When the average values of physiological functions for 30 year olds have been taken as 100%, and the values for increasing age categories are shown as a percentage of this value, bone density decreases about 40% over the age span of 30 to 80 years (1). The decrease of bone density in aging would be the outcome, or the change in calcium metabolism would be needed to maintain normal serum calcium level, despite the reduced calcium intake and absorption (1).

Regulation of calcium metabolism in aging is not completely understood, however, as it is obvious that various factors, such as endocrine factors and nutrients, are involved in the process. Among the nutrients, calcium and protein are important, because they are major constituents of bone. Vitamins A, C, D, and K are also shown to be involved in this process. However, vitamin D is now defined as a hormone (2), thus the changes of vitamins A, C, and K status in aging were discussed in relation to calcium metabolism.

1. Recent trends in vitamin status in Japan

National nutrition survey 1982 in Japan showed that the intakes of all examined nutrients, except for calcium, were above mean RDA (Recommended Dietary Allowances) values for the surveyed subjects. Namely, the 1982 survey revealed that there was no vitamin in which the intake was inadequate (Fig. 1) (3).

However, these values express only means of all surveyed subjects. A national nutrition survey in Japan is carried out on the basis of household units and nutrients intakes are calculated from food composition tables, which list only one value for one item (food). Therefore, we can not estimate the variation of food composition from the table. Moreover, loss of nutrients, especially micronutrients, during storage and cooking will be considerable. Thus, the values might be overestimated.

Moreover, aging may change nutrient intakes, increase the need for vitamins and interfere with their absorption, storage, and utilization. Generally, an overall decrease in food consumption occurs in old age, resulting in lower intake of vitamins, which leads to a lower level of vitamins in the blood, without any characteristic symptoms of vitamin deficiency.

Brin summarized the development of vitamin deficiency as follows (4). In the first stage, tissue stores of vitamins diminish as a result of inadequate dietary intake, malabsorption, or other medical disorders, such as infection or diarrhea. With severe reduction in the amount of vitamins stored in the body, the availability of essential coenzymes decreases, metabolic capacity becomes inadequate to maintain health, biochemical abnormalities are demonstrable and there are nonspecific clinical signs of diseases (the second and third stages). Also evident at this stage is the impairment of psychologic functions. With worsening of vitamin deficiency, specific clinical symptoms appear. If the vitamin deficiency is not corrected, there will be irreversible changes in tissues (the fourth stage). The first three stages might be called a marginal state of vitamin deficiency.

At present, severe vitamin deficiency is rare in Japan. However, marginally vitamin deficient persons may be increasing, especially in old age groups, although the results of the national nutrition survey showed that there was no vitamin inadequacy, compared with the RDA.

2. Changes of vitamin A status in aging

Vitamin A status is evaluated from plasma
Fig. 1. Comparison between nutrients intakes and mean RDA values (100%) for surveyed subjects.

Fig. 2. Plasma RBP levels in individual age groups. Vitamin A level. However, plasma vitamin A level is well correlated with plasma RBP (retinol binding protein) level (5). Therefore, vitamin A status was estimated from the changes in plasma RBP level.

Generally, plasma RBP level increases rapidly after birth and reaches adult levels after 60 days. Muto reported that plasma RBP levels in individual age groups had a slight tendency to increase in the 20 to 50 age groups, however, after 60 years of age, plasma RBP levels decreased (Fig. 2) (5).

When the criteria of plasma RBP levels are considered, with a level of 30 μg/ml, 30% of those in the sixties and 40% in the seventies to eighties showed lower levels of RBP. These results suggest that quite a few persons are in marginal vitamin A deficient status after the sixties, although it is not clear that those persons have some disorders in calcium metabolism or not.

Vitamin A is known to be involved in calcium metabolism via action on differentiation and activity of osteoblasts and osteoclasts. Thus those persons, whose plasma RBP levels are low, might be involved in the high risk group of metabolic calcium disorders in the elderly.

3. Changes of vitamin C status in aging

Sasaki et al. reported that total vitamin C levels in serum also declined with age (6). They examined 200 healthy subjects, 95 males and 105 females, whose ages ranged from 12 to 96 years. None had supplementary vitamin intake.

Total vitamin C level in the serum varied from 0.30–16 μg/ml. It was shown that there was a significant negative correlation between the serum total vitamin C level and age (p<0.001). The regression line is shown by a solid line. A significant negative correlation between the serum total vitamin C level and age was observed in the younger group (p<0.001) and also in the older group, although it was not statistically significant.
The regression line for each group is shown by a dotted line (Fig. 3) (6).

Bates et al. have also reported that in healthy elderly subjects, the marked changes in vitamin C plasma levels, from 3.2–11.1 µg/ml, occurred without any detectable changes in urinary collagen related peptides (7).

However, vitamin C is known to be involved in collagen synthesis, in the step of hydroxylation of proline to hydroxyproline. Therefore, we had better pay attention to the elderly, whose vitamin C level in plasma is low, although no detectable change was reported in urinary collagen related peptides.

4. Changes of vitamin K status in aging

Vitamin K is now known to be involved in the process of γ-carboxylation of glutamic acid to γ-carboxyglutamic acid (Gla). Since the discovery of vitamin K-dependent amino acid, Gla, in prothrombin, one of the vitamin K-dependent blood coagulation factors, has been demonstrated in

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Fig. 4. Serum BGP levels in individual age groups (shaded area shows normal range).

Fig. 5. Serum Ca and P levels in individual age groups (shaded area shows normal range).
other vitamin K-dependent blood coagulation factors (VII, IX, and X), and many other proteins. Among those proteins, bone Gla-containing protein, which is called BGP or osteocalcin, is one of noncollagenous proteins in bone. Because of the discovery of vitamin K-dependent protein in bone, vitamin K is also thought to be involved in calcium metabolism (8).

BGP is a bone protein. However, it appears in small amounts in the blood. Serum BGP level fluctuates in response to the changes in calcium metabolism, and BGP is now thought to be a new marker of calcium metabolism. Therefore, vitamin K status in aging was estimated from serum BGP levels, in relation to calcium metabolism.

We reported that serum BGP levels were high in the young, and decreased to adult levels, but the mean serum BGP levels after 20 years of age did not show any significant change (9). However, the changes in serum BGP levels in healthy elderly subjects over 60 years of age, 69 males and 159 females, were further examined in detail.

As shown in Fig. 4, the mean serum BGP value of each age group was present in normal ranges, within the 30-50 age groups. However, the values which were higher or lower than the normal ranges of the 30-50 age groups increased. Namely, individual variation became evident with age (10).

On the other hand, serum calcium and phosphorus levels of those subjects were mostly within normal ranges (Fig. 5) (10). In other words, the subjects, whose BGP levels in serum are higher or lower, compared with the normal ranges of 30-50 years of age, did not show any significant change in serum calcium and phosphorus levels.

It is reported that serum BGP levels of osteoporotic patients show higher (11) or lower (12) values, compared with normal control levels. Therefore, those subjects, whose BGP levels in serum are extremely high or low, may be involved in high risk group for osteoporosis.

These observations suggest that there are quite a few marginal vitamin deficient persons within the healthy elderly.

At present, it is not clear how changes in vitamin status in aging are related to those of calcium metabolism. However, we should consider the changes of calcium metabolism in aging from the point of the marginal deficient status of multiple vitamins.

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