

HEALTH AND NUTRITION NEWS

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Prefatory Note

Achievements of the National Institute of Health and Nutrition, and future expectations

Prof. Yu Hosokawa

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About Four years has passed since National Institute of Health and Nutrition (NIHN) was transformed into an independent administrative agency in 2001, and now, this is the last year of the midterm plans. In 2006, therefore, the results and achievement levels of the midterm goals will be evaluated. Last autumns, as one of the major achievements, "Dietary Reference Intakes (DRIs) for Japanese, 2005" was officially announced. For examples, the estimation of DRIs for energy is based on the research findings at NIHN on reference value of Japanese energy expenditure. That is, the energy expenditure of general/healthy Japanese was actually measured by the doubly labeled water (DLW), and then, Physical Activity Level (PAL) replaced the existing intensity of daily activity. In addition, new DG (tentative dietary goal for preventing lifestyle related diseases) was set up for some nutrients to reduce the risk of life-style related diseases. In this way, the new DRIs would meet the social needs. Now, the nutrition experts (e.g. dietitians, registered dietitians) are supposed to utilize DRIs as the reference values for nutritional assessment and plans. Since the roles of NIHN comprise the dissemination of research findings to the public, I expect that, in addition to the further development of research, the information is more easily understandable considering the social needs not only for experts but also for general population.

In 2006, the universities for the registered dietitians will be evaluated on the educational efforts and achievements. As the Nutritionists Law revised in 2001 was executed from April, 2002, the present partial exemption for the students

graduated from these universities at the national examination for the registered dietitians will be demolished after March 2006, and then a new framework of the examination guideline will be introduced. In prior to the revision of Nutritionists Law, the expected roles and works of registered dietitians toward 21st century were discussed.

In order to prevent the development and progress of lifestyle related diseases, which is now the major social issues, the most important thing is to improve our diets. Therefore, the registered dietitians with the professional knowledge/skills to assess the physical and nutritional status or dietary pattern of individuals comprehensively, as well as to undertake the appropriate nutrition guidance program, are required.

For which, the educational curriculum at the universities for the registered dietitians' has also been considerably reviewed. Furthermore, these universities also prepare to introduce the curriculums for the nutrition teacher as well. A nutritional teacher is responsible for the children to gain the appropriate diets, since irregular and unbalanced diets among children (e.g. skipping breakfast) become serious issue these days. It is therefore essential to provide the dietary and nutrition education, not only for the children themselves, but also for their families. Now, in order that the registered dietitians will acquire more professional knowledge, the needs of establishing the graduate school have also been discussed. I personally expect that the National Institute of Health and Nutrition will play a core role in education program at the graduate schools.

Current Research Projects

Laboratory of Physical Activity and Health Evaluation

Motohiko Miyachi

Division of Health Promotion and Exercise

Laboratory of Physical Activity and Health Evaluation, Division of Health Promotion and Exercise, mainly works on the research on health promotion and exercise for the human beings. It has been well acknowledged that the exercise and physical activity are useful for developing the physical strength and preventing lifestyle related diseases. In addition, with the accelerated aging in Japan, the positive impacts of exercise and physical activity are now expected for the elderly people in need of nursing care as well. Yet, are there enough scientific evidences on the effectiveness of exercise and physical activity for development of physical strength and prevention of lifestyle related diseases as well as of being in the nursing care? If not, what aspect of knowledge is insufficient?

Now, the questions can be summarized into four categories as below;

1. What types and how much of exercise is effective for the prevention of each disease?
2. Is the possible side-effect of the exercise is explored?
3. Is it based not only on the knowledge in Europe, but also on that for Japanese?
4. Does it focus on improving QOL, in addition to the medical effect?

We, therefore, have been working on the researches based on these questions.

1. "What types and how much of exercise is effective for the prevention of each disease?"

So far, studies have focused on several types of exercises with low intensity for the whole body, so-called aerobic exercise such as walking, jogging, and swimming. Now, we attempt the

research on the exercise with high intensity, so-called "resistance training" such as weight lifting and so on.

2. "Is the possible side-effect of the exercise is explored?"

While many studies have explored the long-lasting impact of exercises on risk factor of lifestyle related diseases, little has been reported on the unfavorable effects (namely, side-effect) of exercise. Thus, we are investigating the possible unfavorable effect of exercise.

3. "Is it based not only on the knowledge in Europe, but also on that for Japanese?"

Only a few researches, well-designed and large-scaled, have been undertaken for Japanese. There is an obvious difference in the disease patterns between Japanese and Europeans, and their genetic background and lifestyle are also very different. Not only working on the laboratory-based research, we are now conducting the field research in Okayama Prefecture entitled "Randomized interventions for several hundreds of local residents".

4. "Does it focus on increasing QOL, in addition to the medical effect?"

Generally, the values of exercise have been examined based on the evidence by medical model. However, in terms of health among the elderly, it is necessary to evaluate the effect of exercise, as well as the QOL properly. We are now organizing the classes for exercise and swimming for the elderly, by which the effects of exercise can be assessed from various aspects.

Our research works in this laboratory are mostly targeted on humans. I would like to provide the better quality of research on exercise for health with the cooperation of the study subjects and collaborative researchers.

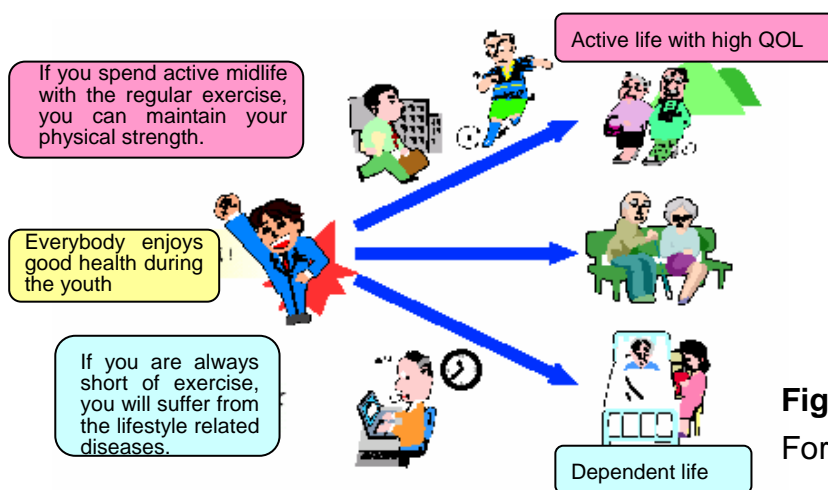


Figure. For healthy life in your old age....

Thoughts on Health and Nutrition Research

Needs of a new QOL evaluation methods for the disease prevention

Osamu Ezaki
Division of Clinical Nutrition

Recently, QOL (quality of life) is often used as a proxy for the “degree of happiness”. It is expressed mostly by comparison such as “lower than...” or “better than...”, and is rarely shown as quantity like “my QOL is...%” or “your QOL is...%”. So, it is difficult to use QOL in the research. In addition, there are two more features/problems; one is that it is the indicator of psychological well-beings for the individuals, and the other is that it is the indicator at one (present) point, not that for the future.

Since it is the indicator of psychological well-beings for the individual person, it can not be estimated unless the questionnaire survey is undertaken. Even though one looks rich and healthy, s/he may have some problems, hence low QOL. Besides, one’s past experience also greatly influences his/her present QOL. Assuming that if the present living condition is physically same... if one experienced hard time in the past, s/he may feel happy with the present condition, whereas if one experienced better time in the past, s/he may feel unhappy now. It is therefore quite difficult to assess the degree of QOL of other persons. However, one’s QOL can be generally estimated low, when s/he is sick or having hard work.

Dietary or exercise therapy for the disease prevention is incompatible with one’s present QOL. In some cases, these therapies could worsen one’s present QOL. For example, one may be forced to eat what s/he doesn’t like, or restricted from what s/he want to eat. One may be unhappy with forcing oneself to do exercise. On the other hand, smoking improves the present QOL of smokers. Nobody knows what will happen in the future, so it is no surprise that one prefers to enjoy oneself at the present point. Yet, it must be noted that the primary prevention of diseases is expected to improve one’s future QOL. Even if you find it hard now, you can expect the improvement of future QOL, by modifying the diet, doing exercise, and stopping smoking.

In order to solve the above inconsistency, it is necessary to develop a new indicator that comprises the present and future QOL till one dies, that is, QOL integral value. For example, for dietary therapy, the new indicator can be introduced, if the

following data are available.

1. QOL is shown properly and quantitatively, in the questionnaire survey,.
2. QOL value without dietary therapy (A), and when one follows the dietary therapy (A')
3. Future morbidity of diabetic mellitus or cerebral infarction without dietary therapy (R), and when one follows the dietary therapy (R').
4. QOL value when one suffered from the diabetic mellitus or cerebral infarction.

$$\text{QOL integral value without dietary therapy} \\ = A + RB + (1 - R)A + \dots$$

$$\text{QOL integral value when one follows the dietary} \\ \text{therapy} = A' + R'B + (1 - R')A' + \dots$$

By investigating which of the above two QOL integral values is higher, we can evaluate if the present dietary therapy is necessary for him/her. Value B could vary by the type of diseases. In order to improve the QOL integral value, more effort is requires for the disease with lower B to reduce R'.

In terms of public health, however, it is necessary to improve QOL of the populations, rather than QOL of each individual. Here, smoking is a typical example. If one’s QOL is quite high when s/he smokes, QOL integral value may be also high, even if the future QOL is estimated lower due to the increasing morbidity of lung cancer and cardiac infarction etc. So, we can say that smoking is good for this person. On the other hand, it can be anticipated that nonsmoker’s QOL could become lower due to the secondhand smoke and increase of medical expenses, leading to the lower average QOL of the population.

As was mentioned earlier, QOL is influenced by many factors not only diets and health, but also economic status, educational level, personal relationships, public security and so on. If all those factors can be included in the calculation of QOL integral value, and if the average QOL integral value of the population can be obtained, it should be very useful for the future policy making.

PCAF and PCAF-B are required for normal Estrogen response in the uterus

Erina Inoue (Division of Applied Food Research)

Estrogen is the main female hormone, which targets genital, bone and brain tissues. The physiological responses are mediated by the transcriptional regulations of target genes with the nuclear receptors for estrogens. In addition, it is also known that not only estrogen receptor but also several transcription co-factors are involved, which form complexes for the transcriptional regulations. Transcription co-factors mediate the basic transcription factors necessary for all the transcriptions and DNA-binding transcription factors by protein-protein interaction. Of which, transcription co-factors called PCAF and PCAF-B are also known to function as the transcriptional coactivators of the receptors for various steroid hormones including Estrogens. In this way, the cooperative effects between the nuclear receptors and the protein complexes are known *in vitro*, though few studies have been done *in vivo*. Under this circumstance, this study aimed to explore the endogenous physiological responses *in vivo*, using the mice with targeted gene disruption of one of the transcription co-factors for the estrogen receptor, PCAF and PCAF-B. And then, this study confirmed that PCAF and PCAF-B are required for the normal estrogen responses in the uterus. Recently, it is recognized as a serious problem that many endocrine disruptors (endocrine disrupting chemicals) like dioxin affect the reproduction and growth of the animals/human beings etc. Even very small amount of endocrine disruptors could disturb the normal hormone responses, with most serious influence on the estrogens. Most of the endocrine disruptors are, perhaps unknowingly, taken orally via foods and utensils. We are concerned that the endocrine disruptors can be easily accumulated in the body, and that the long-termed exposure could cause the serious problems to our health.

* This study was undertaken as a part of Core Research for Evolutional Science and Technology” on the endocrine disrupting chemicals.

Transcriptional Coactivator p300/CBP-Associated Factor and p300/CBP-Associated Factor Type B Are Required for Normal Estrogen Response of the Mouse Uterus

Bioscience, Biotechnology, and Biochemistry, Vol. 68 (2004) , No. 10 pp.2209-2211

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Abstract:

Mice with targeted gene disruption of one of the estrogen receptor coactivators, p300/CBP-associated factor (PCAF), and its counterpart, PCAF-B, were used to investigate the possible involvement of PCAF and PCAF-B in estrogen receptor-mediated actions *in vivo*. Among ovariectomized mice that were treated with estrogen, PCAF and PCAF/PCAF-B knockouts showed abnormal growth of the uterus compared with the wild type. The level of c-fos gene expression in the uterus was not induced by estrogen in the knockouts. These observations suggest that PCAF and PCAF-B are required for estrogen-dependent normal growth of the uterus *via* estrogen receptor-mediated transcriptional regulations.

Functions of the new structured lipids containing n-3 fatty acids (EPA or DHA) and medium-chain fatty acids.

Junichi Nagata (Division of Food Science)

Generally, the edible fat/oil exists in the form of triacylglycerol, which consists of three fatty acids attaching to a glycerol. The fatty acids of triacylglycerol attached to the sn-1,3 positions of the glycerol are hydrolyzed by digestive enzyme "lipase", and a 2-monoacylglycerol and two fatty acids are formed. "Structured lipids (SLs)" can be formed by attaching functional fatty acids to the detached positions (sn-1,3 position) and the sn-2 position of glycerol. SLs are the physiologically advantaged lipid, which can be absorbed into body effectively. So far, most of the studies focused on the effects of fatty acids that compose the fat/oil. In Japan, edible fat/oil that maximized the effects of fatty acid, by attaching optional fatty acids to the glycerol, and processed edible fat/oil designed to improve the absorption by the change of attaching positions and number of fatty acids are now widely available at the market. Fat/oil containing lots of diacylglycerol and medium-chain fatty acids fall into these SLs. In this study, we synthesized new SLs using the enzyme by which the reaction with high specificity positions can be expected, by combining n-3 fatty acids (EPA or DHA) and medium-chain fatty acids (caprylic acid). The effect of n-3 fatty acids is known to reduce the obesity as a risk factor of lifestyle related diseases and serum lipid profiles, and that of medium-chain fatty acids is to reduce the body fat accumulation. Next, the serum- and liver- lipid profiles were compared between the rats fed SLs and those fed the ordinal edible oil, and the differences of the fatty acids and structures were investigated. The findings of this study showed that all the synthesized SLs have the effects to improve the serum lipid profiles. However, it was also explored that the reduced risk factor of the lifestyle related diseases observed in this study were mainly due to the effects of fatty acids, and the differential effects by the triglyceride structures were not confirmed. We, therefore, would like to attempt the further study to develop the SLs which is effective for the prevention of the lifestyle related diseases.

Effects of structured lipids containing eicosapentaenoic or docosahexaenoic acid and caprylic acid on serum and liver lipid profiles in rats.

Biofactors. 2004;22(1-4):157-60.

Nagata J, Kasai M, Negishi S, Saito M.

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Abstract:

The physiological activity and effect on lipid metabolism of four types of structured lipids (SLs), that contain caprylic acid (C8) and either eicosapentaenoic (EPA) or docosahexaenoic acid (DHA), were evaluated in male Wistar rats fed experimental diets containing 7% (wt %) of each SL and 3% (wt %) soybean oil for 28 days. Control rats were fed a diet containing 10% (wt %) soybean oil. The relative perirenal adipose tissue weights of rats fed D-8-8 and 8-D-8 diets were significantly lower than those of other groups. We observed significantly lower serum cholesterol concentrations in rats fed SLs than those of control group over experimental period. The serum lipids concentrations in rats fed diets containing SLs were significantly lower ($P < 0.05$) than those of soybean oil group. The fatty acid compositions of WAT did not reflect the structural differences in the triglyceride. These results suggest that the physiological effects of the SLs used in this study were due to the fatty acids rather than the structural specificity. Therefore, further study will be needed to ascertain the most desirable structural configuration.

Decreased trends of the trace elements involved in antioxidation with ageing

Masao Kondo (Division of Applied Nutrition)

Environmental factors associated with the rapid ageing include the stress, ultraviolet, radiation, nutrition, smoking, alcohol. It has been noted that active enzyme like superoxide produced and accumulated in body through metabolism under these environments for a long time could cause the lipid peroxidation of cell membrane, degeneration of cytoplasm and membrane protein, as well as interference of enzyme, subcellular organelle and cell. In order to prevent these peroxide chain of cellular component, superoxide dismutase and NADPH · GSH system function as an antioxidant, for which the trace elements involved in antioxidation (e.g. Se, Cu, Zn and Ms) are required. This study therefore aimed to investigate the changes of the trace elements in the blood that are involved in the antioxidation mechanism according to age and living environments. One of the interesting findings was the different trends before and after 50 years old (Figure). The possible reasons include the various stress and change in the diets. Besides, more obvious variation in the concentration of elements may be related to the facts that the resistance and immune strength against stress by oxidation is stronger for women than men. Another interesting finding was the associations with the subjective symptoms; those who reported dizzy, palsy, tangled tongue, chest pain, headache, palpitation and insomnia had significantly less Cu, Se, Zn and Mn in the whole blood. Although the increase of mineral intake is recommended to make up for the decrease in the blood, the excessive consumption also brings other functional disorders. It is thus crucial to ensure the intake of appropriate amounts, considering the balance with other nutrients as well.

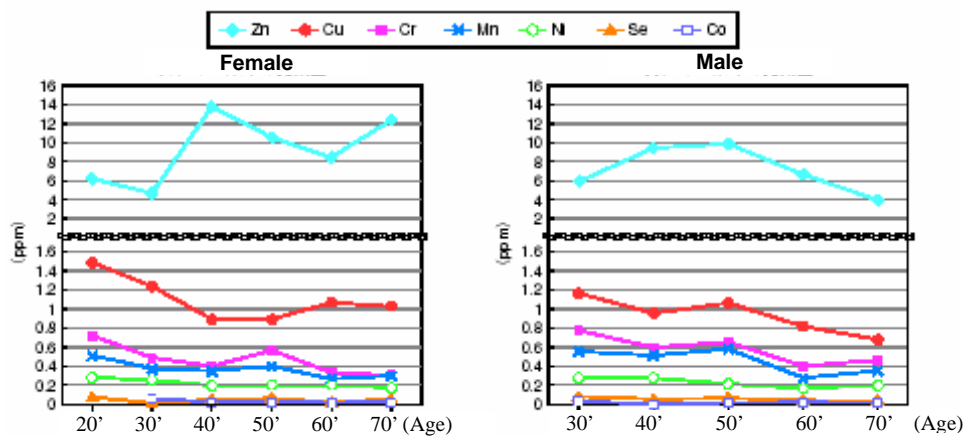


Figure Changes of trace elements in the whole blood with ageing

Changes due to ageing in the concentrations of trace elements in the whole blood that assist with the process of antioxidation

Biomedical Research on Trace Elements, Vol. 15 (2004) , No. 4 342-344

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3) Sagami Women's University

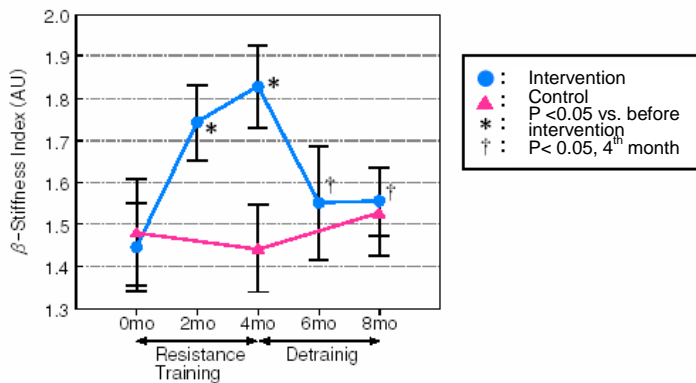
Abstract:

Seven elements, Co, Cr, Cu, Mn, Ni, Se, and Zn, in the whole blood of a total of 94 healthy individuals (36 males and 58 females), ranging from 30 to 79 years of age, were measured by the coupled plasma-mass spectrometer (ICP-MS) method. Gender differences were found only in Cu (p <0.05). By age bracket, low values were measured for Cu in the 70s, Co in the 60-70s, Cr, Ni and Se in the 60s, Zn in the 40s, and Mn in the 30s and 60s. These results reveal that there is a trend for many elements that are involved in antioxidation, except for Zn, to decrease with ageing.

Resistance training "reduces" central arterial compliance in healthy men

Motohiko Miyachi (Division of Health Promotion and Exercise)

Regular exercise is one of the essential parts for the prevention and treatment of the cardiovascular disease. It is known that the regular aerobic exercises like walking could prevent the increase of stiffness of the central artery by ageing, which is an independent risk factor for the cardiovascular disease, and also improve the arterial stiffness among middle- and old-aged people with no habits of regular exercise. Now, it can be questioned if another type of exercise "resistance training" could have the beneficial effect on the arterial stiffness. This study was therefore undertaken under the hypotheses



that the resistance training for 4 months could increase the arterial stiffness. In order to investigate the validity of the hypotheses, the detraining period was set up after the interventions, assuming that the increased stiffness would return to the baseline levels. The findings of this study suggest that it must be cautious to apply the resistance training, especially to those at risk of cardiovascular disease.

Unfavorable effects of resistance training on central arterial compliance: a randomized intervention study.

Circulation. 2004 Nov 2;110(18):2858-63.

Miyachi M, Kawano H, Sugawara J, Takahashi K, Hayashi K, Yamazaki K, Tabata I, Tanaka H.

Division of Health Promotion and Exercise, National Institute of Health and Nutrition, Japan.

BACKGROUND: Reductions in the compliance of central arteries exert a number of adverse effects on cardiovascular function and disease risk. Endurance training is efficacious in increasing arterial compliance in healthy adults. We determined the effects of resistance training on carotid arterial compliance using the intervention study design.

METHODS AND RESULTS: Twenty-eight healthy men 20 to 38 years old were randomly assigned to the intervention group (n=14) and the control group (n=14). Control subjects were instructed not to alter their normal activity levels throughout the study period. Intervention subjects underwent 3 supervised resistance training sessions per week for 4 months and detraining for a subsequent 4 months. The resistance training increased maximal strength in all muscle groups tested (P<0.001). There were no significant differences in baseline arterial compliance and beta-stiffness index between the intervention and control groups. In the intervention group, carotid arterial compliance decreased 19% (P<0.05), and beta-stiffness index increased 21% (P<0.01) after resistance training. These values returned completely to the baseline levels during the detraining period. Arterial compliance did not change in the control group. In both groups, there were no significant changes in brachial and carotid blood pressure, carotid intima-media thickness, lumen diameter, and femoral arterial compliance. Changes in carotid artery compliance were significantly and negatively related to corresponding changes in left ventricular mass index (r=-0.56, P<0.001) and left ventricular hypertrophy index (r=-0.68, P<0.001).

CONCLUSIONS: In marked contrast to the beneficial effect of regular aerobic exercise, several months of resistance training "reduces" central arterial compliance in healthy men.