HEALTH AND NUTRITION NEWS

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Prefatory Note

Expectation to the National Institute of Health and Nutrition

Dr. Yoshiko Kagawa (President of Kagawa Nutrition University)

I have been a member of external evaluation committee for last two years since the NIHN became an incorporated administrative agency. Not surprisingly, facilities and staff are outstanding as expected of being a pioneer in the field of nutrition in Japan.

First of all, their primary research area is on basic human nutrition such as a nutrient and its metabolism, and nutri-genomics. The study of energy metabolism is one of core research areas since the NIHN was found, but it has been upgraded with the new technology. This area is very important to study because many of Japanese are now facing with the problem of consuming too much energy. The study of nutrition is not limited in the basic research, but a research to enhance the public health is well demanded. “Evidence-based Nutrition” (EBN), a study of nutrition based on a scientific evidence, should be at the base. EBN often requires researches on human, so that it is more difficult to conduct compared to an animal study. For instance in the study of gene, researchers are eager to develop an order-made nutritional advice based on one’s physiological constitute in future.

On the other hand, the number of people who is not concerned their diet is increasing due to the change in society, food environment, and family structures. The “National Nutrition Survey” (now changed its name to the National Health and Nutrition Survey) has been providing reliable data concerning the diet of the Japanese every year since 1946, and this survey is now further upgraded with the extended sample size and content. I look forward NIHN to make further efforts to progress in order to obtain enhanced data.

In addition, people who are either less concerned their diet or eating unbalanced diet have been more dependant on dietary supplements, and there are more demands by the public for information on functional foods, BSE, pesticides, genetically modified foods, and false food labeling. Therefore, studies on cooking are inevitable. NIHN has worked on these various areas to meet large expectations from the public.

It is always said that an individual-based nutrition education is important. However, if one does not follow the advice, it is putting the cart before the horse. Yet, it always happens. We have changed the food we eat, so that we need instructions on how to eat. A study of food preference and psychological issues behind diet should be also looked before implementing an education

Japan has the longest life expectancy in the world. On the other hand, the number of people who suffers from lifestyle-related diseases such as diabetes and obesity is also increasing. One of the reasons is lack of physical activity. The study of nutrition and/or physical activity will have a great impact on one’s health and wellbeing in long run. Therefore, we need more data to make a policy. “Health Improvement Law” was enacted last year, and people are now responsible for improvement and maintenance of own heath status. In addition, almost of all target areas in “Health Japan 21” have included nutrition-related topics. The public awareness will continuously increase, so that NIHN should make continuous efforts not only to make great accomplishments in the field of nutritional research, but also to provide valuable information to the public.

Current Research Projects

Diet and energy expenditure

Dr. Toshimasa Osaka (Senior Researcher of Division of Human Nutrition)

Many of you may have experienced the sensation of warmness after eating pot-stew or meals cooked with chili peppers. On the other hand, some may have sweated while you ate meals in hot summer. This is not simply caused by ingestion of hot meals, but rather the heat is induced as a result of the energy synthesis of nutrients during or after the digestion of meals. This type of energy expenditure has been known as “dietary induced thermogenesis.” This takes up to 10% of the total energy intake, and it is taken place in everyone, even for those who do not exercise regularly. Therefore, although it might be thought to be only a little, but this would affect one’s body weight in long-run.

No one consistently consume the same amount of calories everyday, but why one’s body weight relatively stays the same? The reason is that the body not only regulates the energy intake, but also regulates the expenditure to keep the balance. “Obesity” is caused when the energy intake exceeds the expenditure, and that will further lead other lifestyle-related diseases such as diabetes, hypertension, and hyperlipidemia, as many of you have already known. Therefore, if we could control the energy expenditure, it would effectively prevent developing lifestyle-related diseases. However, how the body regulates the energy expenditure is still unknown.

“Dietary induced thermogenesis” is the energy derived from digestion of foods we eat, as well as from absorption, metabolism, and storage of nutrients. In addition, food satiety or chewing will increase the energy expenditure. In addition, we now know that the brain is involved in this regulatory system due to our sense of taste or smell, and our expectation to or experiences with meals. We are currently studying about the basic physiology how food components or hormones secreted for energy metabolism by digestive systems due to ingestion of such foods.

The energy expenditure is mostly regulated by the autonomic nervous system (vagal nerve and sympathetic nerve). For instance, the vagal nerve detects an ingested or digested food component at first, and then transmits a signal to the brain, which then will send an order to the sympathetic nervous system to regulate the energy expenditure. The signal sent to the brain will also influence a food intake. Those food components and hormones will act as “satiety substance” on brain to generate the sense of fullness and to increase the energy expenditure. Overall, it will prevent an accumulation of excess energy in the body. The brain regulates this system, and usually it is unconsciously taken place in the body. If something happens to this mechanism, it may lead to obesity. Our future plan is to clarify how signals from digestive system are sent to the nervous system or brain, how energy metabolism or the sense of fullness is regulated, and which part of the brain is involved in this work.

Thoughts on Health and Nutrition Research

From Index Medicus to Medline: Changes in the method for searching medical research articles and outlook for a research institute

Dr. Satoshi Sasaki (Head of Dietary Reference Intakes)

A decade ago, we referred to “Index Medicus”, a high volume book listed only titles of articles, in order to look for medical research articles. Therefore, we used to spend hours in the library to look for the article we wanted. Even after we found the title, we still had to transcribe the name of the journal, year, volume, and pages. Then we searched shelves or had to ask librarians to order copies by interlibrary loan if they did not have it. In many cases, however, we realized that it was missing out the content we wanted after reading the whole article. The University of Ruben in Belgium is the world oldest catholic university found in 1425, and has a collection of medical journals published worldwide. Through years while I was a doctorate student at that university, I was allowed to use their resources freely, and was able to enhance my knowledge and intelligence.

However, few years later, the National Library of Medicine in the United States started providing medical article database called “Medline” through an internet. Soon after, the service became free of charges. Even at home, we can now access to this database, which contains over 9,000,000 articles, to search and even to read summary of an article. Previously, we had spent a month at a library, but now it only takes an hour in order to get the same outcome. This information infrastructure has contributed a lot to researchers. Furthermore, such intellectual properties, only available for limited number of people at research institutes or universities in one-time, are now open to everyone in the world.

Medline is accessible by anyone. It may need some techniques at first time, but I strongly recommend trying out at least once. For instance, type “Sasaki S” AND (intake OR consumption OR diet OR dietary) in the search box, and hit an enter key. This allows knowing how many articles “Sasaki S” has published or what area of interests he has. However, if more than one “Sasaki S” exist (mostly in this case, “yes”), it is difficult to detect the right one. In addition, if his area of interest is on variety topics, you need to put more keywords and connect with “OR”. If the number of hit articles was not many enough as you expected, there would be two possible reasons: one is “not publishing enough” and the other is “incorrect search keywords.” Furthermore, there are many medical journals not listed in Medline, so that this is one out of many ways to have rough ideas.

After going through such trials, you might understand that Medline is very useful tool but requires some techniques and expertise. In addition, since we can only get access to a summary on Medline, we still need to rely on a library to read whole papers. Information-driven society would also apply to research areas. An effective utilization of resources such as Medline and appropriate library facilities to support it are two keys to determine whether Japan can successfully become an intelligent producing society to produce a high level of research outcomes. For these times, I remember good old days in the Ruben university library.

Research Findings

Are there oils really preventing for fat deposition in the body?

Dr. Nobuyo Kasaoka-Tsuboyama (Researcher of Division of Clinical Nutrition)

In recent days, we see various types of fats and oils in supermarkets, and especially those claiming for “preventing fat deposition in the body” are drawing attention. These types of oils are sold not only as cooking oil, but also as dietary supplements. Quite a lot of people have doubted the consequence, but is that really so?

Fats are made of “fatty acids”, and a number of fatty acids exist in nature. Some of those are indispensable for life, but others are not, even though those still provide some functions to the body. Some fats are less likely to accumulate in the body, and these types of fats are used for manufacturing “oils preventing body fat deposition.” However, some products are enriched with a fatty acid which barely presents in nature, or others contain a fatty acid whose chemical structure was slightly changed from the ordinal one. Furthermore, some products are not clearly confirmed to have a property declared, or whether those are safe enough to consume. We have been studying to evaluate whether these fatty acids truly have such declared properties or how much we should consume, and if there are any adverse effect or not.

We used a conjugated linoleic acid (CLA), a fatty acid often found in meats and dairy products, and we found that the fat mass of CLA-fed mice was significantly reduced. Both visceral and subcutaneous fats were reduced as levels of CLA increased, so that we concluded that CLA has a positive effect on obesity control. On the other hand, feeding too much CLA led extreme reduction of body fat, even those essential to maintain the physiological function, and further conditions like fatty liver and diabetes were developed (1.3gCLA/kg body weight; approximately 70 times more than normally contained in dietary supplements). When feeding smaller amounts of CLA (0.13gCLA/kg body weight; approximately 7 times more than normally contained in dietary supplements), body fat was reduced without causing any adverse effect. In consequence, we found that feeding small amounts of CLA is necessary to control obesity. In addition, even if someone ever consumes larger amounts of CLA than safe levels, we can still avoid developing fatty liver and/or diabetes by eating high-fat diet. This suggests that it is better to add CLA to edible oils, rather than to dietary supplements, in order to prevent obesity.

In addition, after we studied how CLA had caused fatty liver, we found that CLA directly worked on genes involved in the fat synthesis (SREBP-1 and its targeted gene) to enhance the formation of fatty liver.

In this study, we fed 7 to 70 times of CLA more than normally contained in dietary supplements. Therefore, eating regular meals would not cause a health problem. However, if you take some nutrients like CLA that regulate any particular gene, you should be concerned. Those fats and oils declared for “preventing fat deposition” might work differently, but still fats are essential to maintain our physiological function. Therefore, we need to be careful to avoid excessive depletion of body fat stores at any time.

Reference: Increasing the amount of fat in a conjugated linoleic acid-supplemented diet reduces lipodystrophy in mice. Tsuboyama-Kasaoka N, Miyazaki H, Kasaoka S, Ezaki O: J Nutr.: 133:1793-99, 2003

Research Findings

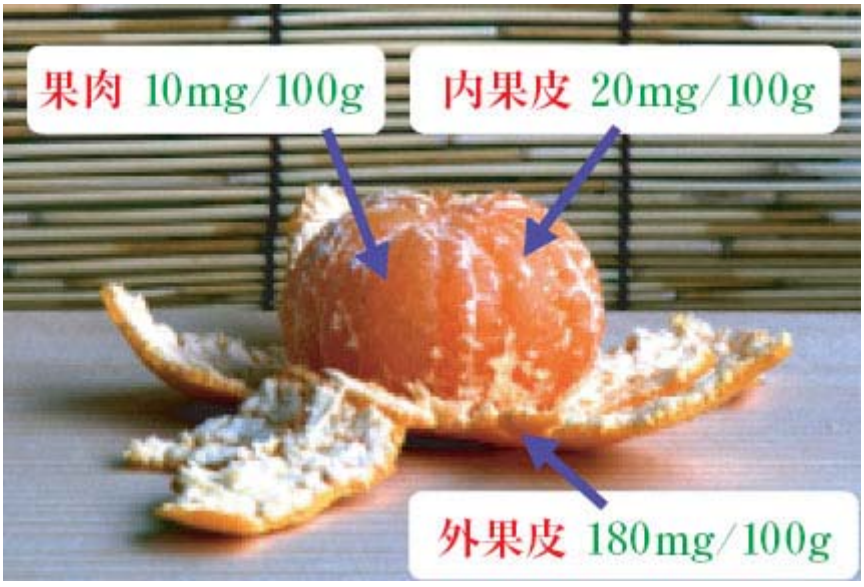
Hesperidin, a citrus flavonoid, inhibits bone loss and decreases serum and hepatic lipids in ovariectomized mice

Dr. Yoshiko Ishimi (Chief of Laboratory of Assessment of Food Function)

The article reported that the synthesis of cholesterol was reduced in statin-fed rats, in the American journal called "*SICENCE*" 4 years ago. This finding had a great impact around the world, and many case-control studies were conducted regarding the relationship between the use of statin and bone mass. As a result, many studies have reported that the incidence of hip bone fracture was lower in statin-taking menopausal women and elderly people, compared to those who did not. The trial was also conducted in Japan with middle-aged women, and increased bone density was observed in those taking statin.

We have conducted nutritional researches to prevent osteoporosis. Recently, we have looked at a citrus flavonoid, which was thought to have a capacity to lower the synthesis of cholesterol, in relation to bone turnover. As a result, hesperidin, a citrus flavonoid predominantly found in an orange peel, inhibited bone loss and decreased serum and hepatic lipids in ovariectomized mice. The peel of "Satsuma mandarins" contains large amounts of hesperidin, but we further need to analyze if the same mechanism would occur in human. The peel of oranges has been popular in Chinese medicines as "Chinpi" to maintain the health of the digestive system and to relieve cough. Why do not you try marmalade for breakfast?

Reference: Chiba H, Uehara M, Wu J, Wang X, Masuyama R, Suzuki K, Kanazawa K, Ishimi Y. Hesperidin, a citrus flavonoid, inhibits bone loss and decreases serum and hepatic lipids in ovariectomized mice. J Nutr. 133: 1892-1897, 2003.



Association of peroxisome proliferators-activated receptor γ coactivator-1α (PGC-1α) to expedite glucose metabolism induced by physical activity

Dr. Shinji Miura (Researcher of Division of Clinical Nutrition)

After engaged in prolonged exercise, body fat is burned due to the increased number of mitochondria in skeletal muscles, and the glucose metabolism is activated by the increased number of glucose transporter (GLUT4) to take blood glucose in skeletal muscles. Regular exercise is thought to prevent developing lifestyle-related diseases like diabetes, and the above mechanism of skeletal muscles is thought to explain it.

Recently, peroxisome proliferators-activated receptor γcoactivator-1α(PGC-1α), a substance regulating genetic transcription, was found to expedite the synthesis of mitochondria. In addition, the study of cultivating skeletal muscle cells has reported that PGC-1αhad increased the number of GLUT4 in skeletal muscles. PGC-1αalso presents in skeletal muscles and we have observed that the number was increased after exercise. According to these results, we have concluded that the change in the structure of skeletal muscles is due to the increased number of PGC-1αinduced by exercise.

In this study, we used transgenic mice with the elevated level of PGC-1αonly in skeletal muscles in order to examine whether or not the increased number of mitochondria and GLUT4 by exercise is as a result of the increased number of PGC-1α, in vivo (figure 1).

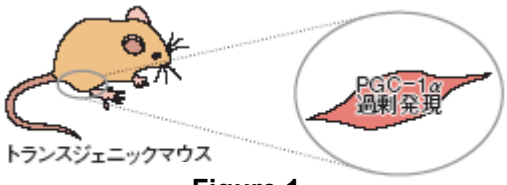


Figure 1

In PGC-1α-transgenic mice, we observed the increased number of mitochondria and red muscles (muscles appropriate for prolonged exercise like marathon), but the level of GLUT4 expression was lowered. In addition, glucose intolerance[1)] was also observed. In conclusion, the number of mitochondria will increase with increasing the number of PGC-1αin skeletal muscles over a long period of time, but it is not associated with overexpression of GLUT4 and the activation of glucose metabolism (figure 2).

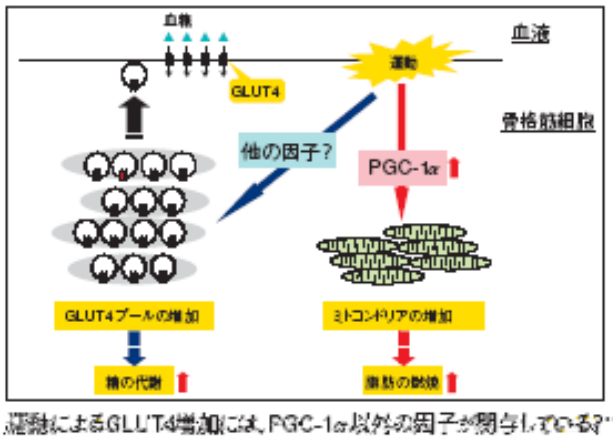


Figure 2

In future, some diabetes medications targeting PGC-1αmay be introduced, but too much PGC-1αmay cause adverse effects such as glucose intolerance. Therefore, we eager to find a GLUT4 enhancing substances, other than PGC-1α, to avoid any possible side effect.

1) Glucose Intolerance: Insulin is secreted from pancreas after ingestion of meals to take blood glucose in skeletal muscles via GLUT4, so that blood glucose is kept within the normal level. However, in people with glucose intolerance, insulin is secreted normally but blood glucose is not taken up by skeletal muscles due to inactivated GLUT4. Accordingly, insulin no longer regulates blood glucose level, and this would result in high blood sugar level. Eating too much food (especially high-fat diet) and sedentary lifestyle are thought to be reasons for developing glucose intolerance. This is a precursor for type 2

diseases in Japan.

Reference: Overexpression of peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α) down-regulates GLUT4 mRNA in skeletal muscles. Miura S, Kai Y, Ono M, Ezaki O: J Biol Chem.: 278(33):31385-31390, 2003.