found to be less than 25 nmol/L in 57% of subjects and below 12.5 nmol/L in 17%. In contrast, none of the formula or mixed-fed infants were found to have an inadequate serum 25OHD level. It should be noted that neonates born in a vitamin D-deficient state may not recover to a vitamin D-sufficient state within a short period, and that the serum 25OHD level of breast milk-fed infants was found to decrease further during the winter months (*43*), indicating that the vitamin D delivered from breast milk may have been unsatisfactory. The vitamin D AI for infants was determined to be 2.5 μg/d by multiplying 0.78 L/d (*15, 16*), the average daily milk intake, by 3.05 μg/L (*44*), the vitamin D concentration in breast milk as reported in the *Standard Tables of Food Composition in Japan*, 5th Revised and Enlarged Edition.

However, this AI value is appropriate only for infants with adequate sun exposure, defined as 2 h/wk to the face or 30 min/wk to the face and extremities. Breast-milk-fed infants with little sun exposure are at higher risk of developing rickets. Considering that previous research found that no infants developed rickets after supplementation with 2.5 μg/d of vitamin D for 6 mo and assuming that infants receive an average of 2.38 μg/d of vitamin D from breast milk, it follows that a daily intake of 4.88 μg/d of vitamin D is satisfactory for avoiding rickets. Based on these data, the AI of vitamin D for infants aged 0 to 5 mo with limited sun exposure was determined to be 5 μg/d. Recently, however, a

Table 2. DRIs for vitamin D (μg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo[1]	—	—	2.5 (5.0)	25	—	—	2.5 (5.0)	25
6–11 mo[1]	—	—	5.0 (5.0)	25	—	—	5.0 (5.0)	25
1–2 y	—	—	2.5	25	—	—	2.5	25
3–5 y	—	—	2.5	30	—	—	2.5	30
6–7 y	—	—	2.5	30	—	—	2.5	30
8–9 y	—	—	3.0	35	—	—	3.0	35
10–11 y	—	—	3.5	35	—	—	3.5	35
12–14 y	—	—	3.5	45	—	—	3.5	45
15–17 y	—	—	4.5	50	—	—	4.5	50
18–29 y	—	—	5.5	50	—	—	5.5	50
30–49 y	—	—	5.5	50	—	—	5.5	50
50–69 y	—	—	5.5	50	—	—	5.5	50
≥70 y	—	—	5.5	50	—	—	5.5	50
Pregnant women (amount to be added)					—	—	+1.5	—
Lactating women (amount to be added)					—	—	+2.5	—

[1] Adequate intakes for an infant who is exposed to appropriate sunlight. The value in parentheses is adequate intakes for those with less sunlight exposure.

study using a novel, highly accurate procedure found the average vitamin D concentration in breast milk to be only 0.6 μg/L (*14*). If this value is employed, the average vitamin D intake of breast-milk-fed infants would be only 0.47 μg/d. Such discrepancies indicate the need for further research into this value (*45*, *46*).

AI for infants aged 6 to 11 mo

The AI of vitamin D for infants aged 6 to 11 mo with adequate sun exposure was determined to be 5 μg/d. This value was also applied to infants aged 6 to 11 mo with limited sun exposure due to lack of evidence for determining the AI.

Additional amount during pregnancy

In a study of pregnant women with limited sun exposure, an inadequate serum 25OHD concentration was observed in those with an average vitamin D intake of less than 5.3 μg/d but not in those an average (*47*) vitamin D intake higher than 7 μg/d (*48*). As these findings indicate that pregnant women require at least 7 μg/d of vitamin D, the additional amount of vitamin D required for pregnant women was determined to be 1.5 μg/d.

Additional amount during lactation

Based on the findings described above, the additional amount of vitamin D required for lactating women was determined to be 2.5 μg/d.

Tolerable upper untake level

Basic considerations

Prolonged intake of excessive quantities of vitamin D can lead to unfavorable outcomes, such as hypercalcemia, renal dysfunction, soft tissue calcification, and growth retardation. As an increased serum 25OHD level itself does not directly cause health problems, the presence of hypercalcemia rather than of a high serum 25OHD level is considered an appropriate indicator for determining the UL.

UL for adults

In an intervention study administering doses of vitamin D for 3 mo, serum calcium concentration was found to exceed the reference value in some subjects receiving 95 μg/d of vitamin D but not in those receiving 60 μg/d of vitamin D (*49*). Thus, the lowest observed adverse effect level (LOAEL) and NOAEL were determined to be 95 μg/d and 60 μg/d, respectively. The latter value was divided by an uncertainty factor of 1.2 yielding a UL for adults of 50 μg/d. Since neither administration of 45 μg/d of vitamin D to elderly subjects for 3 mo (*50*) nor administration of 50 μg/d to pregnant and lactating subjects (*51*) was found to be associated with hypercalcemia, stratification by sex or age group was not performed, and a UL of 50 μg/d was applied to all adult groups.

UL for infants

Based on a study that observed no growth retardation in infants administered an average of 44 μg/d of vitamin D for 6 mo, the NOAEL for infants was determined to be 44 μg/d (*52*), which, assuming an uncertainty factor of 1.8, yielded a UL of 25 μg/d.

UL for children

As data were unavailable for this age group, the UL for children was determined by extrapolating the UL values for adults (50 μg/d) and infants (25 μg/d) based on the reference body weight. Sex differences were not considered.

DRI values for vitamin D are listed in Table 2.

Vitamin E

Background information

Vitamin E is composed of 8 analogues: α-, β-, γ- and

Table 3. DRIs for vitamin E (mg/d).[1]

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	3.0	—	—	—	3.0	—
6–11 mo	—	—	3.5	—	—	—	3.5	—
1–2 y	—	—	3.5	150	—	—	3.5	150
3–5 y	—	—	4.5	200	—	—	4.5	200
6–7 y	—	—	5.0	300	—	—	5.0	300
8–9 y	—	—	6.0	350	—	—	5.5	350
10–11 y	—	—	6.5	450	—	—	6.0	450
12–14 y	—	—	7.0	600	—	—	7.0	600
15–17 y	—	—	8.0	750	—	—	7.0	650
18–29 y	—	—	7.0	800	—	—	6.5	650
30–49 y	—	—	7.0	900	—	—	6.5	700
50–69 y	—	—	7.0	850	—	—	6.5	700
≥70 y	—	—	7.0	750	—	—	6.5	650
Pregnant women (amount to be added)					—	—	+0.0	—
Lactating women (amount to be added)					—	—	+3.0	—

[1] Computation was made on α-tocopherol, not including vitamins E other than α-tocopherol.

δ-forms, of tocopherol and tocotrienol. After intestinal absorption, vitamin E is packaged into chylomicron, transformed into chylomicron remnant by lipoprotein lipase, and transported to the liver. Of the 8 analogues, only α-tocopherol is preferentially bound to α-tocopherol binding protein, whereas the other analogues are metabolized in the liver. Alpha-tocopherol is then formed into very low-density lipoprotein (VLDL), converted into low-density lipoprotein (LDL), and distributed to various tissues (*53*). Due to these metabolic processes, α-tocopherol constitutes the predominant vitamin E analogues present in the blood and various tissues. Based on these facts, only α-tocopherol was considered when determining the current DRI for vitamin E.

Determining DRI

Basis for determining AI

Erythrocytes are susceptible to hemolysis by hydrogen peroxide when the circulating α-tocopherol level is between 6 and 12 μmol/L (*54*), but resistant to it when the serum α-tocopherol level is higher than 14 μmol/L (*55*). Although the data from an intervention study that administered graded doses of vitamin E to vitamin E-deficient subjects are available (*56*), they were not considered appropriate for estimating the EAR and RDA because they were collected many years ago. Several studies that simultaneously studied vitamin E intake and serum α-tocopherol level consistently reported that the average serum α-tocopherol level exceeded 22 μmol/L in all study populations (*40, 41, 57–59*). Average vitamin E intake in these studies ranged from 5.6 to 11.1 mg/d, a range that encompasses the 2005 and 2006 NHNS values (*40, 41*) of an average vitamin E intake of 7.0 mg/d in men and 6.5 mg/d in women. As these findings indicate that the median intake of the Japanese likely yields an adequate vitamin E status, the AI was determined to be the 2005 and 2006 NHNS median values stratified by sex and age group (*40, 41*).

AI for adults

As described above, AI was determined to be the 2005 and 2006 NHNS median values for those aged 18 to 29 y stratified by sex and age group, specifically 7.0 mg/d for men and 6.5 mg/d for women, as these values are expected to yield a blood α-tocopherol level exceeding 12 μmol/L (*40, 41*). As aging has not been reported to be associated with compromised absorption or utilization of vitamin E, the same values were applied to the elderly.

AI for children

The 2005 and 2006 NHNS median values for children stratified by sex and age group were used as the basis for determining the AI for children, as they had been for adults.

AI for infants aged 0 to 5 mo

The AI for infants aged 0 to 5 mo was determined to be 3.0 mg/d by multiplying the average α-tocopherol concentration in breast milk (3.5 to 4.0 mg/L) (*14, 60*) by the average milk intake (0.78 L/d) (*15, 16*).

AI for infants aged 6 to 11 mo

The AI for infants aged 6 to 11 mo old was determined to be 3.5 mg/d by extrapolation from the adult value by the 0.75th power of the BW ratio.

AI during pregnancy

The AI for pregnant women was determined to be the same as that for non-pregnant women because vitamin E deficiency during pregnancy has not been reported.

Additional amount during lactation

Since the average α-tocopherol content provided in breast milk is approximately 3.0 mg/d (*14, 60*), the AI

during lactation was determined to be 3 mg/d.

Tolerable upper intake level

The basis for determining the UL for vitamin E is its possible effect on bleeding tendency. Based on the finding that supplementation with 800 mg/d of α-tocopherol for 28 d did not increase bleeding tendency in healthy males (average body weight, 62.2 kg) (*61*), the NOAEL was determined to be 800 mg/d. Assuming an uncertainty factor of 1.0 and considering that no data regarding LOAEL are available, the sex- and age-group stratified UL was calculated by correcting the 800 mg/d value by BW ratio. Because few data are available regarding the UL for infants aged 0 to 11 mo and because typical feeding with breast milk or baby food does not cause excessive intake, the UL was not determined for this age group.

Additional remarks

Although numerous intervention studies have examined the effect of vitamin E supplementation on the risk of coronary heart diseases, the findings have been inconsistent (*62–65*).

DRI values for vitamin E are listed in Table 3.

Vitamin K

Basic considerations

Naturally occurring vitamin K consists of phylloquinones (PKs; vitamin K_1) and menaquinones (MKs; vitamin K_2). Menaquinones are further subdivided into 11 analogues depending on the number of isoprene units (4–14) in the prenyl side chain. Among the menaquinones, of nutritional importance are menaquinone-4 (MK-4), which is ubiquitously present in animal foods, and menaquinone-7 (MK-7), which is abundantly present in natto, a traditional Japanese food made from soybeans fermented with *Bacillus subtilis*. At present, data are scarce for determining the relative biological activity of these analogues, and no corrections have been made for PK and MK-4 with similar molecular weights. MK-7, which has a much larger molecular weight, can be converted into its MK-4 equivalent using the following formula:

MK-4 equivalent (mg)=MK-7 (mg)×444.7/649.

The sum of the quantity of PK, MK-4, and MK-7 as corrected above was employed in determining the DRI for vitamin K. Although long-chain MKs are produced by intestinal bacteria and MK-4 is also produced by enzymatic conversion from PK, their contribution was not considered sufficiently large to contribute to fulfilling this requirement. Although antibiotic treatment can impair vitamin K status by decreasing the production of MKs by intestinal flora and decreasing vitamin K utilization by inhibiting the enzymatic activity of vitamin K epoxide reductase (*66*), antibiotic treatment itself does not cause vitamin K deficiency if average vitamin K intake is maintained (*67*).

The principal biological action of vitamin K is activation of prothrombin and other serum coagulation factors, thereby enhancing blood coagulation. Other actions include the modulation of bone formation by activation of osteocalcin, a bone matrix protein, and inhibition of arterial calcification by activation of matrix gla protein (MGP), another vitamin-K-dependent matrix protein.

Determining DRI

Evidence for determining AI

Since delayed blood coagulation is the only clinically manifested abnormality attributable to vitamin K deficiency, the intake necessary to maintain normal serum coagulation was considered an appropriate basis for determining the AI for vitamin K. In Japan, however, coagulation abnormalities due to vitamin K deficiency are rarely observed in healthy subjects. An intervention study of young vitamin K-deficient male volunteers weighing 72 kg found that administration of 40 and 32 μg/d of vitamin resulted in a decrease in serum PK level and an elevation in undercarboxylated prothrombin, a serum marker for vitamin K deficiency, respectively, but that administration of 82 μg/d of vitamin K returned these levels to normal values (*68*). Based on these findings, the vitamin K requirement for healthy adults was determined to be approximately 1 μg/[kg·d].

Recent studies have suggested that skeletal vitamin K deficiency is a risk factor for fracture (*69*, *70*), indicating that a much higher vitamin K intake is necessary for skeletal action. Although a recent meta-analysis found that vitamin K administration significantly reduced fracture incidence, it employed a high dosage (45 mg/d) of MK-4, which is considered to be pharmacological rather than nutritional (*71*). Based on the findings of previous research, a vitamin K intake of approximately 1.0 μg/[kg·d] was determined to be satisfactory to avoid even mild deficiency, and thus set as the AI for vitamin K.

AI for adults

As described above, a vitamin K intake of 82 μg/d in those weighing 72 kg was found sufficient to avoid deficiency (*68*). Extrapolation of this value by the 0.75th power of the BW ratio was used as the basis for determining the adult AI. Although the elderly may be more susceptible to vitamin K deficiency due to various factors such as impaired intestinal absorption of vitamin K, at present, the data are scarce, and thus the AI for the elderly was the same as that for those aged 50 to 69 y.

AI for children

The AI for children was determined by extrapolating the AI for adults by the 0.75th power of the BW ratio.

AI for infants aged 0 to 5 mo

Neonates are susceptible to vitamin K deficiency for various reasons, such as poor transplacental vitamin K transport (*72*), low vitamin K content in the breast milk (*14*, *73*), or low production of vitamin K in the intestinal flora (*74*). As neonatal vitamin K deficiency is known to cause neonatal melena, a form of gastrointestinal bleeding, and intracranial bleeding, vitamin K is orally administered just after birth for their prevention. The AI of 4.0 μg/d for this age group was determined by multiplying the average milk intake (0.78 L/d) by the average vitamin K content of milk (5.17 μg/L) and assuming oral administration of vitamin K just after birth in the clinical setting.

Table 4. DRIs for Vitamin K (μg/d).

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	4	—	—	—	4	—
6–11 mo	—	—	7	—	—	—	7	—
1–2 y	—	—	25	—	—	—	25	—
3–5 y	—	—	30	—	—	—	30	—
6–7 y	—	—	40	—	—	—	40	—
8–9 y	—	—	45	—	—	—	45	—
10–11 y	—	—	55	—	—	—	55	—
12–14 y	—	—	70	—	—	—	65	—
15–17 y	—	—	80	—	—	—	60	—
18–29 y	—	—	75	—	—	—	60	—
30–49 y	—	—	75	—	—	—	65	—
50–69 y	—	—	75	—	—	—	65	—
≥70 y	—	—	75	—	—	—	65	—
Pregnant women (amount to be added)					—	—	+0	—
Lactating women (amount to be added)					—	—	+0	—

AI for infants aged 6 to 11 mo

The AI was determined to be 7 μg/d by considering the amount of vitamin K received from sources other than breast milk.

Additional amount during pregnancy

Increased requirements for vitamin K or alterations in circulating vitamin K levels in pregnant women have not been reported. Because of poor transplacental transport, vitamin K intake in pregnant women is unlikely to affect vitamin K status in the fetuses or neonates. Thus, no additional amount required for pregnant women was determined.

Additional amount during lactation

Since lactating women have not been reported to be at higher risk for vitamin K deficiency, no additional amount required for lactating women was determined.

Tolerable upper intake level

Although menadione, a vitamin K metabolite, can cause toxicity, no toxicity has been reported regarding PKs and MKs. As 45 mg/d of MK-4 is clinically administered to many patients in Japan with osteoporosis with no reports of serious adverse events, the UL for vitamin K was not determined.

Other remarks

Due to the abundant vitamin K content of natto, its intake is contraindicated in patients treated with warfarin. In contrast, patients undergoing long-term antibiotic treatment or experiencing chronic obstruction of the biliary tract or impaired fat absorption are at higher risk of vitamin K deficiency.

DRI values for vitamin K are listed in Table 4.

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J Nutr Sci Vitaminol, 59, S67–S82, 2013

Dietary Reference Intakes for Japanese 2010: Water-Soluble Vitamins

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(Received October 26, 2012)

Summary A potential approach for determining the estimated average requirement (EAR) is based on the observation that a water-soluble vitamin or its catabolite(s) can be detected in urine. In this approach, the urinary excretion of a water-soluble vitamin or its catabolite(s) increase when the intake exceeds the requirement. This approach is applied to vitamin B_1, vitamin B_2 and niacin. A second approach is to determine the blood concentration. In this case, the requirement is indicated by a value rather than a threshold level. The second approach is applied to vitamin B_6, vitamin B_{12}, folate, and vitamin C. The recommended dietary allowance (RDA) was calculated by multiplying the EAR by 1.2. For pantothenic acid and biotin, there were insufficient data for determining the EAR. Thus, adequate intakes were set based on food surveillance data.

Key Words water-soluble vitamins, DRI, urine, blood, requirement

Vitamin B_1

Background information

The chemical name of vitamin B_1 is thiamin, and the active form is thiamin diphosphate (TDP). Severe thiamin deficiency results in a nerve and heart disease, termed beriberi. Less severe deficiency results in nonspecific symptoms such as malaise, loss of weight, irritability, and confusion.

In foods, thiamin exists mainly as a TDP-protein complex. Thus, the absorption of thiamin in the digestive tract involves 2 stages: (1) the release of TDP from the complex by the action of proteases and (2) the release of thiamin from TDP by the action of phosphatases and pyrophosphatases. There are 2 mechanisms of absorption. At low luminal concentrations (<2 μmol/L), the process is carrier-mediated; at higher concentrations (e.g., a 2.5 mg dose for humans) passive diffusion also occurs.

Most of the thiamin in serum is bound to protein, mainly albumin. Thiamin is taken up by blood cells and body tissues via active transport. Intracellular thiamin occurs predominantly (80%) as TDP, most of which is bound to proteins. The relative availability of dietary vitamin B_1 to free thiamin in a typical Japanese diet is around 60% (*1*, *2*).

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Determining DRIs

Evidence for determining the estimated average requirement (EAR)

Orally administered thiamin is rapidly converted to TDP in the body tissues. Thereafter, excess thiamin is excreted as free form in the urine. Urinary excretion of thiamin has been shown sharply to increase at a concentration >0.35 mg thiamin/1,000 kcal/d (*3*). Based on this evidence, the EAR of thiamin ($C_{12}H_{17}N_4OS$, molecular weight 265.3) was determined. It should be noted that the Standard Tables of Food Composition in Japan give the content of vitamin B_1 as the value of thiamin hydrochloride ($C_{12}H_{17}ClN_4OS{\cdot}HCl$, molecular weight 337.3). Thus, the EAR of vitamin B_1 becomes 0.45 mg thiamin hydrochloride/1,000 kcal/d. The recommended dietary allowance (RDA) is set by assuming a coefficient of variation of 10%. Thus the RDA becomes 0.54 mg thiamin hydrochloride/1,000 kcal/d.

Table 1. DRIs for vitamin B_1 (mg/d).[1]

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	0.1	—	—	—	0.1	—
6–11 mo	—	—	0.3	—	—	—	0.3	—
1–2 y	0.5	0.5	—	—	0.4	0.5	—	—
3–5 y	0.6	0.7	—	—	0.6	0.7	—	—
6–7 y	0.7	0.8	—	—	0.7	0.8	—	—
8–9 y	0.8	1.0	—	—	0.8	1.0	—	—
10–11 y	1.0	1.2	—	—	0.9	1.1	—	—
12–14 y	1.1	1.4	—	—	1.0	1.2	—	—
15–17 y	1.2	1.5	—	—	1.0	1.2	—	—
18–29 y	1.2	1.4	—	—	0.9	1.1	—	—
30–49 y	1.2	1.4	—	—	0.9	1.1	—	—
50–69 y	1.1	1.3	—	—	0.9	1.1	—	—
≥70 y	1.0	1.2	—	—	0.8	0.9	—	—
Pregnant women (amount to be added)								
Early-stage					+0.0	+0.0	—	—
Mid-stage					+0.1	+0.1	—	—
Late-stage					+0.2	+0.2	—	—
Lactating women (amount to be added)					+0.2	+0.2	—	—

DRIs, Dietary Reference Intakes; EAR, estimated average requirement; RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level.
[1] Calculated by using PAL II of the EER.

For example, the RDAs for 18- to 29-y-old males and females are 1.4 mg/d and 1.1 mg/d, respectively, assuming a physical activity level (PAL) II, i.e., within the estimated energy requirement (EER).

Life stages

0–5 mo. The mean concentration of thiamin hydrochloride in breast milk is 0.13 mg/L (*4–6*). The average intake of breast milk is 0.78 L/d (*7, 8*), representing a daily vitamin B_1 intake of about 0.1 mg/d. This value was set as the adequate intake (AI).

6–11 mo. The AI for infants aged 6–11 mo is calculated using the average of the values from the following 2 expressions: Expression 1, AI for infant boy or girl aged 6–11 mo (extrapolated AI from infants)=AI for infants (0–5 mo)×(average reference infant boy or girl body weight of 6–11 mo/average reference infant boy or girl body weight of 0–5 mo)$^{0.75}$; Expression 2, AI for infant boy or girl aged 6–11 mo (extrapolated AI from adults)=RDA×(average reference infant boy or girl body weight of 6–11 mo/average reference male or female weight of 18–29 y old)$^{0.75}$×(1+growth factor). Thus, the AI of infants aged 6–11 mo is 0.3 mg/d.

Pregnant women. The additional amounts are calculated based on the assumption that the requirement for vitamin B_1 increases according to energy expenditure. In other words, the additional EAR and RDA for pregnant women are calculated by multiplying the EAR or RDA by the additional energy expenditure resulting from pregnancy.

Lactating women. The additional amount is calculated based on the assumption that the excreted amount in breast milk is supplemented. But, the availability of dietary vitamin B_1 is low compared with the free form of vitamin B_1. The relative availability of dietary vitamin B_1 to free thiamin in a typical Japanese diet is around 60% (*1, 2*). Thus, the EAR is divided by 0.6. The additional RDA is calculated by multiplying the additional EAR by 1.2.

Tolerable upper intake level

Chronic intake of thiamin (50 mg/kg body weight/d) has been reported to cause severe toxicity symptoms (*9*). For example, intake of 10 g of thiamin hydrochloride for 2.5 wk daily resulted in headaches, irritability, insomnia, pulsus celer, weakness, contact dermatitis, and itchiness. These symptoms disappeared in 2 d when the intake was discontinued (*10*). Nevertheless, there is insufficient evidence for determining the tolerable upper intake level (UL).

The Dietary Reference Intakes (DRIs) for vitamin B_1 are summarized in Table 1.

Vitamin B_2

Background information

The chemical name of vitamin B_2 is riboflavin, and the active forms are flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). Riboflavin deficiency results in angular cheilitis, glossitis (magenta tongue), seborrheic dermatitis, and other disorders.

Table 2. DRIs for vitamin B_2 (mg/d).[1]

Sex	Males				Females			
Age	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0–5 mo	—	—	0.3	—	—	—	0.3	—
6–11 mo	—	—	0.4	—	—	—	0.4	—
1–2 y	0.5	0.6	—	—	0.5	0.5	—	—
3–5 y	0.7	0.8	—	—	0.6	0.8	—	—
6–7 y	0.8	0.9	—	—	0.7	0.9	—	—
8–9 y	0.9	1.1	—	—	0.9	1.0	—	—
10–11 y	1.1	1.4	—	—	1.0	1.2	—	—
12–14 y	1.3	1.5	—	—	1.1	1.4	—	—
15–17 y	1.4	1.7	—	—	1.1	1.4	—	—
18–29 y	1.3	1.6	—	—	1.0	1.2	—	—
30–49 y	1.3	1.6	—	—	1.0	1.2	—	—
50–69 y	1.2	1.5	—	—	1.0	1.2	—	—
≥70 y	1.1	1.3	—	—	0.9	1.0	—	—
Pregnant women (amount to be added)								
Early-stage					+0.0	+0.0	—	—
Mid-stage					+0.1	+0.2	—	—
Late-stage					+0.2	+0.3	—	—
Lactating women (amount to be added)					+0.3	+0.4	—	—

[1] Calculated by using PAL II of the EER.

In foods, riboflavin exists mainly as a complex of FMN or FAD, non-covalently bound to related enzyme proteins. During digestion, FAD and FMN are firstly liberated in acidic conditions, and are then hydrolyzed by pyrophosphatase and phosphatase. Finally, riboflavin is released and absorbed from the small intestine (*11*). The absorbed riboflavin is incorporated into the body tissues, and used for FAD synthesis. In the rat liver, for example, about 90% of riboflavin exists as FAD, about 10% as FMN, and the remaining 1% as riboflavin.

In the blood, riboflavin exists mainly in the form of FAD, with ~10% FMN and ~4% riboflavin. A large portion of riboflavin is associated with immunoglobulins, but some is bound to albumin (*12*). The absorbed riboflavin is incorporated into the body tissues, and converted mainly to FAD via FMN.

Excess riboflavin is rapidly excreted in the urine, primarily as free riboflavin.

Determining DRIs

Evidence for determining the EAR

Usually only a small amount of riboflavin is excreted in the urine; the level of excretion varies according to the intake of vitamin B_2. If the body requirement is met, urinary excretion shows a rapid increase. A gradual increase in the intake of free riboflavin to ≥1.1 mg/d was shown to result in a rapid rise in urinary excretion by healthy males and females (*13*, *14*). Based on these results, and the involvement of vitamin B_2 in energy metabolism, EAR was determined as the energy intake/d, i.e., 0.50 mg riboflavin/1,000 kcal/d. For example, the EARs for 18- to 29-y-old males and females are 1.3 mg/d and 1.0 mg/d, respectively, assuming a PAL II, i.e., within the EER.

Life stages

0–5 mo. For infants of 0–5 mo, breast milk is the sole source of vitamin B_2. The mean concentration of riboflavin in breast milk is 0.40 mg/L (*4–6*). The average intake of breast milk is 0.78 L/d (*7*, *8*), representing a daily vitamin B_2 intake of about 0.3 mg/d. This value was set as the AI.

6–11 mo. To set the AI for infants aged 6–11 mo, the extrapolated values are calculated from the AI for infants aged 0–5 mo and the EAR for adults, using the weight ratio method described for vitamin B_1. The means of these extrapolated values are determined for each sex. Thus, the AI for infants aged 6–11 mo becomes 0.4 mg/d.

Pregnant women. The additional amounts are calculated based on the assumption that the requirement for vitamin B_2 increases according to energy expenditure. In other words, the additional EAR and RDA for pregnant women are calculated by multiplying the EAR or RDA by the additional energy expenditure resulting from pregnancy.

Lactating women. The additional amount is calculated based on the assumption that the excreted amount in breast milk is supplemented. The mean concentration of riboflavin in breast milk is 0.40 mg/L (*4–6*) and the average secretion of breast milk is 0.78 L/d (*7*, *8*). Thus, the additional EAR becomes 0.3 mg/d. The additional RDA is calculated by multiplying the additional EAR by