

Minerals

(1) Macrominerals

Sodium

1. Background Information

1-1. Definition and Classification

Sodium is an alkali metal element (atomic number: 11, Na).

2. To Avoid Inadequacy

2-1. Factors to be Considered in Estimating Requirements

Determining the Dietary Reference Intakes (DRIs)

The WHO's guideline states that the intake of sodium should be no more than 200 to 500 mg/day⁽¹⁾. Based on the belief that endogenous sodium loss is equal to sodium requirement, the estimated average requirement (EAR) was established with the goal of compensating for endogenous loss, using the same method as the DRIs for Japanese 2010⁽²⁾. However, the value is lower than 1% of the intake distribution value, as determined by the 2010 and 2011 National Health and Nutrition Survey (NHNS)⁽³⁾. Therefore, the sodium requirements are irrelevant with respect to regular dietary intake, and setting an EAR might not be practical. The EAR was calculated for reference. Since the recommended dietary allowance (RDA) has no significance when the amount recommended is utilized, it was not calculated.

The present DRIs for sodium were set with the aim of preventing the increased risk for lifestyle-related diseases (LRDs); therefore, the tentative dietary goal (DG) for preventing LRDs was determined.

2-2. Method Used to Set the EAR and RDA

2-2-1. Background Information

Under conditions of normal renal function, sodium deficiency does not occur, as sodium balance is maintained through sodium reabsorption in the kidneys. The unavoidable sodium loss is the sum of the excretion via urine, stool, skin, or others at a dietary sodium intake of 0. The required sodium intake has been regarded as the loss because the sodium consumed is mainly absorbed by the intestine⁽⁴⁾.

2-2-2. Adults and Children (EAR, RDA)

From the results of a review of traditional studies, the endogenous sodium loss of adults was calculated to be 0.023 mg (0.001 mmol)/kg body weight (BW)/day from the feces, 0.23 mg (0.01 mmol)/kg BW/day from urine, and 0.92 mg (0.04 mmol)/kg BW/day from skin (total: 1.173 mg (0.051 mmol)/kg BW/day)⁽⁴⁾. On applying these values to men aged 18 to 29 years, the endogenous sodium loss was 74 (1.173 × 63.0) mg/day or 3.2 (0.051 × 63.0)

mmol/day. The endogenous sodium loss was set at 115 mg/day (5 mmol/day) in the American dietary requirement 1989⁽⁵⁾, and 69 to 490 mg/day (3 to 20 mmol/day) in the DRIs for the UK 1991⁽⁶⁾. Thus, the endogenous sodium loss of adults is lower than 500 mg/day or 600 mg/day (sodium chloride equivalent of 1.5 g/day) even after considering interindividual variations (with a coefficient of variation of 10%). This value was set as the EAR for adults. In practical terms, the regular dietary intake of salt is lower than 1.5 g/day.

Working or exercising in hot environments can lead to the loss of a significant amount of sodium through profuse perspiration; hydration with a small amount of added salt may be needed in such cases⁽⁷⁾. In view of the rising summer temperatures in Japan, it is necessary to consume a moderate amount of salt. However, excessive intakes can be unfavorable in the prevention of the onset and progression of LRDs, and improvement in their severity.

For children, since no data were available, the EAR was not determined.

2-2-3. Additional Amount for Pregnant and Lactating Women (EAR, RDA)

The amount required by pregnant women was estimated to be approximately 21.85 g (950 mmol) for the maintenance of the increase of the mothers' tissues, fetus and placenta⁽⁸⁾. These increases occur over a period of 9 months, which is equivalent to 0.08 g (3.5 mmol)/day (a sodium chloride equivalent of 0.2 g/day). Since the regular dietary intake of salt is considered to be sufficient, pregnant women do not require an additional intake of sodium.

The average concentration of sodium in the breast milk of Japanese mothers is 135 mg/L^(9,10). Considering the daily milk secretion is 0.78 L/day, the amount of sodium consumed is 105 mg/day (a sodium chloride equivalent of 0.27 g/day). Since their regular dietary intake of salt is considered sufficient, lactating women do not require an additional intake of sodium.

2-3. Method Used to Set the Adequate Intake (AI)

2-3-1. Infants (AI)

For infants aged 0-5 months, the AI was calculated using the average concentration of sodium in breast milk (135 mg/L)^(9,10) and average milk intake (0.78 L/day)^(11,12), yielding 100 mg/day (a sodium chloride equivalent of 0.3 mg/day).

For infants aged 6 to 11 months, the AI was calculated using the average consumption of sodium from breast milk^(13,14) and complementary food⁽¹⁵⁾.

The daily sodium intake was calculated as 559 mg/day (72 mg/day (135 mg/L × 0.53 L/day) from breast milk and 487 mg/day from complementary food); therefore, the AI was set at 600 mg/day (a sodium chloride equivalent of 1.5 g/day).

3. To Avoid Excessive Intake

3-1. Dietary Intake

The major sources of sodium intake are dietary salt (sodium chloride), and sodium-containing seasonings. The amount of sodium chloride can be calculated as follows:

Sodium chloride equivalent (g) = sodium (g) × 58.5/23 = sodium (g) × 2.54

The Standard Tables of Food Composition in Japan 2010⁽¹⁶⁾ used the above-stated formula to measure the sodium content in food. There are various kinds of sodium compounds other than sodium chloride in various foods, especially in processed foods that contain sodium chloride.

Although sodium exists in foods as sodium salt or sodium ion, humans consume most of the sodium as sodium chloride (NaCl). Therefore, sodium intake is often expressed as sodium chloride equivalents.

3–2. The Tolerable the Tolerable Upper Intake level (UL)

The ULs for sodium have not been determined, as DGs have been set for similar purposes.

4. For the Prevention of the Development and Progression of LRDs

4–1. The Association between Sodium and Major LRDs

The development and maintenance of hypertension are based on the interaction of heritable factors and environmental factors (lifestyle habits). Lifestyle modification plays an important role in the prevention and treatment of hypertension. In addition to patients with hypertension, those with heritable factors for hypertension or a high normal blood pressure (130-139/85-89 mmHg) should work on modifying their lifestyle habits, especially in terms of diet.

Results from large Western clinical studies^(17–22) showed that the blood pressure was significantly reduced when the sodium intake was within 6 g/day. Worldwide, the major guidelines for the treatment of hypertension recommend that the salt intake be reduced to 6 g/day or less, based on the above-stated findings. The Japanese Guideline for the Management of Hypertension by the Japanese Society of Hypertension (JSH2009)⁽²³⁾ also set a threshold of 6 g/day for salt intake.

In Western countries, the guidelines for salt reduction are stricter. In 2010, the American Heart Association issued a recommendation stating that the goal for sodium intake should be 2,300 mg (a sodium chloride equivalent of 5.8 g/day) for healthy adults, and 1,500 mg (a sodium chloride equivalent of 5.8 g/day) for those at risk (having hypertension, belonging to a black race, or being middle-aged)⁽²⁴⁾. The 2013 WHO guideline for the general population strongly recommends a dietary salt intake goal of 5 g/day⁽¹⁾. Although the 2005 US-Canada DRIs set a salt intake lower than 1,500 mg/day as a dietary goal⁽²⁵⁾, this goal has been deleted in the recent DRIs due to a lack of relevant data⁽²⁶⁾. Several studies have reported on the association between dietary salt and cancer, especially gastric cancer. According to a review of the World Cancer Research Fund/American Institute for Cancer Research, the intake of salted foods and dietary salt are likely to increase the risk of gastric cancer⁽²⁷⁾. Japanese cohort studies have reported that dietary salt intake is positively associated with gastric cancer prevalence and

mortality⁽²⁸⁻³⁰⁾, while the frequency of the intake of salt-cured foods was associated with the risk of gastric cancer⁽²⁸⁾. A meta-analysis reported that a high salt intake increased the risk of gastric cancer⁽³¹⁾, while another meta-analysis reported the presence of a dose-response relationship between salt intake and gastric cancer risk⁽³²⁾.

4-2. Method Used to Set the DG

In the DRIs for Japanese 2010⁽²⁾, the target DG to attain over a period of 5 years was calculated to be less than 9 g/day for men, and less than 7.5 g/day for women. Since that point, the average intake of salt has decreased by approximately 0.5 g in men, and 1 g in women (the median intake was 10.5-11.8 g in men, and 8.8-10.0 g in women in the 2010 and 2011 NHNS)⁽³⁾. Although the current intake does not meet the DGs set in the previous DRI, the new DG should be set as low as possible, as a salt intake less than 6 g/day is favorable for the prevention and management of hypertension.

The 2013 WHO guideline for the general population strongly recommends achieving a dietary salt intake goal of 5 g/day⁽¹⁾. However, this goal was achieved in only about 5% of the participants in the 2010 and 2011 NHNS⁽³⁾. Considering that the intraindividual variation of dietary salt intake (34-36%) is greater than the interindividual variation (15-20%)⁽³³⁾, some individuals may consume less than 5 g/day habitually. Therefore, for the sake of feasibility, the DG should not be lower than 5 g/day.

Accordingly, the DG for sodium was set at the median of 5 g/day and the current intake (the median intake from the 2010 and 2011 NHNS⁽³⁾). This value was applied for the DG, except among those aged 50-69 years; in such cases, smoothing was conducted.

The 2013 WHO guideline for the general population strongly recommends a dietary salt intake goal of 5 g/day⁽¹⁾, through the calculation of the values for children by adjusting the adults' values for energy requirement. The current DRIs also extrapolated the values for adults aged 18 to 29 years into the values for children, using estimated energy requirement (level 2 of physical activity). The DG was set at the median of both these values, and the current intake (the median intake from the 2010 and 2011 NHNS⁽³⁾) as follows:

$$\text{DGx} = (5.0 \times (\text{EERx}/\text{EERo}) + \text{Ix} [\text{g/day}])/2$$

EERx: Estimated Energy Requirement for each age and sex group (kcal/day)

EERo: Estimated Energy Requirement for adults aged 18-29 years (kcal/day)

Ix: the median intake (sodium chloride equivalent) in the 2010 and 2011 NHNS⁽³⁾ (g/day)

Smoothing was conducted for girls aged 12-14 years, and those aged 15-17 years. No additional amount was set for pregnant or lactating women.

Table 1. Methods to determine the DG for sodium (salt equivalent: g/day)

Gender	Male				Female			
Age (years)	(A)	(B)	(C)	(D)	(A)	(B)	(C)	(D)
1-2	1.8	4.3	3.0	3.0	2.3	4.2	3.3	3.5
3-5	2.5	5.9	4.2	4.0	3.2	5.4	4.3	4.5
6-7	2.9	7.2	5.1	5.0	3.7	7.0	5.3	5.5
8-9	3.5	7.8	5.7	5.5	4.4	8.1	6.2	6.0
10-11	4.2	9.1	6.7	6.5	5.4	8.4	6.9	7.0
12-14	4.9	10.7	7.8	8.0	6.2	9.0	7.6	7.5 ↓
15-17	5.4	11.0	8.2	8.0	5.9	9.1	7.5	7.5 ↓
18-29	5.0	10.5	7.8	8.0	5.0	8.7	6.9	7.0
30-49	5.0	10.7	7.9	8.0	5.0	8.8	6.9	7.0
50-69	5.0	11.8	8.4	8.5 ↓	5.0	10.0	7.5	7.5 ↓
70+	5.0	10.7	7.8	8.0	5.0	9.4	7.2	7.0

(A) Recommendation in guideline of WHO in 2013. The values for 1-17 years old were extrapolated using estimated energy requirement.

(B) Median value of the sodium intake (salt equivalent) in NHNS2010 and NHNS2011 (g/day)

(C) Intermediate value of (A) and (B)

(D) Value after rounding, ↑ and ↓ present the way to smooth the calculated value (up and down)

Potassium

1. Background Information

1-1. Definition and Classification

Potassium is an alkali metal element (atomic number: 19: K) that is found in high quantities in fruits and vegetables; the amount of potassium decreases as the degree of processing or refinement increases^(34,35).

1-2. Function

As the main cation contained in intracellular fluid, potassium has an important role in the determination of the osmotic pressure of the aqueous humors and maintaining acid-base balance. It also participates in nerve transmission, muscle contraction, and regulation of vascular tone⁽³⁶⁾.

Potassium deficiency is rarely observed in healthy individuals, and typically affects only those with diarrhea or heavy perspiration, or those taking diuretics. The average sodium intake in Japan is higher than that in many other countries⁽³⁾. As the urinary excretion of sodium is related to potassium intake, it is believed that increasing the ingestion of potassium is important for Japanese individuals. Moreover, recent animal and epidemiological studies indicated that an increased potassium intake may be associated with a reduction in blood pressure and the prevention of stroke⁽³⁴⁾.

1-3. Digestion, Absorption and Metabolism

Although the absorption of potassium is passive, it is released actively in the ileum and large intestine. It is released in the large intestine at 25 mEq/L. In the case of severe diarrhea, the plasma potassium level sharply decreases, as more than 16 L/day of intestinal juices could be lost (hypokalemia).

2. To Avoid Inadequacy

2-1. Factors to be Considered in Estimating Requirements

Since potassium is present in various foods, its deficiency rarely occurs with the consumption of a regular diet. Few scientific data are available for the establishment of the EAR and RDA.

Therefore, the AI was determined to compensate for endogenous potassium loss and the maintenance of potassium balance at the present intake level. Moreover, the DG was determined for the prevention of the onset and progression of LRDs.

2-2. Method Used to Set the AI

2-2-1. Adults (AI)

The endogenous potassium loss has been estimated as follows: stool, 4.84 mg/kg BW/

day; urine, 2.14 mg/kg BW/ day; skin, 2.34 mg/kg BW/day (5.46 mg/kg BW/ day at high temperatures, at rest); and total, 9.32 mg/kg BW/day (12.44 mg/kg BW/day at high temperatures, at rest)⁽⁴⁾. Another study reported the total endogenous potassium loss to be 15.64 mg/kg BW /day⁽³⁷⁾. A study reported that when the loss from stool is 400 mg/day, and that from urine is 200 to 400 mg/day, the loss from sweat or others can be ignored, indicating that an intake of 800 mg/day is sufficient to maintain balance⁽⁴⁾. However, in that study, the plasma potassium levels of some participants decreased at this level; thus, 1,600 mg/day (23 mg/kg BW/day) was reported to be an appropriate amount. In research conducted in other countries, an intake of 1,600 mg was found to be adequate in the maintenance of potassium balance⁽³⁸⁾. From these findings, 1,600 mg/day can be considered as the amount at which balance can be maintained safely.

Based on data from the 2010 and 2011 NHNS, the median intakes of potassium were 2,309 mg/day and 2,138 mg/day in men and women, respectively⁽³⁾. The current intake of Japanese individuals was found to exceed the amount required for the maintenance of balance. The median intake of potassium in men aged over 50 years was approximately 2,500 mg/day; therefore, AIs of 2,500 mg/day and 2,000 mg/day were set for men and women, respectively; these values are not unrealizable, considering the differences in energy intake.

2-2-2. Children (AI)

Based on the AI of adults aged 18 to 29 years, the AI was extrapolated by the 0.75th power of the BW ratio, in consideration of the growth factors.

2-2-3. Infants (AI)

The AI for infants aged 0-5 months infants was calculated using the average concentration of potassium in breast milk (470 mg/L)^(9,10), and the daily intake of breast milk (0.78 L/day)^(11,12), yielding 367 mg/day.

The AI for infants aged 6 to 11 months was calculated using the amount of potassium obtained from breast milk (249 mg/day (470 mg/L × 0.53 L)^(13,14)) and complementary food (492 mg/day)⁽¹⁵⁾.

By rounding, the AIs were set at 400 mg/day and 700 mg/day for infants aged 0-5 months and 6-11 months, respectively.

2-2-4. Pregnant and Lactating Women (AI)

During pregnancy, the potassium demand increases, for the development of fetal tissues. This demand was reported to be 12.5 g⁽³⁷⁾. Considering this value as the demand over a period of 9 months, the daily requirement was calculated as 46 mg/day. This amount can be obtained from regular meals; therefore, an increase in the intake of potassium is not required during pregnancy. The median value from the 2007 to 2011 NHNS⁽³⁹⁾ was calculated to be 1,902 mg/day. The AI for women of childbearing age is 2,000 mg/day. From these data, the AI

for pregnant women was determined to be 2,000 mg/day.

For lactating women, the median value of the 2007 to 2011 NHNS⁽³⁹⁾ was calculated to be 2,161 mg/day. This value is considered to be sufficient for the maintenance of potassium balance, and thus, was adopted as the AI, yielding a value of 2,200 mg/day by rounding.

3. To Avoid Excessive Intake

If renal function is normal, the potassium intake from regular meals will not lead to excessive potassium levels. Therefore, the UL was not determined. However, caution must be exercised in terms of potassium intake, if renal disorders are present.

4. For the Prevention of the Development and Progression of LRDs

4-1. The Association between Sodium and Major LRDs

A meta-analysis of cohort studies⁽⁴⁰⁾ reported that, while increased potassium levels increased the risk of stroke, they did not affect the risk of cardiovascular diseases. An epidemiological study showed that the Na/K intake ratio was significantly associated with the risk of cardiovascular disease or all-cause mortality in the healthy population⁽⁴¹⁾. Thus, potassium intake should be evaluated in relation with salt intake. A recently published WHO guideline⁽³⁴⁾ recommends a potassium intake higher than 90 mmol (3,510 mg)/day. This value was determined from a meta-analysis which showed that a potassium intake of 90 to 120 mmol/day decreased the systolic blood pressure by 7.16 mmHg.

However, the presence of renal disorders requires attention, as these can cause hypokalemia in their milder forms; therefore, those with renal function disorders should avoid the aggressive intake of potassium.

4-2. Method Used to Set the DG

The WHO reported that an intake of 3,510 mg potassium/day is desirable for the prevention of high blood pressure⁽³⁴⁾. This value is considered an intake goal. However, considering the current intake of Japanese adults, this intake may be difficult to realize. Therefore, the DG was calculated using the following method. The reference was set at the current median intake of Japanese adults--2,384 mg for men and 2,215 mg for women--based on the 2010 and 2011 NHNS⁽³⁾. Then, the DGs were calculated by extrapolating by the 0.75th power of the BW ratio using the average reference BW (57.8 kg for adults) and reference BWs for each age and sex group (the average potassium intake and average reference BW were calculated solely from all the age and sex groups) as follows:

$$2,856 \text{ mg/day} \times (\text{reference BW for each age and sex group} / 57.8 \text{ kg})^{0.75}$$

The higher of the two values was adopted as the DG. In this method, rounding at each 200 mg/day and smoothing were conducted.

No additional DG was set for pregnant and lactating women.

For children aged 1 to 5 years, few reports present quantitative evidence on potassium

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Potassium

intake, and its association with the prevention of LRDs. It is difficult to assess potassium intake, and no relevant data were available in Japan. Thus, for children aged 6 to 17 years alone, the DG was determined using the same method as that used for adults. The current average intake was adopted when the calculated amount exceeded it. In the WHO guideline⁽³⁴⁾, the DG for adults was adjusted for energy requirement; however, the value for girls would be higher if the same DG as that used for boys is employed. Therefore, in the current DRIs, extrapolation was performed using the reference BW.

Table 2. Method to determine the DG for Potassium (mg/day)

Gender	Male				Female			
	Age (years)	(A)	(B)	(C)	(D)	(A)	(B)	(C)
6-7	1,393	1,861	(B)	1,800	1,379	1,822	(B)	1,800
8-9	1,658	1,986	(B)	2,000	1,632	1,977	(B)	2,000
10-11	1,986	2,198	(B)	2,200	2,015	2,052	(B)	2,000
12-14	2,523	2,450	(A)	2,600	2,465	2,211	(A)	2,400
15-17	2,926	2,332	(A)	3,000	2,634	1,939	(A)	2,600
18-29	3,054	2,004	(A)	3,000	2,562	1,700	(A)	2,600
30-49	3,244	2,077	(A)	↓ 3,000	2,680	1,843	(A)	2,600
50-69	3,130	2,452	(A)	↓ 3,000	2,676	2,341	(A)	2,600
70+	2,937	2,459	(A)	3,000	2,543	2,293	(A)	2,600

(A) Extrapolated value from the reference value for DG calculation (mg/day).

(B) Median value of the sodium intake (salt equivalent) in NHNS2010 and NHNS2011.

(C) Value of the DG determined.

(D) Value after rounding, ↑ and ↓ present the way to smooth the calculated value (up and down)

Calcium

1. Background Information

1-1. Definition and Classification

Calcium is an alkali earth metal (atomic number: 20: Ca) that accounts for 1%- 2% of the total BW of humans, with more than 99% present in the bones and teeth, and the remaining 1% in the blood, tissue fluid, and cells.

1-2. Function

The calcium concentration in the blood is controlled within a very narrow range (8.5 to 10.4 mg/dL). If the concentration decreases, the parathyroid hormone stimulates the absorption of calcium from bone, which undergoes repeated bone resorption (resorption of calcium from the bones) and bone formation (accumulation of calcium in the bones). Bone mass increases during growth, and begins to decrease in menopause or later, and then continues to decrease during the aging process. Calcium deficiency can cause osteoporosis, high blood pressure, or arteriosclerosis, while excessive calcium intake can cause hypercalcemia, hypercalciuria, calcification of soft tissues, urinary system calculus, prostate cancer, absorption disorders of iron and copper, or constipation.

1-3. Digestion, Absorption and Metabolism

Orally digested calcium is predominantly absorbed in the upper part of the small intestine through active transport. The absorption rate is comparably low, at 25 to 30%, and is affected by various factors such as age, pregnancy/lactation, or other food compositions. Vitamin D promotes calcium absorption.

Absorbed calcium is regulated by bone accumulation, and the urine excretion pathway through the kidney. Therefore, calcium nutrient status should take into account intake, absorption from the intestine, bone metabolism, and urine excretion.

2. To Avoid Inadequacy

2-1. Factors to be Considered in Estimating Requirements

As a biomarker for the requirement of calcium, bone health is important. This apart, calcium has been reported to be associated with LRDs such as blood pressure or obesity, although the effect has not been established⁽⁴²⁾. At present, the requirement cannot be set using biomarkers other than bone health.

A meta-analysis showed a significant association between calcium intake, bone mass and bone mineral density⁽⁴³⁻⁴⁵⁾. A Japanese epidemiological study demonstrated a significant association between increased bone fracture prevalence and low calcium intake⁽⁴⁶⁾. A meta-analysis of studies conducted in other countries reported no significant association between calcium intake and bone fracture prevalence⁽⁴⁷⁾. While intervention studies reported that

calcium supplementation alone was not associated with the prevention of bone fracture^(48,49), calcium supplementation with vitamin D inhibited bone fracture development according to a meta-analysis^(50,51). However, another report negated the above-stated finding⁽⁵²⁾; therefore, the results of epidemiological studies are not necessarily consistent.

In contrast, useful data have been accumulated for the estimation of the calcium intake required for the maintenance of bone mass using factorial methods. The US-Canada DRIs have set the EAR and RDA instead of the AI previously used⁽⁵³⁾. Although the US-Canada DRIs used data from balance studies, the current DRIs adopted factorial modeling, as no balance study has been conducted in recent times.

2-2. Method Used to Set the EAR and RDA

2-2-1. Background

For those aged over 1 year, the EAR and RDA were calculated using the factorial method, which considers the amount of calcium accumulated in the body, excreted through urine and lost via dermal tissue, as well as the apparent rates. For the RDA, the interindividual difference in the requirement is unclear; however, the coefficient of variation was set as 10%. For infants, the AI was determined.

2-2-2. Factors for Factorial Modeling

2-2-2-1. Calcium Accumulation in the Body

Few longitudinal studies have examined calcium accumulation in Japanese populations, especially among children. A Chinese study reported that the calcium accumulation in the body was 162.3 mg/day in girls aged 9.5 to 10.5 years, and the accumulation rate was 40.9%⁽⁵⁴⁾. In that study, the mean calcium intake was 444 mg/day, which is approximately 200 mg/day lower than that of Japanese girls of a similar age. In a study that examined adolescents, the greatest calcium accumulation was observed at 13.4 years of age in boys with an average calcium intake of 359 mg/day (standard deviation [SD] 82), and at 11.8 years of age in girls with an average calcium intake of 284 mg/day (SD 59)⁽⁵⁵⁾. Another study reported that the maximum accumulation was observed at 628.9 mg/day in boys, and the difference between the sexes was 171 mg/day⁽⁵⁶⁾. It is known that calcium accumulation varies between ethnicities. A study reported that a calcium intake of 700 mg/day resulted in an accumulation of 367 mg/day in black participants; this value was 183 mg/day in white participants, among adolescent girls⁽⁵⁷⁾. Although increased calcium intakes are not associated with race-related differences in the increase in the calcium accumulation, increased calcium intakes are associated with an increase in calcium accumulation, indicating that using the aforementioned results pertaining to calcium intakes higher than those in the normal Japanese diet may be problematic. Taking these into consideration, the accumulation for Japanese individuals was calculated.

The calcium accumulation per year was calculated based on the results of several

studies that examined the total body bone mineral content using dual-energy X-ray absorptiometry⁽⁵⁸⁻⁶⁷⁾, for each age and sex category. In a cross-sectional study on Japanese children, the accumulation was quite similar to that obtained from the current calculation⁽⁶⁷⁾. For children younger than 6 years of age, the calcium accumulation was determined according to increases in the bone mineral content per year⁽⁶⁸⁾.

2-2-2-2. Urine Excretion and Percutaneous Loss of Calcium

Urine calcium excretion can be calculated as $BW^{0.75} \times 6$ mg/day, when calcium balance is maintained⁽⁶⁹⁾. This calculation is similar to the 24-hour urine calcium excretion observed in a balance study in Japanese women^(70,71). Another study estimated the percutaneous loss to be approximately one-sixth of the urine excretion⁽⁷²⁾. Based on these findings, the percutaneous loss was calculated by estimating the urine calcium excretion calculated by the reference BW for each age and sex category.

2-2-2-3. Apparent Absorption

The apparent absorption rate varies inversely with the calcium intake⁽⁵⁷⁾. The intake level is higher in studies conducted in countries other than Japan; therefore, this rate may underestimate the requirement when applied to the Japanese population. The actual absorption rate estimated by the double-isotope method tends to be higher than the apparent rate. Therefore, the apparent rate was estimated based on studies that reported the results of balance tests (through which the apparent rate can be examined), and isotope procedures (through which the actual rate can be examined)⁽⁷³⁻⁹⁰⁾.

Table 3. Factors for factorial modeling to determine the EAR and RDA

Age (years)	Reference BW(kg)	(A) Body accumulation (mg/day)	(B) Urinary excretion	(C) Percutaneous loss(mg/day)	(A)+(B)+(C)	Apparent absorption rate (%)	EAR (mg/day)	RDA (mg/day)
Male								
1-2	11.5	99	37	6	143	40	357	428
3-5	16.5	114	49	8	171	35	489	587
6-7	22.2	99	61	10	171	35	487	585
8-9	28.0	103	73	12	188	35	538	645
10-11	35.6	134	87	15	236	40	590	708
12-14	49.0	242	111	19	372	45	826	991
15-17	59.7	151	129	21	301	45	670	804
18-29	63.2	38	135	22	195	30	648	778
30-49	68.5	0	143	24	167	30	557	668
50-69	65.3	0	138	23	161	27	596	716
70+	60.0	0	129	21	150	25	601	722
Female								
1-2	11.0	96	36	6	138	40	346	415
3-5	16.1	99	48	8	155	35	444	532
6-7	21.9	86	61	10	157	35	448	538
8-9	27.4	135	72	12	219	35	625	750
10-11	36.3	171	89	15	275	45	610	732
12-14	47.5	178	109	18	305	45	677	812
15-17	51.9	89	116	19	224	40	561	673
18-29	50.0	33	113	19	165	30	550	660
30-49	53.1	0	118	20	138	25	552	662
50-69	53.0	0	118	20	138	25	552	662
70+	49.5	0	112	19	131	25	524	629

2-2-3. Adults and Children (EAR, RDA)

The EAR and RDA were calculated using the factorial method, which considers the amount of calcium accumulated in the body, excreted by urine, and lost via dermal tissue, as well as the apparent rate. For the RDA, the interindividual difference in the requirement is unclear; however, the coefficient of variation was set as 10%.

2-2-4. Additional Amount for Pregnant and Lactating Women (EAR, RDA)

A newborn accrues about 28 to 30 g of calcium, most of which is obtained from the

mother and stored⁽⁹¹⁾. The intestinal calcium absorption rate in mothers doubles beginning early in pregnancy⁽⁹²⁾. A balance study in Japanese women reported that an increased absorption (42 ± 19%) was observed in the late stages of pregnancy compared to when they were not pregnant (23 ± 8%)⁽⁸⁸⁾. As a result, calcium is transferred to the fetus. At the same time, excess calcium absorption increases the urinary excretion in the mother. Therefore, an additional intake of calcium is not required for pregnant women. The US-Canada DRIs adopted this estimation⁽⁵³⁾. However, Hacker et al. reported that women with an insufficient calcium intake (less than 500 mg/day) may require an additional amount of calcium to meet both their demands and those of the fetus⁽⁹³⁾.

During lactation, the intestinal calcium absorption slightly increases⁽⁸⁸⁾, and the urine calcium excretion decreases^(82,94), so as to provide calcium to the breast milk. Thus, there is no requirement for additional calcium intake.

2-3. Method Used to Set the AI

2-3-1. Infants (AI)

The AI for infants was calculated based on the calcium concentration, and the volume of breast milk. For infants aged 0-5 months, the calcium concentration of breast milk was estimated to be 250 mg/L based on Japanese studies^(9,10). Using 0.78 L/day as the average milk intake^(11,12), the AI was determined to be 200 mg/day by rounding. Infant formula includes nutrient values that are similar to those of breast milk; however, the absorption rates are lower than in the case of breast milk^(73,95).

For infants aged over 6 months, the calculation of intake needs to consider breast milk as well as other food. Calcium intake from breast milk was calculated using the average milk intake (0.53 L/day)^(9,11,15), and the mean calcium concentration of breast milk (250 mg/L)^(9,11,15), and was estimated as 131 mg/day. The calcium intake from foods was estimated to be 128 mg/day for this age group; thus, the total calcium intake was estimated to be 261 mg/day, and the AI was set at 250 mg/day after rounding.

3. To Avoid Excessive Intake

3-1. Method Used to Set the UL

Excess calcium intake can cause hypercalcemia, hypercalciuria, soft tissue calcification, calculus development in the urinary system, prostate cancer, iron and zinc absorption disorders, and constipation⁽⁵³⁾. The previous DRIs set the lowest observed adverse effect level (LOAEL) using data pertaining to milk-alkali syndrome. Patel and Goldfarb suggested that the name of the syndrome be changed to “calcium-alkali syndrome”⁽⁹⁶⁾, and the US-Canada DRIs set the UL according to the results of this case report⁽⁵³⁾. High serum calcium levels were observed at a calcium intake greater than 3,000 mg/day in a case report on calcium-alkali syndrome⁽⁵³⁾.

From these data, the LOAEL was set at 3,000 mg/day, and the UL was set at 2,500

II Energy and Nutrients

Minerals (1) Macrominerals

Calcium

mg/day using an uncertainty factor of 1.2. The current dietary pattern among Japanese individuals is not considered to exceed 2,500 mg/day. However, calcium supplementation can lead to excessive intake. Bolland et al. reported that the use of calcium supplements elevated the risk of cardiovascular diseases^(97,98). Although these reports have attracted debate⁽⁹⁹⁾, it should be noted that calcium intake through supplementation or calcium medication may lead to excessive intake. For those aged under 18 years, the UL was not determined due to a lack of data.

Magnesium

1. Background Information

1-1. Definition and Classification

Magnesium is an alkaline earth metal (atomic number: 12, Mg) that contributes to the maintenance of bone health, and various enzymatic reactions. Approximately 25 g of magnesium exists in the adult body, and is present in bones at levels of 50% to 60%⁽¹⁰⁰⁾.

2. To Avoid Inadequacy

2-1. Factors to be Considered in Estimating Requirements

The EAR was calculated on the basis of the results obtained by previous studies on magnesium balance. For infants, the AI was determined using the magnesium concentration of breast milk and average milk volume.

2-2. Method Used to Set the EAR and RDA

2-2-1. Adults (EAR, RDA)

A magnesium balance study reported 4.7 mg/kg BW/day as the amount required for the maintenance of magnesium balance in 86 Japanese participants aged 18 to 28 years⁽¹⁰¹⁾. However, another Japanese study reported that the amount was 4.4 mg/kg BW/day among 109 participants aged 18 to 29 years⁽¹⁰²⁾. A report examining 31 Japanese participants aged 18 to 26 years from 13 studies pointed to a value of 4.18 mg/kg BW/day after adjusting the magnesium balance⁽¹⁰³⁾.

In contrast, an American study suggested that 4.3 mg/kg BW/day is the amount required for the maintenance of magnesium balance⁽¹⁰⁴⁾. A reanalysis of 243 Americans from 27 studies reported that, at an intake of 2.36 mg/kg BW/day of magnesium, the magnesium balance was 0⁽¹⁰⁵⁾.

Compared these findings, as the studies for Japanese individuals were given priority, and 4.5 mg was set as the EAR per an adult's BW. The RDA was set after multiplying it by the reference BW, applying a factor of 1.2, and assuming a coefficient of variation of 10%.

2-2-2. Children (EAR, RDA)

A magnesium balance study examining Japanese children aged 3 to 6 years estimated the EAR to be 2.6 mg/kg BW/day, based on the observation under conditions of the consumption of a regular diet⁽¹⁰⁶⁾. The results of an American balance test examining 12 boys and 13 girls, aged 9 to 14 years, using a stable magnesium isotope, determined the EAR to be 5 mg⁽⁷⁴⁾; this value was adopted since isotope procedures are considered reasonably accurate. This value was subsequently adopted as the RDA after multiplying it by the reference BW, and applying a factor of 1.2, as had been applied to the adult EAR.

2-2-3. Additional Amount for Pregnant and Lactating Women (EAR and RDA)

According to the results obtained in a magnesium balance study of pregnant women⁽¹⁰⁷⁾, an intake of 430 mg/day of magnesium maintained the plus balance in most participants. Considering that the lean BW during pregnancy is 6-9 kg (average 7.5 kg)⁽¹⁰⁸⁾, and the magnesium content per lean BW is 40 mg/kg BW⁽¹⁰⁹⁾, the additional amount of magnesium required can be calculated as 31.5 mg, using 40% as the apparent absorption rate for this period⁽⁷³⁾. Thus, the additional EAR was determined to be 30 mg. This value was subsequently adopted as the RDA after multiplying it by the reference BW and applying a factor of 1.2.

For lactating women, some studies reported that the urine magnesium concentration does not differ by the presence or absence of lactation^(110,111). Therefore, the additional amount required for lactating women was not determined.

2-3. Method Used to Set the AI

2-3-1. Infants (AI)

The AI for infants aged 0-5 months was calculated using the average concentration of magnesium in breast milk (27 mg/L^(9,10)), and average milk intake (0.78 L/day^(11,12)), yielding a value of 20 mg/day by rounding 21.1 mg/day.

The AI for infants aged 6-11 months was calculated using the consumption of magnesium from breast milk, calculated from the concentration of magnesium in breast milk (27 mg/L^(9,10)) and average milk intake (0.53 L/day^(13,14)), and complementary food (46 mg/day⁽¹⁵⁾). From these values, the AI was determined to be 60 mg/day.

3. To Avoid Excessive Intake

3-1. Method Used to Set the UL

The first stage of the unfavorable effects of excessive magnesium intake from sources other than food is diarrhea. Many individuals may experience mild transient diarrhea even without increased magnesium intake. Therefore, it is thought that the development of diarrhea symptoms may be the clearest index for the determination of the UL. The LOAEL was determined to be 360 mg/day based on reports from Western countries pertaining to intake through supplements⁽¹¹²⁻¹¹⁵⁾.

However, Japan-centric data were not available. As the diarrhea caused by excessive magnesium intake is not severe, and it is a reversible symptom, the uncertainty factor can be set at nearly 1. The US-Canada DRIs adopted these methods⁽¹¹⁶⁾. Similarly, the UL was determined to be 350 mg/day for adults, and 5 mg/day for children, for intake sources other than food.

In addition, data on unfavorable outcomes due to an excessive intake of magnesium from typical food sources were not found. Therefore, the UL for the intake of typical foods was not determined.

Phosphorus

1. Background Information

1-1. Definition and Classification

Phosphorus is a nitrogen family element (atomic number: 15, P), a maximum of 850 g of which is present in an adult individual, with 85% in the bones, 14% in soft tissues, and the remaining 1% in extracellular fluid.

2. To Avoid Inadequacy

2-1. Factors to be Considered in Estimating Requirements

Phosphorus balance studies conducted among Japanese women, aged 18-28 years, reported that the requirement amounts were 18.7 mg/kg BW /day⁽¹⁰³⁾ and 22.58 mg/kg BW/day⁽¹⁰²⁾. Based on these values, the EAR can be calculated as 946 mg/day or 1,143 mg/day, both of which are higher than the RDA value in the US-Canada DRIs (700 mg/ day⁽¹¹⁶⁾). Another study reported that the amount required for even balance was 1,180 mg/day for men, and 970 mg/day for women, among elderly Japanese individuals (the mean age was 74.1 years for men, and 71.9 years for women)⁽¹¹⁷⁾, which would yield a remarkably higher EAR. In the US-Canada DRIs, the EAR was calculated using the phosphorus intake required for the maintenance of the lowest normal level of plasma phosphorus⁽¹¹⁶⁾. However, due to a lack of evidence in determining the presumed Japanese EAR and RDA, the AI for phosphorus was determined.

2-2. Method Used to Set the AI

2-2-1. Adults and Children (AI)

According to the 2010 and 2011 NHNS⁽³⁾, the median phosphorus intake was 944 mg/day. However, the actual intake may be higher, since the phosphorus content of processed foods was not added to this value. A study using a duplicate method reported that the average phosphorus intake was $1,019 \pm 267$ mg/day⁽¹¹⁸⁾, which is comparable to the above-stated value.

Therefore, the AI for those aged over 1 year was adopted from the median intake from the 2010 and 2011 NHNS⁽³⁾, in relation to the US-Canada DRIs⁽¹¹⁶⁾. The same AI was set for adults aged over 18 years, based on the lowest intake among the age and sex groups.

2-2-2. Infants (AI)

The AI for infants aged 0-5 months was calculated using the average concentration of phosphorus in breast milk (150 mg/L)^(9,10) and the average milk intake (0.78 L/day)^(11,12), yielding 120 mg/day (rounding 117 mg/day).

The AI for infants aged 6 to 11 months was calculated using the average consumption of phosphorus from breast milk (80 mg/day) and complementary food (183 mg/day⁽¹⁵⁾), yielding 260 mg/day.

2-2-3. Pregnant and Lactating Women (AI)

The phosphorus body storage of newborns is reported to be 17.1 g⁽¹¹⁹⁾. If this value is considered the additional requirement for non-pregnant women, the total dietary requirement can be calculated as 61 mg/day. However, the dietary phosphorus absorption rate is 70% during pregnancy and 60-65% when not pregnant⁽¹¹⁶⁾. On multiplying the AI for non-pregnant women aged 18-29 years (800 mg/day) and the above-stated values, the phosphorus absorption can be estimated at 560 mg/day for pregnant women, and 480 mg/day for non-pregnant women. As the difference (80 mg/day) is greater than the 61 mg/day above mentioned, pregnant women do not require an additional phosphorus intake.

According to the 2007-2011 NHNS⁽³⁹⁾, the median phosphorus intake of pregnant Japanese women was 846 mg/day. As mentioned above, sufficient evidence was not available to increase the requirement, in comparison to non-pregnant women. Therefore, the AI was set at 800 mg/day, which is the same as that for non-pregnant women.

The serum phosphorus concentration has been reported to be high in lactating women, although there may be loss due to lactation⁽¹²⁰⁾. Furthermore, lactating women exhibit an elevated bone absorption of phosphorus and decreased urinary excretion⁽¹¹⁶⁾. Therefore, pregnant women do not require an additional amount of phosphorus. The median phosphorus intake of lactating women was 979 mg/day in the 2007-2011 NHNS⁽³⁹⁾. The AI was set at 800 mg/day, which is the same as that for non-pregnant women.

3. To Avoid Excessive Intake

3-1. Dietary Intake

Phosphorus is present in various foods. Although many processed foods use phosphorus as a food additive, the contribution of such phosphorus to the overall phosphorus intake is unclear since presenting information on the amount present, on food labels, is not mandatory.

3-2. Method Used to Set the UL

If renal function is normal, a high intake of phosphorus may enhance the secretion of parathyroid hormone and fibroblast growth factor 23 (FGF23), which promote phosphorus excretion from the kidney and maintain blood phosphorus concentrations⁽¹²¹⁾. Therefore, the fasting serum phosphorus concentration cannot be used as an indicator of excess phosphorus intake. Postprandial serum phosphorus concentration, urinary phosphorus excretion rate, parathyroid hormone level, and FGF23 level may be indicators for the determination of the UL.

The association between phosphorus intake and parathyroid hormone has been examined^(120,122-130). A study reported that hyperparathyroidism occurred when the phosphorus intake from food additives exceeded 2,100 mg/day⁽¹²²⁾. Additionally, an intake of 1,500-2,500 mg/day of inorganic phosphorus (phosphoric acid)^(123,124) or 400-800 mg/meal of inorganic phosphorus elevated postprandial parathyroid hormone levels⁽¹²⁵⁾. Excess phosphorus intake

reduces the calcium absorption in the intestine and acutely increases the postprandial serum inorganic phosphorus concentration, decreases the serum calcium ion concentration, and elevates the serum parathyroid hormone concentration⁽¹²⁰⁾. A report questioned if these reactions may lead to decreased bone mass⁽¹²⁶⁾. In contrast, a study reported that phosphorus intake elevated the blood parathyroid hormone concentration, dose-dependently, and bone resorption marker type 1 collagen cross-linked N-telopeptide level, and decreased the bone formation marker level (bone-type alkaline phosphatase) in women, under conditions of low calcium intake⁽¹²⁷⁾. The phosphorus and calcium intake ratio may also be considered. However, few human studies have focused on this issue, and it is difficult to determine the UL using the parathyroid hormone level as an indicator.

An increasing number of studies are focusing on FGF23 as an indicator of phosphorus load^(121,125,128–136). However, the methods used for the measurement of serum FGF23 levels were different between studies. Moreover, evidence on the effect of serum FGF23 function on human health is scarce, while the association between dietary phosphorus and serum FGF23 in Japanese individuals is unclear.

Several studies have reported an association between dietary phosphorus intake and adverse health effects in body parts other than the bones^(137–141). Although it may be possible to use these data for the determination of the UL, the intake levels leading to adverse effects ranged from 1,347–3,600 mg/day across the studies. Due to data insufficiency, it was difficult to set a threshold value.

One study examined the diurnal changes in serum phosphorus concentrations according to phosphorus intake⁽¹⁴²⁾. In that study, an intake of 1,500 mg/day phosphorus resulted in normal serum concentrations, while an intake of 3,000 mg/day led to a high serum phosphorus level. A Japanese study reported that an intake of 800 mg/meal (2,400 mg/day) did not lead to serum concentrations that exceeded the normal range, while 1,200 mg/meal (3,600 mg/day) exceeded the normal range⁽¹²⁵⁾. There is no standard value for urinary phosphorus excretion, and data on the relationship between urinary phosphorus excretion and adverse health effects are scarce.

The UL was determined based on the relationship between dietary phosphorus intake and the elevation of serum phosphorus concentration.

Serum inorganic phosphorus = 0.00765 × absorbed phosphorus + 0.8194 × (1-e(-0.2635 × absorbed phosphorus))

This equation includes both inorganic phosphorus (mmol/L), and absorbed phosphorus (mmol/day)⁽¹⁴³⁾. Assuming an absorption rate of 60%⁽¹²⁰⁾, serum inorganic phosphorus level of 4.3 mg/dL⁽¹⁴⁴⁾ (upper limit of the normal range) and phosphorus molar weight of 30.97, the phosphorus intake can be estimated as 3,686 mg/day, which is the upper limit of the normal range of the serum inorganic phosphorus level. This value was used as the LOAEL. Using an uncertainty factor of 1.2, the UL for adults was set at 3,000 mg/day by rounding 3,072 mg/day.

For children, the UL was not determined due to a lack of data.

II Energy and Nutrients
Minerals (1) Macrominerals

DRI_s for Sodium (mg/day. Values in parentheses are salt equivalent [g/day])

Gender	Males			Females		
	EAR	AI	DG	EAR	AI	DG
0-5 months	—	100(0.3)	—	—	100(0.3)	—
6-11 months	—	600(1.5)	—	—	600(1.5)	—
1-2 years	—	—	(<3.0)	—	—	(<3.5)
3-5 years	—	—	(<4.0)	—	—	(<4.5)
6-7 years	—	—	(<5.0)	—	—	(<5.5)
8-9 years	—	—	(<5.5)	—	—	(<6.0)
10-11 years	—	—	(<6.5)	—	—	(<7.0)
12-14 years	—	—	(<8.0)	—	—	(<7.0)
15-17 years	—	—	(<8.0)	—	—	(<7.0)
18-29 years	600(1.5)	—	(<8.0)	600(1.5)	—	(<7.0)
30-49 years	600(1.5)	—	(<8.0)	600(1.5)	—	(<7.0)
50-69 years	600(1.5)	—	(<8.0)	600(1.5)	—	(<7.0)
70+ years	600(1.5)	—	(<8.0)	600(1.5)	—	(<7.0)
Pregnant women	—			—	—	—
Lactating women				—	—	—

DRIs for Potassium (mg/day)

Gender	Males		Females	
Age etc.	AI	DG	AI	DG
0-5 months	400	—	400	—
6-11 months	700	—	700	—
1-2 years	900	—	800	—
3-5 years	1,100	—	1,000	—
6-7 years	1,300	≥1,800	1,200	≥1,800
8-9 years	1,600	≥2,000	1,500	≥2,000
10-11 years	1,900	≥2,200	1,800	≥2,000
12-14 years	2,400	≥2,600	2,200	≥2,400
15-17 years	2,800	≥3,000	2,100	≥2,600
18-29 years	2,500	≥3,000	2,000	≥2,600
30-49 years	2,500	≥3,000	2,000	≥2,600
50-69 years	2,500	≥3,000	2,000	≥2,600
70+ years	2,500	≥3,000	2,000	≥2,600
Pregnant women			2,000	—
Lactating women			2,200	—

DRI_s for Calcium (mg/day)

Gender	Males				Females			
	EAR	RDA	AI	UL	EAR	RDA	AI	UL
0-5 months	—	—	200	—	—	—	200	—
6-11 months	—	—	250	—	—	—	250	—
1-2 years	350	450	—	—	350	400	—	—
3-5 years	500	600	—	—	450	550	—	—
6-7 years	500	600	—	—	450	550	—	—
8-9 years	550	650	—	—	600	750	—	—
10-11 years	600	700	—	—	600	750	—	—
12-14 years	850	1,000	—	—	700	800	—	—
15-17 years	650	800	—	—	550	650	—	—
18-29 years	650	800	—	2,500	550	650	—	2,500
30-49 years	550	650	—	2,500	550	650	—	2,500
50-69 years	600	700	—	2,500	550	650	—	2,500
70+ years	600	700	—	2,500	550	650	—	2,500
Pregnant women					—	—	—	—
Lactating women					—	—	—	—

DRIs for Magnesium (mg/day)

Gender	Males				Females			
Age etc.	EAR	RDA	AI	UL ¹	EAR	RDA	AI	UL ¹
0-5 months	—	—	20	—	—	—	20	—
6-11 months	—	—	60	—	—	—	60	—
1-2 years	60	70	—	—	60	70	—	—
3-5 years	80	100	—	—	80	100	—	—
6-7 years	110	130	—	—	110	130	—	—
8-9 years	140	170	—	—	140	160	—	—
10-11 years	180	210	—	—	180	220	—	—
12-14 years	250	290	—	—	240	290	—	—
15-17 years	300	360	—	—	260	310	—	—
18-29 years	280	340	—	—	230	270	—	—
30-49 years	310	370	—	—	240	290	—	—
50-69 years	290	350	—	—	240	290	—	—
70+ years	270	320	—	—	220	270	—	—
Pregnant women (additional)					+30	+40	—	—
Lactating women (additional)					—	—	—	—

¹ No UL is developed for dietary intake from normal food. For dietary intake from sources other than normal food, ULs of 350 mg/day and 5 mg/kg body weight/day are set for adults and children, respectively.

DRIs for Phosphorus (mg/day)

Gender	Males		Females	
	AI	UL	AI	UL
0-5 months	120	—	120	—
6-11 months	260	—	260	—
1-2 years	500	—	500	—
3-5 years	800	—	600	—
6-7 years	900	—	900	—
8-9 years	1,000	—	900	—
10-11 years	1,100	—	1,000	—
12-14 years	1,200	—	1,100	—
15-17 years	1,200	—	900	—
18-29 years	1,000	3,000	800	3,000
30-49 years	1,000	3,000	800	3,000
50-69 years	1,000	3,000	800	3,000
70+ years	1,000	3,000	800	3,000
Pregnant women			800	—
Lactating women			800	—

References

1. WHO. (2012) *Guideline: Sodium intake for adults and children*. Geneva: World Health Organization (WHO).
2. Ministry of Health, Labour and Welfare (2009) *Dietary Reference Intakes for Japanese, 2010*. Tokyo: Daiichi Shuppan Publishing Co., Ltd.
3. Ministry of Health, Labour and Welfare, National Health and Nutrition Survey in Japan, Results of 2010-2011.
http://www.mhlw.go.jp/bunya/kenkou/dl/kenkou_eiyou_chousa_tokubetsuuukei_h22.pdf.
4. Aitken FC. (1976) *Sodium and potassium in nutrition of mammals*. Farnham Royal, Slough: Commonwealth Agricultural Bureaux.
5. National Research Council. (1989) *Recommended Dietary Allowances*. 10th ed. Washington, D.C.: National Academies Press.
6. Department of Health. (1991) *Report on health and social subjects 41 dietary reference values of food energy and nutrients for the United Kingdom*. London: Her Majesty's Stationery Office.
7. Maughan RJ & Shirreffs SM (1997) Recovery from prolonged exercise: restoration of water and electrolyte balance. *J Sports Sci* **15**, 297–303.
8. Lindheimer M, Conrad K & Karumanchi A (2008) Renal physiology and disease in pregnancy. In *Seldin and Giebisch's the Kidney: physiology and pathophysiology*, 4th ed., pp. 2339–2398 [Alpern R, Hebert R, editors]. Burlington: Academic Press.
9. Yamawaki N, Yamada M, Kan-no T, et al. (2005) Macronutrient, mineral and trace element composition of breast milk from Japanese women. *J Trace Elem Med Biol* **19**, 171–181.
10. Itoda T (2007) Analysis of breast milk composition: as a target of infant formula composition (in Japanese). *Obstet Gynecol Pract* **56**, 315–325.
11. Suzuki K, Sasaki S, Shizawa K, et al. (2004) Milk intake by breast-fed infants before weaning (in Japanese). *Japanese J Nutr* **62**, 369–372.
12. Hirose J, Endo M, Shibata K, et al. (2008) Amount of breast milk sucked by Japanese breast feeding infants (in Japanese). *J Japanese Soc Breastfeed Res* **2**, 23–28.
13. Yoneyama K (1998) Growth of breast-fed infants and intake of nutrients from breast-milk (in Japanese). *J Child Heal* **57**, 49–57.
14. Yoneyama K, Goto I & Nagata H (1995) Changes in the concentrations of nutrient components of human milk during lactation (in Japanese). *Japanese J public Heal* **42**, 472–481.
15. Nakano T, Kato K, Kobayashi N, et al. (2003) Nutrient intake from baby foods infant formula and cow's milk -results from a nation wide infant's dietary survey- (in Japanese). *J Child Heal* **62**, 630–9.

16. The Council for Science and Technology, Ministry of Education, Culture, Sports and Technology (2010) *Standard tables of food composition in Japan - 2010*. Tokyo: Official Gazette Co-operation.
17. The Trials of Hypertension Prevention Collaborative Research Group. (1992) The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: Results of the Trials of Hypertension Prevention, Phase I. *JAMA* **267**, 1213–1220.
18. Whelton PK, Appel LJ, Espeland MA, et al. (1998) Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA* **279**, 839–46.
19. He J, Whelton PK, Appel LJ, et al. (2000) Long-term effects of weight loss and dietary sodium reduction on incidence of hypertension. *Hypertension* **35**, 544–549.
20. Sacks FM, Svetkey LP, Vollmer WM, et al. (2001) Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med* **344**, 3–10.
21. The Trials of Hypertension Prevention Collaborative Research Group. (1997) Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, Phase II. *Arch Intern Med* **157**, 657–667.
22. Espeland MA, Whelton PK, Kostis JB, et al. (1999) Predictors and mediators of successful long-term withdrawal from antihypertensive medications. TONE Cooperative Research Group. Trial of Nonpharmacologic Interventions in the Elderly. *Arch Fam Med* **8**, 228–36.
23. Committee for Guidelines for the Management of Hypertension (2009) *The Japanese Guideline for Hypertension 2009* (in Japanese). Japanese Society of Hypertension.
24. Lloyd-Jones DM, Hong Y, Labarthe D, et al. (2010) Defining and setting national goals for cardiovascular health promotion and disease reduction: The american heart association's strategic impact goal through 2020 and beyond. *Circulation* **121**, 586–613.
25. Food and Nutrition Board, Institute of Medicine (2005) *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate*. Washington, D.C.: National Academies Press.
26. Food and Nutrition Board, Institute of Medicine (2013) Sodium intake in Populations Assessment of evidence. <http://www.iom.edu/Reports/2013/Sodium-Intake-in-Populations-assessment-of-Evidence.aspx>.
27. World Cancer Research Fund/ American Institute for Cancer Research (2007) *Food, nutrition, physical activity and the prevention of cancer, a global perspective*. .
28. Tsugane S, Sasazuki S, Kobayashi M, et al. (2004) Salt and salted food intake and

subsequent risk of gastric cancer among middle-aged Japanese men and women. *Br J Cancer* **90**, 128–134.

29. Kurosawa M, Kikuchi S, Xu J, et al. (2006) Highly salted food and mountain herbs elevate the risk for stomach cancer death in a rural area of Japan. *J Gastroenterol Hepatol* **21**, 1681–1686.

30. Shikata K, Kiyohara Y, Kubo M, et al. (2006) A prospective study of dietary salt intake and gastric cancer incidence in a defined Japanese population: The Hisayama study. *Int J Cancer* **119**, 196–201.

31. Ge S, Feng X, Shen L, et al. (2012) Association between habitual dietary salt intake and risk of gastric cancer: A systematic review of observational studies. *Gastroenterol Res Pract* **2012**, 808120.

32. D'Elia L, Rossi G, Ippolito R, et al. (2012) Habitual salt intake and risk of gastric cancer: A meta-analysis of prospective studies. *Clin Nutr* **31**, 489–498.

33. Fukumoto A, Asakura K, Murakami K, et al. (2013) Within- and between-individual variation in energy and nutrient intake in Japanese adults: effect of age and sex differences on group size and number of records required for adequate dietary assessment. *J Epidemiol* **23**, 178–86.

34. WHO. (2012) *Guideline: Potassium intake for adults and children*. Geneva: World Health Organization (WHO).

35. Webster JL, Dunford EK & Neal BC (2010) A systematic survey of the sodium contents of processed foods. *Am J Clin Nutr* **91**, 413–420.

36. Young D (2001) *Role of potassium in preventive cardiovascular medicine*. Boston: Kluwer Academic Publishers.

37. Preuss HG. (2006) Electrolytes: sodium, chloride, and potassium. In *Present knowledge in nutrition*, 9th ed., pp. 409–421 [Bowman B, Russel R, editors]. Washington D.C.: ILSI Press.

38. Frank H, Hastings T & Brophy T (1952) Fluid and electrolyte management in pediatric surgery. *West J Surg Obstet Gynecol* **60**, 25–31.

39. Ministry of Health, Labour and Welfare, National Health and Nutrition Survey in Japan, Results of 2007-2011.
http://www.mhlw.go.jp/bunya/kenkou/dl/kenkou_eiyou_chousa_tokubetsuuukei_ninpu_h19.pdf.

40. Aburto NJ, Hanson S, Gutierrez H, et al. (2013) Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ* **346**, f1378.

41. Yang Q, Liu T, Kuklina E V, et al. (2011) Sodium and potassium intake and mortality among US adults: prospective data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med* **171**, 1183–91.

42. Onakpoya IJ, Perry R, Zhang J, et al. (2011) Efficacy of calcium supplementation for

management of overweight and obesity: Systematic review of randomized clinical trials. *Nutr Rev* **69**, 335–343.

43. Sasaki S & Yanagibori R (2001) Association between current nutrient intakes and bone mineral density at calcaneus in pre- and postmenopausal Japanese women. *J Nutr Sci Vitaminol* **47**, 289–94.
44. Cumming RG & Nevitt MC (1997) Calcium for prevention of osteoporotic fractures in postmenopausal women. *J Bone Miner Res* **12**, 1321–1329.
45. Welten DC, Kemper HC, Post GB, et al. (1995) A meta-analysis of the effect of calcium intake on bone mass in young and middle aged females and males. *J Nutr* **125**, 2802–13.
46. Nakamura K, Kurahashi N, Ishihara J, et al. (2009) Calcium intake and the 10-year incidence of self-reported vertebral fractures in women and men: The Japan Public Health Centre-based Prospective Study. *Br J Nutr* **101**, 285–294.
47. Xu L, McElduff P, D'Este C, et al. (2004) Does dietary calcium have a protective effect on bone fractures in women? A meta-analysis of observational studies. *Br J Nutr* **91**, 625.
48. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. (2007) Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr* **86**, 1780–90.
49. Winzenberg T, Shaw K, Fryer J, et al. (2006) Effects of calcium supplementation on bone density in healthy children: meta-analysis of randomised controlled trials. *BMJ* **333**, 775.
50. Tang BMP, Eslick GD, Nowson C, et al. (2007) Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* **370**, 657–66.
51. Boonen S, Lips P, Bouillon R, et al. (2007) Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. *J Clin Endocrinol Metab* **92**, 1415–23.
52. Jackson RD, LaCroix AZ, Gass M, et al. (2006) Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med* **354**, 669–83.
53. Food and Nutrition Board Institute of Medicine. (2011) *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, D.C.: National Academies Press.
54. Zhu K, Greenfield H, Zhang Q, et al. (2008) Growth and bone mineral accretion during puberty in Chinese girls: A five-year longitudinal study. *J Bone Miner Res* **23**, 167–172.
55. Bailey DA, Martin AD, McKay HA, et al. (2000) Calcium accretion in girls and boys during puberty: A longitudinal analysis. *J Bone Miner Res* **15**, 2245–2250.
56. Braun M, Martin BR, Kern M, et al. (2006) Calcium retention in adolescent boys on a range of controlled calcium intakes. *Am J Clin Nutr* **84**, 414–418.

57. Braun M, Palacios C, Wigertz K, et al. (2007) Racial differences in skeletal calcium retention in adolescent girls with varied controlled calcium intakes. *Am J Clin Nutr* **85**, 1657–1663.
58. van der Sluis IM, de Ridder MAJ, Boot AM, et al. (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**, 341-7; discussion 341-7.
59. Bachrach LK, Hastie T, Wang MC, et al. (1999) Bone mineral acquisition in healthy Asian, Hispanic, black, and Caucasian youth: a longitudinal study. *J Clin Endocrinol Metab* **84**, 4702–12.
60. Maynard LM, Guo SS, Chumlea WC, et al. (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**, 1111–7.
61. Kalkwarf HJ, Zemel BS, Gilsanz V, et al. (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.
62. Mølgaard C, Thomsen BL & Michaelsen KF (1999) Whole body bone mineral accretion in healthy children and adolescents. *Arch Dis Child* **81**, 10–15.
63. Zhu K, Zhang Q, Foo LH, et al. (2006) Growth, bone mass, and vitamin D status of Chinese adolescent girls 3 y after withdrawal of milk supplementation. *Am J Clin Nutr* **83**, 714–21.
64. Abrams SA, Copeland KC, Gunn SK, et al. (2000) Calcium absorption, bone mass accumulation, and kinetics increase during early pubertal development in girls. *J Clin Endocrinol Metab* **85**, 1805–9.
65. Martin AD, Bailey DA, McKay HA, et al. (1997) Bone mineral and calcium accretion during puberty. *Am J Clin Nutr.* **66**, 611–5.
66. Whiting SJ, Vatanparast H, Baxter-Jones A, et al. (2004) Factors that affect bone mineral accrual in the adolescent growth spurt. *J Nutr* **134**, 696S–700S.
67. Nishiyama S, Kiwaki K, Inomoto T, et al. (1999) Bone mineral density of the lumbar spine and total body mass in Japanese children and adolescents (in Japanese). *J Japan Pediatr Soc* **103**, 1131–1138.
68. Butte NF, Hopkinson JM, Wong WW, et al. (2000) Body composition during the first 2 years of life: an updated reference. *Pediatr Res* **47**, 578–85.
69. Schaafsma G (1992) The scientific basis of recommended dietary allowances for calcium. *J Intern Med* **231**, 187–94.
70. Uenishi K, Ishida H, Kamei A, et al. (2000) Calcium requirement among young women: Comparison with elderly people (in Japanese). *Osteoporos Japan* **8**, 217–219.
71. Uenishi K, Ishida H, Kamei A, et al. (2001) Calcium requirement estimated by balance study in elderly Japanese people. *Osteoporos Int* **12**, 858–63.
72. Charles P, Eriksen EF, Hasling C, et al. (1991) Dermal, intestinal, and renal obligatory

losses of calcium: relation to skeletal calcium loss. *Am J Clin Nutr* **54**, 266S–273S.

- 73. Abrams SA, Wen J & Stuff JE (1997) Absorption of calcium, zinc, and iron from breast milk by five- to seven-month-old infants. *Pediatr Res* **41**, 384–390.
- 74. Abrams SA, Grusak MA, Stuff J, et al. (1997) Calcium and magnesium balance in 9-14-y-old children. *Am J Clin Nutr* **66**, 1172–7.
- 75. Tahiri M, Tressol JC, Arnaud J, et al. (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.
- 76. Cifuentes M, Riedt CS, Brolin RE, et al. (2004) Weight loss and calcium intake influence calcium absorption in overweight postmenopausal women. *Am J Clin Nutr* **80**, 123–30.
- 77. Lynch MF, Griffin IJ, Hawthorne KM, et al. (2007) Calcium balance in 1-4-y-old children. *Am J Clin Nutr* **85**, 750–4.
- 78. Kohlenberg-Mueller K & Raschka L (2003) Calcium balance in young adults on a vegan and lactovegetarian diet. *J Bone Miner Metab* **21**, 28–33.
- 79. Abrams SA, Griffin IJ, Hawthorne KM, et al. (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.
- 80. O'Brien KO, Abrams SA, Liang LK, et al. (1996) Increased efficiency of calcium absorption during short periods of inadequate calcium intake in girls. *Am J Clin Nutr* **63**, 579–83.
- 81. Weaver CM, McCabe LD, McCabe GP, et al. (2008) Vitamin D status and calcium metabolism in adolescent black and white girls on a range of controlled calcium intakes. *J Clin Endocrinol Metab* **93**, 3907–14.
- 82. Moser-Veillon PB, Mangels AR, Vieira NE, et al. (2001) Calcium fractional absorption and metabolism assessed using stable isotopes differ between postpartum and never pregnant women. *J Nutr* **131**, 2295–9.
- 83. Heany RP, Recker RR & Hinders SM (1988) Variability of calcium absorption. *Am J Clin Nutr* **47**, 262–264.
- 84. Miller JZ, Smith DL, Flora L, et al. (1988) Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* **48**, 1291–4.
- 85. Abrams SA, O'Brien KO, Liang LK, et al. (1995) Differences in calcium absorption and kinetics between black and white girls aged 5-16 years. *J Bone Miner Res* **10**, 829–33.
- 86. Bryant RJ, Wastney ME, Martin BR, et al. (2003) Racial differences in bone turnover and calcium metabolism in adolescent females. *J Clin Endocrinol Metab* **88**, 1043–7.
- 87. Weaver CM, Martin BR, Plawecki KL, et al. (1995) Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* **61**, 577–81.

88. Uenishi K, Ishida H, Kamei A, et al. (2003) Calcium balance of pregnant and lactating women in consuming regular meals (in Japanese). *Osteoporos Japan* **11**, 249–251.
89. Heaney RP, Recker RR, Stegman MR, et al. (1989) Calcium absorption in women: Relationships to Calcium intake, Estrogen status, and age. *J Bone Miner Res* **4**, 469–475.
90. Roughead ZK, Johnson LK, Lykken GI, et al. (2003) Controlled high meat diets do not affect calcium retention or indices of bone status in healthy postmenopausal women. *J Nutr* **133**, 1020–6.
91. King JC (2000) Physiology of pregnancy and nutrient metabolism. *Am J Clin Nutr* **71**, 1218S–25S.
92. Cross NA, Hillman LS, Allen SH, et al. (1995) Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: a longitudinal study. *Am J Clin Nutr* **61**, 514–23.
93. Hacker AN, Fung EB & King JC (2012) Role of calcium during pregnancy: maternal and fetal needs. *Nutr Rev* **70**, 397–409.
94. Ritchie LD, Fung EB, Halloran BP, et al. (1998) A longitudinal study of calcium homeostasis during human pregnancy and lactation and after resumption of menses. *Am J Clin Nutr* **67**, 693–701.
95. Rigo J, Salle BL, Picaud JC, et al. (1995) Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* **49 Suppl 1**, S26-38.
96. Patel AM & Goldfarb S (2010) Got Calcium? Welcome to the Calcium-Alkali Syndrome. *J Am Soc Nephrol* **21**, 1440–1443.
97. Bolland MJ, Barber PA, Doughty RN, et al. (2008) Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. *BMJ* **336**, 262–6.
98. Bolland MJ, Avenell A, Baron JA, et al. (2010) Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. *BMJ* **341**, c3691.
99. Spence LA & Weaver CM (2013) Calcium intake, vascular calcification, and vascular disease. *Nutr Rev* **71**, 15–22.
100. Fleet JC & Cashman KD (2001) Magnesium. In *Present knowledge in nutrition*, 8th ed., pp. 292–301 [Bowman B, Russell R, editors]. Washington, D.C.: ILSI Press.
101. Nishimuta M, Kodama N, Yoshida Y, et al. (2001) Magnesium intake and balance in the Japanese population. In *Advances in Magnesium Research: Nutrition and Health*. pp. 197–200 [Rayssiguier Y, Mazur A, Durlach J, editors]. John Libbey and Company Ltd.
102. Nishimuta M, Kodama N, Eiko M, et al. (2004) Balances of calcium, magnesium and phosphorus in Japanese young adults. *J Nutr Sci Vitaminol* **50**, 19–25.
103. Nishimuta M, Kodama N, Shimada M, et al. (2012) Estimated equilibrated dietary intakes for nine minerals (Na, K, Ca, Mg, P, Fe, Zn, Cu, and Mn) adjusted by mineral

balance medians in young Japanese females. *J Nutr Sci Vitaminol* **58**, 118–28.

104. Lakshmanan FL, Rao RB, Kim WW, et al. (1984) Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* **40**, 1380–9.

105. Hunt CD & Johnson LAK (2007) Calcium requirements: New estimations for men and women by cross-sectional statistical analyses of calcium balance data from metabolic studies. *Am J Clin Nutr* **86**, 1054–1063.

106. Kazuharu S (1991) Mineral intake and its balance in Japanese young children (in Japanese). *J Japan Soc Nutr Food Sci* **44**, 89–104.

107. Mildred S (1980) *Magnesium deficiency in the pathogenesis of disease*. New York: Plenum Medical.

108. Subcommittee on Nutrition during Lactation Committee on Nutritional Status during Pregnancy and Lactation. Food and Nutrition Board Institute of Medicine (1991) *Nutrition during lactation*. Washington, D.C.: National Academies Press.

109. Widdowson E & Dickerson J (1964) The chemical composition of the body. In *Mineral metabolism: An advanced treatise, Volume II The elements. Part A*, pp. 1–247 [Comer C, Bronner F, editors]. New York: Academic Press.

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

111. Klein CJ, Moser-Veillon PB, Douglass LW, et al. (1995) A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* **61**, 779–86.

112. Bashir Y, Sneddon JF, Anne Staunton H, et al. (1993) Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* **72**, 1156–1162.

113. Fine KD, Santa Ana CA & Fordtran JS (1991) Diagnosis of magnesium-induced diarrhea. *N Engl J Med* **324**, 1012–7.

114. Marken PA, Weart CW, Carson DS, et al. (1989) Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* **77**, 37–42.

115. Ricci JM, Hariharan S, Helfgott A, et al. (1991) Oral tocolysis with magnesium chloride: a randomized controlled prospective clinical trial. *Am J Obstet Gynecol* **165**, 603–10.

116. Food and Nutrition Board Institute of Medicine (1997) *Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride*. Washington D.C.: National Academies Press.

117. Okuda T, Miyoshi-Nishimura H, Matsudaira T, et al. (1995) Dietary intake, absorption and balance of calcium, phosphorus and magnesium in elderly people (in Japanese). *Japanese J Nutr Diet* **53**, 33–40.

118. Nakamura K, Hori Y, Nashimoto M, et al. (2003) Nutritional covariates of dietary calcium in elderly Japanese women: Results of a study using the duplicate portion

sampling method. *Nutrition* **19**, 922–925.

- 119. Fomon SJ, Haschke F, Ziegler EE, et al. (1982) Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* **35**, 1169–1175.
- 120. Anderson JJB (1991) Nutritional biochemistry of calcium and phosphorus. *J Nutr Biochem*, 300–307.
- 121. Bergwitz C & Jüppner H (2010) Regulation of phosphate homeostasis by PTH, vitamin D, and FGF23. *Annu Rev Med* **61**, 91–104.
- 122. Bell RR, Draper HH, Tzeng DY, et al. (1977) Physiological responses of human adults to foods containing phosphate additives. *J Nutr* **107**, 42–50.
- 123. Calvo MS & Heath H (1988) Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* **47**, 1025–1029.
- 124. Silverberg SJ, Shane E, Clemens TL, et al. (1986) The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* **1**, 383–8.
- 125. Nishida Y, Taketani Y, Yamanaka-Okumura H, et al. (2006) Acute effect of oral phosphate loading on serum fibroblast growth factor 23 levels in healthy men. *Kidney Int* **70**, 2141–2147.
- 126. Zemel MB & Linkswiler HM (1981) Calcium metabolism in the young adult male as affected by level and form of phosphorus intake and level of calcium intake. *J Nutr* **111**, 315–24.
- 127. Kemi VE, Kärkkäinen MUM & Lamberg-Allardt CJE (2006) High phosphorus intakes acutely and negatively affect Ca and bone metabolism in a dose-dependent manner in healthy young females. *Br J Nutr* **96**, 545–52.
- 128. Vervloet MG, van Ittersum FJ, Büttler RM, et al. (2011) Effects of dietary phosphate and calcium intake on fibroblast growth factor-23. *Clin J Am Soc Nephrol* **6**, 383–9.
- 129. Ferrari SL, Bonjour J-P & Rizzoli R (2005) Fibroblast growth factor-23 relationship to dietary phosphate and renal phosphate handling in healthy young men. *J Clin Endocrinol Metab* **90**, 1519–24.
- 130. Antoniucci DM, Yamashita T & Portale AA (2006) Dietary phosphorus regulates serum fibroblast growth factor-23 concentrations in healthy men. *J Clin Endocrinol Metab* **91**, 3144–9.
- 131. Faul C, Amaral AP, Oskouei B, et al. (2011) FGF23 induces left ventricular hypertrophy. *J Clin Invest* **121**, 4393–408.
- 132. Burnett SAM, Gunawardene SC, Bringhurst FR, et al. (2006) Regulation of C-terminal and intact FGF-23 by dietary phosphate in men and women. *J Bone Miner Res* **21**, 1187–96.
- 133. Sigrist M, Tang M, Beaulieu M, et al. (2013) Responsiveness of FGF-23 and mineral metabolism to altered dietary phosphate intake in chronic kidney disease (CKD):

Results of a randomized trial. *Nephrol Dial Transplant* **28**, 161–169.

- 134. Mirza MAI, Larsson A, Lind L, et al. (2009) Circulating fibroblast growth factor-23 is associated with vascular dysfunction in the community. *Atherosclerosis* **205**, 385–390.
- 135. Mirza MAI, Hansen T, Johansson L, et al. (2009) Relationship between circulating FGF23 and total body atherosclerosis in the community. *Nephrol Dial Transplant* **24**, 3125–3131.
- 136. Mirza MAI, Larsson A, Melhus H, et al. (2009) Serum intact FGF23 associate with left ventricular mass, hypertrophy and geometry in an elderly population. *Atherosclerosis* **207**, 546–551.
- 137. Yamamoto KT, Robinson-Cohen C, De Oliveira MC, et al. (2013) Dietary phosphorus is associated with greater left ventricular mass. *Kidney Int* **83**, 707–714.
- 138. Shuto E, Taketani Y, Tanaka R, et al. (2009) Dietary phosphorus acutely impairs endothelial function. *J Am Soc Nephrol* **20**, 1504–12.
- 139. Elliott P, Kesteloot H, Appel LJ, et al. (2008) Dietary phosphorus and blood pressure: international study of macro- and micro-nutrients and blood pressure. *Hypertension* **51**, 669–75.
- 140. Alonso A, Nettleton JA, Ix JH, et al. (2010) Dietary phosphorus, blood pressure, and incidence of hypertension in the atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. *Hypertension* **55**, 776–784.
- 141. Berkemeyer S, Bhargava A & Bhargava U (2007) Urinary phosphorus rather than urinary calcium possibly increases renal stone formation in a sample of Asian Indian, male stone-formers. *Br J Nutr* **98**, 1224–1228.
- 142. Portale AA, Halloran BP & Morris RC (1987) Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* **80**, 1147–54.
- 143. Nordin BEC. (1989) Phosphorus. *J Food Nutr* **45**, 62–75.
- 144. Ogawa A & Kawaguchi Y (1989) Hyper- and hypo-phosphataemia (in Japanese). *Japanese J Med Pharm Sci* **22**, 321–328.