The aging process as a modifier of metabolism

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ABSTRACT Because elderly adults have distinct metabolic characteristics that alter various nutrient requirements, simple extrapolations of nutrient requirements for younger adults are not warranted. Gastrointestinal function is well preserved with aging regarding the digestion and absorption of macronutrients, but the aging gastrointestinal tract becomes less efficient in absorbing vitamin B-12, vitamin D, and calcium. The new dietary reference intakes considered recent studies in aging adults and concluded that the recommended dietary allowances (RDAs) should be 1200 mg and 15 μg for calcium and vitamin D, respectively, for persons over the age of 70 y. The new RDAs for riboflavin, niacin, thiamine, folate, vitamin B-6, and vitamin B-12 are not different for persons in the oldest age category (> 70 y) than for those aged 51–70 y. Because this is a quickly advancing field, it will be important to closely follow new research on nutrient requirements and aging over the next several years. Am J Clin Nutr 2000;72(suppl):529S–32S.

KEY WORDS Aging, elderly, nutrient requirements, metabolism, dietary requirements, absorption, gastrointestinal function, dietary reference intakes, DRIs, recommended dietary allowances, RDAs

This paper delineates some of the nutritional and metabolic differences between young and old humans. Scientists in other fields are now beginning to realize what gerontologists have known for some time: older adults are not simply a more aged version of younger adults but rather have distinct metabolic characteristics that alter the requirements for specific nutrients. In addition, as humans age, variability in nutrient needs becomes wider rather than narrower. Thus, it is difficult to make gross generalizations about the nutritional needs of the elderly.

An example of the metabolic differences between young and elderly subjects was well illustrated by Roberts et al (1), who showed that after a period of deliberate overfeeding, young men subsequently decreased their voluntary intake of food. In contrast, elderly men continued to overfeed themselves after a period of enforced overfeeding. Conversely, after a period of enforced underfeeding, young men increased their energy intake to make up for the energy deficit, whereas elderly men continued to underfeed themselves for a period of 9–10 d. These findings have important implications for elderly persons who for one reason or another (eg, a hospital stay due to illness) undergo a period of energy restriction. It cannot be assumed that these elderly persons will quickly return to higher energy intakes once an illness is over.

Bodily functions such as cardiac output, lung capacity, and kidney function decline with advancing age (2). Whether these declines can be modified by, for example, improved nutrition or conditioning is currently a matter of intense interest. Over the years, gastroenterologists have speculated that the functioning of the gastrointestinal tract also declines with aging; specifically, it was thought that the efficiency of the digestive and absorptive functions of the gastrointestinal tract declines with aging. Once this hypothesis was rigorously tested, however, this assumption was found not to be true (3). For example, it was shown that with advancing age into the 90s, humans display no increase in fat malabsorption. Similar results were shown for protein; that is, protein loss in the feces does not increase with advancing age except when elderly persons are placed on extremely high-protein diets.

Interpreting tests of carbohydrate maldigestion and malabsorption with age is complicated by the increased numbers of bacteria that can overgrow in the intestines of elderly adults as a result of hypochlorhydria of aging (4). Hypochlorhydria comes about in advanced age as a result of a high prevalence of atrophic gastritis, which affects as many as 10–30% of elderly persons over the age of 60 y (5, 6). The decreased gastric acid secretion in persons with atrophic gastritis results in increased survivability of swallowed bacteria in the stomach and small intestine, which in younger, normal-chlorhydric persons would be killed by stomach acid.

Carbohydrate malabsorption is clinically diagnosed with breath tests. For example, when a sugar or starch is given to a normal person, it is digested and absorbed in the jejunum. If that does not occur (ie, if the carbohydrate is malabsorbed), the carbohydrate enters the colon, where increased numbers of bacteria reside and cause fermentation resulting in a rise in breath carbon dioxide, hydrogen, and methane (7). These gases rapidly diffuse into the portal system and are excreted in the breath in measurable quantities. However, the proximal small bowel of persons with atrophic gastritis also contains many bacteria (4). Thus, an abnormal result on a breath test in these persons might not reflect carbohydrate malabsorption but rather simply exposure of the carbohydrate load to the bacteria residing in the small intestine, where fermentation and gas formation take place.

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Feibusch and Holt (8) tested the effects of diets of increasing carbohydrate content on carbohydrate absorption in young and elderly persons. They found that elderly persons consuming the higher-carbohydrate meals had a high prevalence of abnormal results on breath tests. This finding is difficult to interpret, however, because the authors did not test for the presence of bacteria in the small intestines of the elderly persons who tested positive (that is, in those who had abnormal test results).

Thus, gastrointestinal function appears to be well preserved with aging, at least regarding macronutrients. Encountering true malabsorption in an elderly person should raise concerns as to whether a significant disease process is underway in the pancreas or the small intestine.

The generalization that the intestine ages well regarding macronutrients does not necessarily extend to micronutrients. To explore this difference it is important to review the present US recommendations for vitamin and mineral intakes in the elderly. In the 1989 recommended dietary allowances (RDAs), elderly was defined as ≥51 y (9). The 1989 RDA committee found insufficient data to create additional age categories for the elderly age group (for example, 51–70 y and ≥70 y). In the 1989 RDA tables, values for only a few nutrients differed between persons aged 23–50 y and those aged ≥51 y. For example, the ≥51-y-old category had lower RDAs for thiamine, riboflavin, niacin, and iron than did younger persons because the first 3 of these nutrients are known to be linked to energy and protein metabolism and because energy and protein intakes are known to diminish with age. The decrement in iron for ≥51-y-old females was the result of the absence of menstrual periods. However, the data examined by the 1989 RDA committee for the most part were not derived from studies on elderly adults. Rather, they were extrapolations from younger adult values with a step down for the elderly because aged persons are less active and consume less food. The new edition of the dietary reference intakes (DRIs) considers data from studies in elderly persons, and for some nutrients enough data exist to provide RDAs for several adult age categories, namely, 31–50, 51–70, and ≥71 y (10).

Low riboflavin intakes [defined as less than two-thirds of the contemporaneous RDA (11)] are prevalent in elderly persons in most of the societies in which riboflavin intakes have been measured. Various surveys estimate low intakes among elderly people in Europe and the United States ranging from 20% to 27%. In an elderly population in a developing country such as Guatemala, 50–70% of persons consume less than two-thirds of the recommended amount (12). By use of a blood measure of riboflavin deficiency (in this case, a rise in the erythrocyte glutathione reductase activity coefficient), anywhere from 5–16% of persons in the United States and 17–76% of elderly persons in Guatemala have evidence of riboflavin deficiency (11, 12).

The data that were primarily relied on by the 1989 RDA committee for setting the riboflavin RDA were the classic data of Horwitt et al (13) on young adults, which showed that riboflavin urinary excretion increased abruptly at an intake of ≈1.1 mg/d. This abrupt increase in urinary excretion of riboflavin was thought to be due to saturation of riboflavin body stores at this intake.

A study on riboflavin requirements was carried out in Guatemala among elderly adults in a metabolic setting (14). The study subjects did not have malabsorption, had been cleared of intestinal parasites, and were known to be riboflavin deficient. A riboflavin repletion protocol was instituted, beginning with quantities below and advancing to those above the new RDA values of 1.3 mg/d for men and 1.1 mg/d for women (10). The so-called critical intake point at which the slope of the urinary riboflavin excretion curve increased in the elderly persons was exactly the same as for the younger persons studied by Horwitt et al (13) (ie, 1.1 mg/d). Thus, despite the 1989 RDA committee’s assumption that the riboflavin requirement would be lower in the elderly than in younger persons, in fact the requirements are exactly the same. The 1998 DRIs recognize that the riboflavin requirement is not different for any adult age category and set the adult RDA at 1.3 mg/d for men and 1.1 mg/d for women (10).

About 10% of the elderly populations in both the United States and Europe can be defined as being vitamin B-6 deficient on the basis of an elevated transferase activity coefficient (11). If one looks at a different measure of vitamin B-6 status (in this case, pyridoxal phosphate concentrations), however, higher estimates of deficiency can be obtained in the same population (11). A group of patients were studied in Boston with use of a repletion-depletion protocol in which persons were first depleted in vitamin B-6 but given adequate amounts of all other nutrients for 17–20 d (15). Volunteers then underwent 3 repletion periods, the second of which was the amount on which the 1989 RDA was based (0.016 mg/g protein). Xanthurenic acid was used as the measure of vitamin B-6 nutriture because with vitamin B-6 deficiency, 3-hydroxykynurenine is not metabolized to anthranilic acid but rather is short-circuited to xanthurenic acid, which is rapidly excreted in the urine. In both elderly men and women, urinary xanthurenic acid concentrations declined, but only during the third repletion period (intake above the 1989 RDA) did urinary xanthurenic acid excretion return to baseline. It is not known why the vitamin B-6 requirement may increase with age. From initial studies, it does not appear to be an absorptive problem, but rather a problem of cellular uptake or metabolism of the vitamin.

Subclinical nutrient deficiencies in elderly persons may not necessarily be benign, as shown by the work of Meydani et al (16) in the same subjects as those described above. By measuring various aspects of immune function, Meydani et al found that during the vitamin B-6 depletion period, interleukin-22 dropped significantly from baseline, only to rise back to normal during the third repletion period. Thus, subclinical deficiency of vitamin B-6 might result in immune dysfunction and an increase in infectious disease or other chronic immune-related diseases. The 1998 DRIs recognize a greater need for vitamin B-6 in older adults than in younger adults; the RDA for adults aged ≥71 y was set higher (1.7 mg/d for men, 1.5 mg/d for women) than that for younger adults (1.3 mg/d for both sexes) (10). This is a change from the 1989 RDA edition, which had a lower RDA for the ≥51-y age category than for the 20–50-y age category.

Vitamin B-12 presents a particular problem for elderly persons with atrophic gastritis (5, 6, 17). Young adults have the highest serum B-12 concentrations, elderly adults without atrophic gastritis have midrange concentrations, and elderly adults with atrophic gastritis have the lowest concentrations. Vitamin B-12 normally enters the body bound to food protein, which then becomes dissociated in the stomach under the action of pepsin and hydrochloric acid to free vitamin B-12. The free vitamin then binds with R binders (small proteins secreted by the salivary glands and stomach) in the stomach, and the R binder–B-12 complex then migrates to the proximal small bowel, where pancreatic enzymes digest the R protein. It is here, in the proximal small bowel, under more neutral pH conditions that intrinsic factor
binds the vitamin B-12 and allows for the subsequent absorption of the vitamin in the ileum. As mentioned earlier, persons with atrophic gastritis have increased amounts of bacteria growing in their stomachs and small intestines because of survivability of swallowed bacteria in a low-acid environment (4).

King et al (18) were among the first to show that food-bound vitamin B-12 was not very available for absorption in persons with atrophic gastritis. They studied protein-bound vitamin B-12 absorption in 5 persons with atrophic gastritis and found it to be below normal. This finding was not due to a lack of intrinsic factor secretion by the stomach, because when intrinsic factor was added to the oral protein-bound vitamin B-12, there was no increase in urinary excretion (a proxy measure for how much is absorbed). However, when acid or acid plus pepsin was added back, normal vitamin B-12 excretion was seen in most patients.

My laboratory was interested in the effect of bacterial overgrowth on vitamin B-12 bioavailability in persons with atrophic gastritis (19). Persons with atrophic gastritis could not absorb protein-bound vitamin B-12 even though they could normally absorb crystalline, free vitamin B-12 (the type found in a vitamin pill). When patients with atrophic gastritis were subsequently treated with an antibiotic to reduce bacterial counts in the stomach and small intestine, the bioavailability of protein-bound vitamin B-12 increased to normal in the persons with atrophic gastritis. Tetracycline did not affect the absorption of protein-bound vitamin B-12 in elderly persons without atrophic gastritis.

Thus, there are at least 2 reasons elderly persons with atrophic gastritis have problems with bioavailability of dietary vitamin B-12. First, the diminished dissociation of the vitamin from food proteins results in little of the vitamin becoming free for subsequent binding to intrinsic factor, which would allow for its ultimate absorption. Second, the small amount of vitamin B-12 that does get freed from food is rapidly taken up by the increased numbers of bacteria residing in the proximal small intestine. The 1998 DRI committee report set the RDA for vitamin B-12 for the oldest age category (≥71 y) at the same amount as that for younger adults (10). However, because of the prevalence of atrophic gastritis in a significant proportion of the elderly population, the committee recommended that the elderly’s vitamin B-12 requirement be met by taking supplements containing vitamin B-12 or by eating fortified food products (eg, vitamin-fortified cereals) (10). There is, of course, great interest in preventing vitamin B-12 deficiency among the elderly and in treating those who are deficient, because vitamin B-12 deficiency can result in both higher plasma homocysteine concentrations, which confers an increased risk of vascular disease, and neurologic damage and brain dysfunction (20–22).

Calcium absorption is also diminished with advancing age, but this is primarily thought to be related to problems in vitamin D metabolism. For example, elderly persons have decreased dietary intakes of vitamin D and decreased sun exposure. Moreover, even if their skin is exposed to ultraviolet light, it is less able to synthesize vitamin D (23). In addition, the kidneys of elderly persons are less likely to dihydroxylate 25-hydroxyvitamin D to the active 1,25-dihydroxy form (24). Finally, the decreased numbers of vitamin D receptors in the intestinal mucosa of elderly persons result in a diminished capacity to absorb vitamin D (25). Together, all of these problems in vitamin D metabolism result in decreased calcium absorption in the elderly. The clinical effects of this decrease are increased parathyroid hormone secretion and increased remodeling of bone with bone loss. It is clear that a vitamin D intake of 5 µg/d is inadequate for the elderly. Moreover, the Consensus Conference on Calcium Requirements (published in 1994) set the calcium requirement for the elderly in the range of 1000–1500 mg/d, which is a substantial increase over the 800 mg/d currently recommended in the 1989 RDAs (26). The 1998 DRI committee recommended the following as adequate vitamin D intakes: 5 µg/d for persons aged 31–50 y, 10 µg/d for those aged 51–70 y, and 15 µg/d for those aged ≥71 y (27). The recommendations for calcium are 1000 mg for persons aged 31–50 y and 1200 mg for those aged ≥51 y (27).

Vitamin A presents a different problem in that the 1989 RDA may be overly generous for elderly persons. It is known that with advancing age, both mean and median liver values for vitamin A do not decrease (the liver is the primary storage organ for vitamin A) (28). It is surprising not to see a decrease in hepatic vitamin A concentrations with advancing age because it is known from the National Health and Nutrition Examination Surveys that 42–65% of elderly Americans (depending on the subpopulation) eat less than two-thirds of the current RDA for this nutrient (29). Part of the reason for the well-maintained body stores (despite diminished dietary intake) is that vitamin A absorption may actually increase with age. Hollander and Dadulfalza (30) showed that as rats age, uptake and absorption of vitamin A by the intestine increase. My laboratory investigated blood response curves after feeding physiologic doses of vitamin A to elderly and young adults and found that elderly persons had significantly higher blood responses than did young adults. This finding could be due to either an increased absorption or a decreased clearance of the vitamin by peripheral tissues. To differentiate these effects, groups of young and old persons were fed meals high in fat and vitamin A (31). Three hours later, a unit of blood was drawn and subjected to plasmapheresis, and red cells were given back to the volunteers. Twenty-four hours later, the chylomicron remnants, now laden with vitamin A, were reinjected into elderly and young adults. The young adults were found to clear the reinjected vitamin A twice as quickly as the older adults.

What is the significance of the decreased clearance? When retinyl esters remain in serum associated with chylomicron remnants for any length of time, they begin to transfer to low-density lipoproteins and gradually become transformed to retinol, a nonspecific delivery system for vitamin A that is toxic to cell membranes. In a cross-sectional population, we looked at the possibility that vitamin A supplementation would increase fasting serum retinyl esters in elderly and young adults. In fact, elderly persons did accumulate more retinyl esters in serum than did younger adults, depending on the dose of the supplement taken (32). Specifically, intake of vitamin A of >3000 µg/d (>1000 g/d) resulted in significantly elevated circulating retinyl esters. Thus, vitamin A supplementation in amounts >3000 µg/d is probably not a desirable practice on a long-term basis. The updated report of the DRI committee for vitamin A is not yet available.

Further research in the area of aging and nutritional metabolism should include studies on elderly persons who are affected by disease and physical stress. In all such studies, drug-nutrient interactions must be taken into account. Additionally, the role of several nutrients (eg, folic acid, calcium, and vitamin D) in preventing various diseases and disorders associated with aging (eg, cardiovascular disease and osteoporosis) are in need of study. Functional indexes as well as disease endpoints should be correlated with intakes or blood values of the nutrients. Various factors
that affect appetite control must be better understood and researched to explain the anorexia of aging. Finally, in the elderly, as in other vulnerable populations, there is a tendency for overuse of supplements. The possible detrimental effects of long-term chronic overuse of supplements, particularly at high doses, should be studied in elderly populations. All of these are high-priority research areas with regard to understanding aging as a modifier of nutritional metabolism.

In summary, elderly persons are not simply older versions of younger adults; rather, they have unique metabolic characteristics that are just beginning to be defined. Little is known about how specific nutrient requirements are affected by physical stress or disease. The edition of the DRIs currently being prepared has more than the 2 customary adult age categories of 23–50 and ≥71 y. For many nutrients, enough data are now available to split the elderly into young-old (51–70 y) and old-old (≥71 y). Because this is a quickly changing field, it will be important to follow developments closely over the next several years.

REFERENCES


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