An approach to providing supplement advice in health evaluation and promotion

– Including experiences from our anti-aging health check-up system –

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ABSTRACT

Nutritional status is the balance between intake and expenditure, the assessment of which is highly complex and individualized. Dietary supplements can be beneficial for covering the shortcomings of some people's diets, but must not be used to replace the balanced variety of foods necessary for a healthy diet.

In Japan, the term "supplement" is used without a clear legal definition. Many supplements contain active ingredients that may have strong and unpredictable detrimental biological effects on the human body. Some dangerous products may carry illegal health claims or contain pharmaceutical ingredients with a high risk of adverse effects. When using dietary supplements, it is important to consider their necessity and efficacy, and to obtain the advice of health-care professionals who have sufficient knowledge about nutrition.

Our anti-aging health check-up provides personal nutrition advice based on serum vitamin levels and detailed information about dietary habits. To help people make informed decisions, the doctors and dietitians work together to decide how people can achieve a balance between the foods and nutrients they personally need. We do not always find that people need supplements, and sometimes we find those who use supplements inappropriately.

This article presents a current overview of dietary supplements in Japan and our approach to providing supplement advice in our anti-aging health check-up system, and gives a helpful perspective in evaluating and promoting good health.

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Key words supplement, supplement advice, health evaluation and promotion, anti-aging health check-up system

1. Introduction

In modern society, nutritional excess is a major health problem leading to lifestyle-related diseases, whereas nutritional deficiency can also be caused by an unbalanced diet due to eating alone and using instant foods. Even if three proper meals were eaten each day, the quantity of nutrients may be insufficient compared to that in the past due to changes in the global environment. The ideal situation for most people is to eat a wide variety of nutrient-rich foods to obtain the nutrients needed to be healthy and reduce the risk of chronic disease.

Dietary supplements can be beneficial for covering the shortcomings of some people's diets, but must not be used to replace the balanced variety of foods necessary for a healthy diet. The purpose of using supplements may be to improve optimal health and performance, prevent disease, or maintain a youthful appearance. Another possible advantage is that dietary supplements contain fewer calories than the food required to achieve sufficient

nutrient status. When using dietary supplements, it is important to consider their necessity and efficacy, and to obtain the advice of health-care professionals who have sufficient knowledge about nutrition.

Our anti-aging health check-up provides not only various examinations and health guidance before the occurrence of aging-related problems, but also nutritional advice including on dietary supplements that the examinees personally need. This article presents a current overview of dietary supplements in Japan and our approach to providing supplement advice in our anti-aging health check-up system, and gives a helpful perspective in evaluating and promoting good health.

2. Current overview of dietary supplements in Japan

1) What is a dietary supplement?

A dietary supplement is described in the United States by the Dietary Supplement Health and Education Act (DSHEA) of 1994 as a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet¹⁾. According to the DSHEA, the "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be prepared in the form of tablets, capsules, softgels, gel-caps, liquids, or powders.

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In Japan, the term “supplement” is used without a clear legal definition. Supplements may belong to either the legally defined “Food with Health Claims (FHC)” or the legally undefined so-called “health food” (Fig. 1)²⁻⁵⁾. Supplements may be in the form of common foods as well as tablets or capsules, and the legally defined FHC is more often likely to be in the food form rather than “health foods”. As a result, it is more complicated to interpret what constitutes a dietary supplement in Japan.

2) Difference between “Food with Health Claims (FHC)” and “health food” – from a legal point of view

The FHC system was originally established under the Nutrition Improvement Law, which was replaced by the Health Promotion Law in 2003⁵⁾. FHC comprises two categories: “Food for Specified Health Use (FOSHU)” and “Food with Nutrient Function Claims (FNFC)”²⁻⁵⁾ (Fig. 1), which is described later.

For “health food” on the other hand, there are no legal provisions. “Health food” itself is a generic term for food products that carry nutrient functions and health claims or that are designed to be more effective than common foods in helping people maintain and improve their health, or at least are expected to have such an effect. Health foods are sometimes distributed and sold without substantiation of the safety and quality of the individual product. Even so, health foods are regulated by several laws in terms of manufacturing, quality, labeling and advertising for the purpose of consumer protection^{6, 7)}. For example, false/exaggerated labeling and advertising are restricted by the Health Promotion Law. It is prohibited by the Food Sanitation Law to indicate health claims or function claims that might be confused with FHC. If a health food carries a claim that is intended for use in the prevention or treatment of disease, this would conflict with the Pharmaceutical Affairs Law.

3) Food for specified health use (FOSHU)⁸⁾

FOSHU refers to food containing ingredients with beneficial functions for health and for which it is officially permitted to claim its physiological effects on the human body. FOSHU is

intended to be consumed for the maintenance and improvement of health or special health use by people who wish to control aspects of their health, such as blood pressure and serum levels of cholesterol or triglycerides. In order to sell a food labeled as FOSHU, its safety and the effectiveness of its beneficial health functions must be assessed, and the health claim must be approved by the Ministry of Health, Labour, and Welfare (MHLW).

A detailed review process with scientific evidence for each application is required for FOSHU approval, such as clearly proven effectiveness on the human body, absence of any safety issues (animal toxicity tests, confirmation of effects in the case of excess intake, etc.), use of nutritionally appropriate ingredients, guarantee of compatibility with product specifications by the time of consumption and established quality control methods.

Since 2005, the following three types of FOSHU have been available in addition to “regular” FOSHU.

- 1. Qualified FOSHU: Food with a beneficial health function that is not substantiated by scientific evidence that meets the level of FOSHU, or food with some effectiveness but without an established mechanism of the effective ingredient for the function that will be approved as qualified FOSHU.
- 2. Standardized FOSHU: Standards and specifications are established for foods with sufficient FOSHU approval and accumulation of scientific evidence. Standardized FOSHU is approved when it meets the standards and specifications.
- 3. Reduction of disease risk FOSHU: This claim is permitted when a reduced disease risk is clinically and nutritionally established in an ingredient.

4) Foods with nutrient function claims (FNFC)⁹⁾

FNFC refers to all food that is labeled with the nutrient function claims specified by the MHLW. To date, standards and specifications for indicating nutritional function have been established for 17 ingredients (12 vitamins: niacin, pantothenic acid, biotin, vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin C, vitamin D, vitamin E, and folic acid; and 5 miner-

Fig. 1 Relationship of supplements to food and drugs

als: zinc, calcium, iron, copper, and magnesium).

These foods may be freely manufactured and distributed without permission from or notification to the national government, provided that the established standards and specifications are met. However, the nutrient function claims must be accompanied by warning indications.

3. Safety and risk of dietary supplements

1) What we need to know about supplements

Many supplements contain active ingredients that may have strong and unpredictable detrimental biological effects on the human body. Some dangerous products may carry illegal health claims or contain pharmaceutical ingredients with a high risk of adverse effects. With the rapid development of the information society, it is increasingly important to distinguish between reliable and unreliable information. Moreover, online shopping has made it very easy to obtain health products even from foreign countries. The use of health foods is an international trend, and the rising volume of illegal health foods imported from overseas has caused an increase in health food problems.

2) Confusing products – drug or food?

Some products that are positioned as “supplements” in Japan are designated as “drugs” in foreign countries, and vice versa. Examples of the former are ginkgo leaf extract, echinacea, St. John’s wort and milk thistle. Ginkgo leaf extract is a popular drug in Europe for amelioration of cerebral vascular circulation¹⁰⁾. However, it must be noted that not every ginkgo leaf extract has the same physiological action: both pharmaceutical grade and food grade products are marketed; only the pharmaceutical grade product is proven to be effective based on scientific evidence including clinical trials, and there is a difference in the manufacturing process between Western countries and Japan.

By contrast, *Angelica acutiloba* (Tang-kuei) is classified as a drug (Chinese medicine prescription also known as Kanpo) in Japan, whereas it is used as a supplement in the U.S. for menstrual and menopausal problems.

3) Safety concerns

Not only are there unexpected risks posed by the nutritional ingredients themselves, but health hazards are also created by illegal and dangerous products. Products purchased over the Internet may contain pharmaceutical ingredients or ingredients prohibited in Japan. Examples are: erectile dysfunction drugs (sildenafil or tadalafil) contained in foods claiming “a tonic effect”, sibutramine contained in diet foods, and steroids and non-steroidal anti-inflammatory drugs contained in products claiming “good for arthritis”. A database of evidence-based information on the effectiveness, safety, warnings, and interactions with drugs and so-called “health foods” is publicly provided on the web by the National Institute of Health and Nutrition¹¹⁾.

4) Need for supplement advisors

In order to help people in need of reliable information and advice on dietary supplements, a qualification system for supplement advisors was proposed by the MHLW in 2002. Several organizations such as the Japanese Clinical Nutrition Association (JCNA), the Japanese Association of Food Science and Risk

Analysis, and the Japan Health and Nutrition Food Association initiated training programs for advisory staff. In April 2012, the “Supplement Advisor” of the JCNA and the “Nutrition Representative (NR)” of the National Institute of Health and Nutrition were integrated, and the “NR-Supplement Advisor” was established¹²⁾.

Advisory staffs require accurate knowledge on food and nutrition to provide useful information to consumers. They can act in various health care businesses including hospitals/clinics, public health centers, stores and consumer information centers for supplement manufacturers. They are also expected to focus on consumer protection and prevention of health hazards.

4. Current status of supplement usage in our anti-aging health check-ups

Tokai University Tokyo Hospital began offering anti-aging health check-ups in June 2006¹³⁾. The examinations carried out in our hospital are divided into those that are related to the present “aging level” and those that focus on “factors affecting aging”. The former includes the degree of arteriosclerosis, body composition analysis, bone densitometry, muscle strength, balance function and hormone levels (dehydroepiandrosterone and sex hormones). The latter includes metabolic parameters, advanced glycation end products, oxidation and anti-oxidation balance, immunity, lifestyle and stress.

Serum concentrations of several vitamins are measured as part of the anti-oxidative factors, and the levels of vitamin A, C, E (fractions of α , β , γ , δ), β -carotene, vitamin B₁₂ and folic acid are obtained. In addition, the use of prescribed drugs and dietary supplements are surveyed through a self-administered questionnaire. Dietary habits are assessed by a questionnaire asking about the regularity of meals, habits of daytime or late-evening snacks and food preferences. Some of the doctors are qualified as “Supplement Advisors”. When abnormal values are found in the vitamin levels, the doctors seek detailed information through a medical interview. The dietitians give nutritional guidance based on the information from the questionnaire and medical data.

We previously reported on the awareness of supplements and the proportion of users in our anti-aging health-check examinees during the year 2005–2006¹⁴⁾. More than 85% of the respondents were interested in dietary supplements, and 31.4% were already actively taking supplements (**Fig. 2**). Among the various supplements, foods accounted for 39%, vitamins 24%, minerals 9%, polyphenols 7%, amino acids 7% and others included docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), dietary fiber and lactobacillus¹⁵⁾. More specifically, vitamin C was the most commonly used supplement, followed by coenzyme Q10 (CoQ10), calcium, vitamin E, DHA and EPA. As vitamins are so widely used, we next asked about awareness of vitamins and the proportion of users in the same subjects¹⁴⁾. We found that 27.2% were already actively taking vitamins, and more than 90% answered that they knew about vitamins (**Fig. 3**).

Generally, the anti-aging health-check examinees are more health-conscious. Even if they eat a wide variety of foods and take some dietary supplements, it is difficult to ensure an ade-

Fig. 2 Degree of awareness of supplements and rate of use
The health-check examinees were asked if they were taking supplements. More than 30% were already taking supplements and more than 85% showed an interest in taking supplements. (Cited from Ref. 13)

Fig. 3 Degree of awareness of vitamins and proportion of vitamin users
The question was “Do you know about vitamins?” Vitamin users accounted for 27.2% but more than 90% answered that they had knowledge of vitamins. (Cited from Ref. 13)

quate dietary intake of essential nutrients. Moreover, as people become older, nutritional needs may change. Acquisition of vitamin levels and detailed nutritional information from the examinees greatly help us determine whether their intake of a specific nutrient might be too low or too high.

5. Supplement advice in our anti-aging health check-up system

Here, we present two typical cases with under- and over-nutrition respectively, and explain how we gave supplement

advice in each case.
1) Case 1: Vitamin C deficiency
The subject was an 81-year-old man with remission status of chronic hepatitis C and liver cancer, who had smoked three cigarettes daily for the past 60 years. He had the first anti-aging health check-up in 2011. He was found to be extremely deficient in vitamin C, the serum concentration of which was only 2.6 μg/ml (Table 1), while all the other vitamins were within the normal range. Judging from the questionnaire and interview, he had no apparent problems in his dietary habits and was not taking any

Table 1 Serum vitamin concentrations in Case 1

	2011/10/6	2012/11/6	Reference range
Vitamin A	44.6	36.1	27.2 - 102.7 $\mu\text{g/dl}$
Vitamin C	2.6	13.0	4.7 - 17.8 $\mu\text{g/ml}$
Vitamin E α	10.95	10.09	4.90 - 13.80 $\mu\text{g/ml}$
β	0.12	0.13	0.06 - 0.28 $\mu\text{g/ml}$
γ	1.12	1.19	0.10 - 2.40 $\mu\text{g/ml}$
δ	0.03	0.03	≤ 0.14 $\mu\text{g/ml}$
β -carotene	9.9	21.9	< 96.4 $\mu\text{g/dl}$
Vitamin B ₁₂	283	419	223 - 914 pg/ml
Folic acid	5.2	7.3	3.6 - 12.9 ng/ml

dietary supplements. The attending doctor considered that smoking caused vitamin C depletion, and prescribed 200 mg of ascorbic acid three times a day. The dietitian recommended eating more vegetables and fruits, and also adding foods rich in dietary fiber (e.g., grains, mushrooms and seaweed) because of occasional constipation. At the examination in 2012, he was still smoking but his vitamin C level had improved to 13.0 $\mu\text{g/ml}$.

2) Case 2: Vitamin E excess

The subject was a 67-year-old woman with osteoporosis and euthyroid state of chronic thyroiditis. She and her husband had had four anti-aging health check-ups (2007, 2009, 2011 and 2012). The couple took regular meals together, did not eat out, and took the same kinds of supplements (an over-the-counter gastrointestinal remedy containing digestive enzymes, lactobacillus, 3.4 mg of vitamin B₁, 2.0 mg of B₂ and 2.0 mg of nicotinic-acid amide in a daily dose, and glucosamine, CoQ10 and blueberry). At the first visit, no abnormality was observed in their vitamin levels. In 2009, the woman's serum concentration of vitamin E α fraction and folate were slightly above the upper limits (**Table 2**); the attending doctor told her that she was nutritionally sufficient and the dietitian advised her to maintain a balanced diet. During 2009 and 2011, they started taking two other supplements instead of glucosamine, CoQ10 and blueberry while continuing the abovementioned gastrointestinal remedy. One of the new supplements contained 360 mg of DHA, 210 mg of bilberry extract, 30 mg of grape seed extract and 30 mg of Nikko maple (*Acer maximowiczianum*) extract in a daily dose. The other contained 300 mg of DHA, 100 mg of EPA and 55 mg of vitamin E in a daily dose. Thereafter, their vitamin E levels continued to increase (**Fig. 4**). As the woman's vitamin E α fraction was 17.83 $\mu\text{g/ml}$ at the examination in 2012, the doctor advised her not to take the supplement containing vitamin E and the dietitian emphasized the importance of taking nutrients from meals.

In our anti-aging health-check examinees, a high vitamin E level is one of the most frequently observed abnormalities. On the other hand, we find a vitamin deficiency relatively infrequently. Vitamin E itself is popular because it is widely advertised as being good for blood circulation, but vitamin E is also often added to products such as DHA, EPA or sesamin. We think that an overlapped vitamin intake from products that are not easily

Table 2 Serum vitamin concentrations in Case 2

	2009/9/4	2011/10/21	2012/11/30	Reference range
Vitamin A	37.2	46.2	37.7	27.2 - 102.7 $\mu\text{g/dl}$
Vitamin C	12.9	11.5	13.7	4.7 - 17.8 $\mu\text{g/ml}$
Vitamin E α	14.48	16.64	17.83	4.90 - 13.80 $\mu\text{g/ml}$
β	0.19	0.13	0.13	0.06 - 0.28 $\mu\text{g/ml}$
γ	0.85	0.82	0.82	0.10 - 2.40 $\mu\text{g/ml}$
δ	0.07	0.05	0.04	≤ 0.14 $\mu\text{g/ml}$
β -carotene	106.1	129.4	102.4	< 96.4 $\mu\text{g/dl}$
Vitamin B ₁₂	786	599	516	223 - 914 pg/ml
Folic acid	15.2	12.8	13.0	3.6 - 12.9 ng/ml

Fig. 4 Transition of serum vitamin E levels in Case 2

Since the subject and her husband started taking a supplement containing vitamin E, their vitamin E levels continued to increase. The subject's vitamin E concentration reached 17.83 $\mu\text{g/ml}$ in 2012, and the doctor told her not to take the supplement.

recognizable as containing the vitamin is a major cause of high vitamin levels found in our examinees. The woman in case 2 was probably unaware that she had been taking vitamin E and also two kinds of DHA supplements. As vitamin E is fat soluble, excess vitamin E is stored in the body tissues leading to a condition called hypervitaminosis. Taking vitamin E together with antiplatelet and/or anticoagulant drugs is known to increase the potential for internal bleeding. Moreover, it was recently reported in a rodent model that vitamin E stimulates bone resorption and decreases bone mass by inducing osteoclast fusion, suggesting that serum vitamin E is a determinant of bone mass¹⁶. It is important to note that nutrients work best when taken in the proper amounts: more is not always better.

6. Conclusion

Nutritional status is the balance between intake and expenditure, the assessment of which is highly complex and individualized. Scientific evidence has shown that some dietary supplements are beneficial for overall health and for managing health conditions. However, dietary supplements are not intended to prevent, mitigate or cure disease, and must not be used to replace the balance of the variety of foods necessary for a healthy diet. The decision to use a dietary supplement may provide health benefits, but it may be unnecessary for good health or even bring unexpected risks under certain circumstances.

To help people make informed decisions, the doctors and dietitians must work together to decide how people can achieve a balance between the foods and nutrients they personally need. Our anti-aging health check-up provides personal nutrition advice based on serum vitamin levels and detailed information about dietary habits. We do not always find that people need supplements, and sometimes we find those who use supplements inappropriately. Our approach to supplement advice in anti-aging health check-ups is unique, and we hope that more people will use our system in order to ensure that they maintain an adequate nutritional status for successful aging.

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