

Foreword

Characteristics of health and diet in Japan

International comparison of demographic findings indicates that the life expectancy at birth is at present the longest in Japan, i.e. 84 years for females and 77.2 years for males in 1999. Furthermore, the World Health Organization (WHO) recently reported that the rank of Japan was the highest in the 'New Health Life Expectancy Rankings' which were estimated for 191 countries using a newly developed indicator 'Disability Adjusted Life Expectancy (DALE)'. The estimate of DALE for the Japanese is 74.5 years, whereas that for the United States is 70 years.

Among many factors of Japanese socioeconomic conditions, the traditional Japanese diet has attracted the attention of many researchers since its low-fat low-calorie characteristics are beneficial for preventing ischemic heart disease and certain types of cancer, e.g. colorectal, breast, prostatic and lung cancer. In the Japanese diet, a wide variety of marine products including seaweeds and vegetables including root-vegetables are utilized. In general, a marked correlation is seen between the average total calorie intake per day and the annual income per head when compared for different nations. Interestingly, Japan exhibits an exceptional feature, namely the total calorie intake has remained constant at the level of developing countries during the past 40 years, during which the nation's income has increased to the highest in the world.

However, there is a problem that such a traditional diet has been gradually changing or deteriorating because of internationalization of food, particularly in younger generations, so that the morbidity pattern of Japanese has concurrently been gradually but slowly changing. Therefore, many studies of nutrition and health science have claimed the necessity of preservation of the traditional diet and further clarification of the scientific bases of the benefits and faults, if any, of Japanese food and dietary style. In addition, research of non-nutrient functional components of food, such as catechins, isoflavonoids and lignans, which are rich in Japanese food has begun to attract a great deal of attention because of the anti-carcinogenic and anti-atherosclerotic actions of these compounds, currently being disclosed by cell biological and molecular biological studies.

Another important problem to be investigated more extensively in Japan may be the improvement of the nutritional state of elderly persons, whose population is now rapidly increasing. This increase naturally brings about an increase in old persons with weaknesses or in a bedridden state. Most researchers involved in health promotion of the elderly, therefore, are interested in the establishment of knowledge of nutrition and life-style necessary for maintaining health until the later stages of life and for ultimately attaining natural death without disease (Friess, 1980).

The purpose of the Shizuoka Forum on Health and Longevity

Shizuoka Prefecture, one of 47 prefectures in Japan, is located in the central part of Japan. The inhabitants of the prefecture (population 3.8 million) preserve the typical Japanese diet and drink green tea more frequently than the average Japanese. The prefecture has a mild climate and is rich in agricultural and marine products. Also, there are many industries, including those of automobiles, musical instruments and pharmaceuticals in this area. Its gross domestic product ranks about tenth in the forty-seven prefectures.

The health status level of inhabitants of the prefecture is relatively high as indicated by the high ranks of average life expectancy at birth for both males and females (within the fifth highest among the forty-seven prefectures) and the lowest medical expenditure for the elderly. The prefecture government has a policy to maintain or further promote the health status of the inhabitants. As one of the ways of realization of this policy, they determined to support scientific research on health and longevity within the prefecture and to have international conferences concerning this issue to accumulate modern and useful knowledge and to stimulate relevant research. With such ideas, the Shizuoka Forum on Health and Longevity was commenced in 1996 under the total sponsorship of the prefectural government. The Forum has been held every year thereafter under different topics. The organizing committee of the Forum has been formed by inviting outstanding specialists of various fields from all over Japan including nutrition, biochemistry/molecular biology, physiology, public health/epidemiology, and gerontology/geriatrics. Participants have been invited from both outside and inside Japan, and advanced knowledge has been discussed concerning ageing mechanisms, age-related diseases and their preventive means, and the roles of nutrition in the prevention of diseases and maintenance of health.

Thus far, the following problems have been discussed in the Shizuoka Forum on Health and Longevity. In the first forum (1996), recent advances in research of etiology, epidemiology and treatment of age-associated dementia, Alzheimer's disease and dementia of other origins, were discussed. At the present time, there is no effective means of prevention of age-associated dementia, nevertheless, possible measures for prevention were discussed by all participating specialists. In a separate session, current problems of viral infection were also discussed. The second forum was held in 1997 under the main theme of 'Compression of morbidity of the elderly and how to reduce the number of bed-bound old persons'. The presentations were made on recent advances in etiology of hypertension, brain stroke and osteoporosis, and discussions were made on how to

prevent these pathological conditions. There are relatively many bed-bound patients in Japan compared with European countries. This may, in part, be due to the differences in living customs, family structure, and a tradition of medical treatment stressing more bed-rest in Japan. Anyway, it is one of the most urgent and important problems to decrease bed-bound old persons because the aged population is rapidly increasing. In the third forum (1998), new aspects of cancer research were extensively discussed in four separate sessions: (1) New strategies for cancer treatment, (2) New resources for chemoprevention and cancer treatment, (3) New modalities of cancer diagnosis and treatment, and (4) New aspects of cancer metastasis and its inhibition. It was emphasized that about 60 % of cancer patients are now curable and more than 40 % of cancers are preventable. Knowledge of the mechanisms of chemoprevention of cancer by functional elements of food at the level of the cell membrane (receptor), signal transduction within cells, and metastatic migration is rapidly expanding at present.

The fourth forum was held in November 1999 under the main theme of 'Wise dietary life-style and healthy longevity'. The relation of healthy longevity to diet was discussed in separate sessions: (1) Strategy for prevention of lifestyle-related diseases — cause, treatment and prevention of diabetes mellitus, (2) Nutrition and health — research messages from Shizuoka, Asia and Europe, (3) Frontiers of molecular nutrition. Special aspects of the fourth forum are described below. A satellite conference on 'Nutrition in Asia: present and future' was held on the day immediately following the scientific sessions described above. Fifteen presentations selected from the academic sessions and the Asian conference are published in this supplement.

Special aspects of the fourth Shizuoka Forum on Health and Longevity

The fourth Forum was organized to disclose four main points. The first was to clarify the specific aspects of non-insulin-dependent diabetes mellitus (NIDDM) in Japanese from both genetic and nutritional aspects. The second point was to compare the nutritional problems in relation to health status of the elderly among European, Mediterranean and Asian countries and to present new findings of health and nutritional status of Shizuoka Prefecture inhabitants. The third point was to discuss up-to-date knowledge of nutrition-related control of gene expression.

It has long been pointed out that the features of NIDDM in Japanese are somewhat different from those of European and American people. A special feature is that the hyperinsulinemia which develops under the conditions of insulin-resistance is not marked in Japanese, particularly during the chronic stage. Therefore, obesity is not frequently seen in Japan although people with insulin-resistance have, in recent years, steadily increased. It is obvious that development of insulin-resistance can be ascribed to imbalance of energy intake and expenditure or over-nutrition/low physical activities, which are very common in modern civilized daily life. It has been clarified that more than 90 % of Japanese have the thrifty genotype,

indicating that Japanese are to acquire insulin-resistance when they intake fatty or calorie-rich food and maintain low physical activity. Fortunately, the Japanese diet is both low-fat and low-calorie, therefore, preservation of the traditional diet custom is particularly important in Japan. This was extensively discussed in this Forum.

The traditional Mediterranean diet was known to be beneficial for compression of ischemic heart disease and certain types of cancer like the Japanese diet. However, it was pointed out that, in Greece, the morbidity pattern is gradually approaching that of Western Europe more rapidly than in Japan. This is interpreted as the result of a more rapid internationalization of food, and consequently the deterioration of traditional dietary customs. It was reported that there was no substantial difference today in the incidence of ischemic heart disease between Greece and the UK or USA. In the UK, the dietary strategy to lower fat intake and to replace the energy with that from starchy foods was shown to be prevailing.

As described above, the health status of Shizuoka Prefecture is ranked highly among the forty-seven prefectures. Studies of the regional differences of the incidence of cancer, especially gastric cancer, within the prefecture showed a good correlation to the consumption of green tea; the larger the consumption, the smaller the incidence. Blood and urine analyses done for inhabitants of selected regions showed that urinary excretion of iso-flavonoids was high in regions where the cancer incidence was low and other indices of health status were relatively high.

The molecular biological knowledge of the actions of some vitamins and nutrients is rapidly accumulating at present. In the third session, 'Frontiers of molecular nutrition', the focus was placed on the nuclear receptors for lipid soluble vitamins and other nutrients which act as ligand-inducible transcription factors. Nuclear receptors are also known to serve as nuclear targets for a broad range of hormones and therapeutic agents. Retinoid X receptor (RXR) plays a central role in the regulation of many intracellular signaling pathways. Peroxisome proliferator-activated receptors (PPAR) heterodimerize with RXR and alter the transcription of target genes after binding to specific elements. This was shown to be the case in the regulation of transcription of the cellular retinol-binding protein (CRBP) gene, which is stimulated by fat intake. PPAR/RXR is also known to be involved in glucose homeostasis and fat metabolism. The growth rate, controlled by protein nutrition, is also explained by the transcription of insulin-like growth factor and its binding protein. In this process, the amino acid responsive element (AARE) of the genes for these factors is known to play an important role. Nuclear receptor-mediated control of transcription has also been shown for the substrate-induction of disaccharidases of the intestinal epithelium.

The satellite conference entitled 'Nutrition in Asia: present and future' was held in a semi-closed style. Representative researchers of nutrition were invited to this meeting from eight countries; Bangladesh, Malaysia, Vietnam, Thailand, Philippines, Singapore, Korea and China, discussions were held between them and with Japanese researchers. The common interest was health and

nutrition, but there were a wide variety of specific problems in these countries. One of the problems seen in developing countries is the coexistence of under-nutrition and over-nutrition and also the regional differences in health and nutritional status depending on the degree of economic development.

Future problems to be discussed in the Forum

The ultimate purpose of the Forum is to systematize our knowledge towards healthy ageing and natural death without disease and to derive the maxims for people useful for maintenance of a high quality of life until the terminal stage of life. For this purpose, it is fundamentally important to clarify the time course of the integrated vitality of our body and its relation to changes in homeostatic controls. The concept of the homeodynamic vitality developed by Yates (1993) appears to be useful as a fundamental principle. This proposes that human life is maintained for 100 years if premature death due to external (environmental) factors and chronic diseases due to intrinsic or internal factors (morbid constitution due to gene mutations and risky life-style) are ideally avoided. Natural death may occur as a result of failure of integration of physiological functions and homeostatic control of the internal environment due to narrowing of the width of regulation of individual physiological functions by ageing.

Due to the holistic nature of health and longevity, many aspects of human life must be taken into consideration for systematization of knowledge for attaining healthy longevity, therefore, not only biomedical aspects but also mental and socioeconomic aspects are important. One of the ways of obtaining fundamental principles of human healthy longevity is to investigate the life styles of inhabitants of villages or districts where many nonagenarians and centenarians are living. In Japan, Okinawa is a special district where many healthy centenarians are living. Many observations and investigations have been made for this area thus far, the findings are to be discussed in the coming Forum (the fifth Forum, 2000). However, basic research of ageing and age-related diseases is progressing. The Forum is always making efforts to absorb recent knowledge of these fields. In the coming Forum, new findings of cellular and mitochondrial ageing, and their relation to ageing of the whole body will be discussed together with the above issue.

The organizing committee has an idea that genomic diagnosis of morbid constitution and pharmacogenomics should be dealt with in a Forum in the near future. The genomic diagnosis using DNA tips or microarrays is considered to rapidly progress in the near future with

advancement of post-genomic bioscience. Since most of the diseases of the elderly are related to both genetic constitution and life-style, it will become possible in the near future to clarify individual constitution before suffering from a particular disease and to prevent disease more effectively by changing one's life-style to avoid risk factors relevant to a particular disease. This may be one of the ways of assisting the attainment of longevity and ultimately healthy dying.

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