

HEALTH AND NUTRITION NEWS

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Prefatory Note

Dietary Life as a Philosophy

Junzoh Hayashi
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While diet is an everyday expression, it is one of the most important things in health and nutrition. In about 1980, this popular term has become one of the subjects in universities and junior colleges as “Studies on Dietary Life”. After the World War , many courses related to dietary life has come in education of domestic science or dietary nutrition as follows: “nutritional science”, derived from biochemistry or physiology, “food science” and “food hygiene” from agriculture, “food economics” from economics, and “cookery”. When the purpose of the education and research of these courses is fostering of dietitians or education in domestic science, the area was likely to be preoccupied with its segmentation. Isn't it also necessary to look them from total point of view, although an academic advancement is necessary? If we succeed in systematizing dietary life academically, it will become deeply involved in health and nutrition.

At such demands, “Studies on Dietary Life” was arisen. “Studies on Dietary Life” was, therefore, dietary life that theorized and practiced human's health and nutrition. It was as if Dr. Tadasu Saeki who created the Institute of Nutrition emphasized on practice of nutrition improvement. In 1981, “Studies on Dietary Life” was fit in a curriculum of domestic science course of women's college where I belonged to, and then I took charge of it. At the beginning, it was made of a

variety of knowledge of food and nutrition. But with extreme difficulty, we finally build it up as “Studies on Dietary Life”. When Dietitian's Law was conducted in 1985, “Studies on Dietary Life” became mandatory in a training course of dietitians and registered dietitians (currently it is not mandatory). In 1989, I retired, and I was freed from duties of college administration. At this time, I had an opportunity to discuss several times with Dr. Tatsuyuki Sugawara, then professor of Kagawa Nutrition University (present professor of Seitoku Univ.) and Mr. Yoshio Tsukushi, president of Kenpakusha and organized a workshop on “Studies on Dietary Life”. And we named a meeting of promoters “Dietary Life General Workshop” and about 20 people got together at the private hall in March, 1990. A few people left from the workshop in several times for supreme academic learning. In October 27, 1990, the first workshop was conducted at Japan Publishing Club Conference Room and about 100 people attended. I gave a lecture of “Focusing on Dietary Habits ”. Also, the concept of Dietary Life General Workshop was recognized on the day. Some parts are introduced as followed: “It is believed to be useful in human health maintenance and their happiness by expanding the issue of food and nutrition from the viewpoint of dietary life and systematize the knowledge.” The workshop was named “The Japan Association for the Integrated Study of Dietary Habits” since 1994, and has been published 4 times a year. In 1998, it became science council registered association, and increased the membership of 700 people or more.

I am expecting the Japan Association for the Integrated Study of Dietary Habits to contribute to public health and nutrition, and also subjected in the National Institute of Health and Nutrition.

Current Research Projects

In the Laboratory Now

Tomomi Yamazaki
Division of Clinical Nutrition

In the Division of Clinical Nutrition, we are researching on the relationship between metabolic syndrome such as diabetes, hyperlipidemia, or obesity that leads to metabolic syndrome, and nutrition and exercise, by molecular biology.

Acutely, an exercise bout increases glucose uptake in skeletal muscles by translocating intracellular GLUT4, the insulin-responsive glucose transporter, to plasma membrane. Exercise stimulated translocation of GLUT4 is considered to be mediated by activation of AMP kinase. Chronically, endurance exercise training decreases the incidence rate of diabetes mellitus. This might be due to increased GLUT4 and number of mitochondria in skeletal muscle, respectively. Development of diabetes caused by high fat diet can be prevented by overexpressing as twice of GLUT4 in muscle and adipose tissue so that new treatment for diabetes can be expected by increase in GLUT4. We are now investigating the mechanisms of exercise-mediated increase of GLUT4 and mitochondria. We found exercise responsive elements that control the expression of GLUT4, and are searching the transcription factors that bind to the elements. We also created transgenic mice over expressed PGC-1, co-factor that promote mitochondria biosynthesis, in skeletal muscle. As a result, mitochondrion increased in the muscle of the transgenic mouse, and changed to red muscle. We are now analyzing more.

Next, it is nutrition. High fat diet causes visceral obesity, and it also accumulates fats in the liver and muscle. High fat diet accumulates fats in each tissue and insulin resistance and hyperlipemia. However, the mechanism is still not clear. Now we created the transgenic mouse that over expressed UCPs, thermogenic proteins, in tissue specifically and analyzed. First, we found improvement of obesity caused by high fat diet or insulin resistance in the mouse that over expressed UCP2 in fat tissue specifically. But, there was no response in the mouse that over expressed UCP3 in the muscle tissue specifically. Then we found increasing of heat production of the fat tissue was effective in prevention of metabolic syndrome. Currently we create the

mice that over express UCP2 in the liver tissue specifically.

On the other hand, high consumption of fish has been advanced for low incidence of arteriosclerosis among Japanese people. Then we are identifying the suppressive mechanism of fat synthesis by consuming fish oil. Fish oil feeding activates PPAR, the transcription factor, promotes β -oxidation of fatty acid, decreases an amount of the transcription factor that controls expression of SREBP-1c, sterol regulatory element binding protein, decreases lipogenesis and blood lipid concentration. In the laboratory, we examined a mechanism of decrease in lipogenesis by consuming both high and low concentration of fish oil. As a result, it became clear that high fish oil diet leads to

Thoughts on Health and Nutrition Research

The Falling Birthrate ~What Can Nutrition Do? ~

Nobuyo Kasaoka-Tsuboyama
Division of Clinical Nutrition

I had a bad dream the other night.

A child plays all alone at the large park, talking to oneself with no expression.

I shuddered with horror at the thought of Japan's future that there are no brothers and sisters, even neighborhood kid.

Many people still remember of "1.29 shock", Japan's birth rate (total birth rate) was the lowest in the past. In fact, a number of Japanese children are getting smaller and smaller each year. It is assumed that total population will be decrease in 2 years of 2006. It is estimated that total population is going to be half after 100 years.

I'm not going to discuss about unprecedented problem of the falling birthrate now in here because it is out of place to do so. However, measures to the various problems that working women face fall far behind. Japan introduces 3 years of child-care leave. However, how many mothers can leave their job for 3 years? If they want to keep their job, most mothers will leave their baby in the day-care center, and come back to work. Actually, I am one of them. I took one and half month of child-care leave, and came back to work in 3 months when my child's neck was not stabilized yet. While it is unusual that a researcher take a child-care leave, I stayed with my child as much as I can since it was hard to leave after I actually delivered the baby. But I always felt guilty.

Because it is believed of a legend, called "3-year-old myth," in Japan that mothers stay close and have to raise their children until age of three. Scientific and theoretical ground of this myth is weak, but power of mental pressure to working women is enough. And many of early childhood educators say that parents should raise their children by their side for at least 1 year.

But recently, another research result reported from different point of view. Many people may remember that a study group of the Health and Welfare Ministry reported that whether children eat meals at home or not influences their growth while length of stay in the nursery doesn't. According to the Prof. Yasuume and others' survey of night nursery, "children who rarely have chance to eat meals with their family have 70 times more risk of underdeveloped interpersonal skills and 44 times more risk of underdeveloped

understanding than children who does have meals with their family. Of course, we shouldn't believe everything of this result. But even the concept of hospitalism which was often quoted to "3-year-old myth" - "infants who spent long time in the orphanage for children or infants, or pediatric hospitals, may develop psychosomatic disorder" that Spitz advocated reported that nurse can improve the disorder by caring with maternity. It leads to the result that meals with full of maternity is the most important factor to the way of raising the quality of child-care.

I am researching the function of nutrient on a genetic level and I must confess that I was surprised with this result. Meals may have immeasurable power that can not be explained with just nutrient. For example, isn't it possible that "atmosphere" or "with whom" of eating may make a difference in taking the same nutrient? Isn't eating of "tasty" or "fun" influence on regulation of nutrient on a genetic level? My work willingness fills up.

In addition, well utilization of meals as a communication tool, it may lead to realization of family ties, lower anxiety of child care, and halt of the declining birth rate. Since I at least tried to have dinner with my child in a relaxed mood, guilt toward child-care outside home reduced. This lower guilt may lead to the next birth. And I can't help expecting a possibility of meals.

From now on, we may add an option of a declining birth rate by approaching from nutrition.



Research Findings

Swimming Works Gene Everyday to Improve Physical Fitness

Izumi Tabata
Division of Health Promotion and Exercise

According to the recent survey, swimming always ranks in the top of the exercise that people want to do from now. This time, I'm going to explain a little further about a trick of gaining physical fitness by swimming and training that everyone want to do.

Swimming gradually builds up endurance. This means that exercise increases mitochondria in everyone's meat (indicates skeletal muscle. It doesn't mean fat.) Mitochondrion is a subcellular organelle which produces a lot of energy by utilizing oxygen taken up from lung. It doesn't produce lactic acid, substance of fatigue, and it is a fundamental building block for endurance.

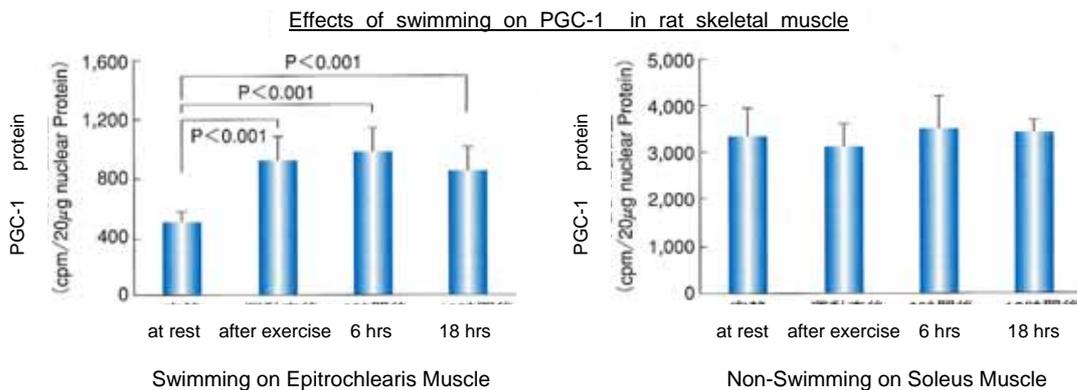
Increase in mitochondria by exercise was already reported 40 years ago. Although how the mitochondria increase by exercise, in other words, its' mechanism was not clear, recently it's getting reveal.

Mitochondrion is a soul of protein. To increase protein, it is necessary to work with the corresponding gene. Gene exists in DNA, mRNA is produced from DNA, and protein, which is an amino acid chain, is synthesized from RNA. Recently, we are focusing on PGC-1, gene

transcription coactivator. Transcription coactivator is needed when making mRNA from DNA (It is called transcription because DNA sequence (template) transfers precisely to mRNA sequence). It is like a printer cable that connects a printer which copies mRNA from DNA and gene, in other words, it is like a line that connects a computer which everyone use and printer (basic transcription factor). If this cable increases, it receives the information fast (like a broadband), produces lots of mRNA, and increases products of protein, mitochondria. We found on rats that this printer cable like substance increases only on muscle (epitrochlearis muscle) used by swimming (Figure).

Therefore, either building up endurance, or increase in mitochondria by exercise means that everyone's gene are activated by swimming. Although gene, DNA, and mRNA are not very familiar words, actually those are the words that are related to inside of everyone's body, especially the muscle taken place in swimming.

Currently, it is reported that brain gene can be worked by exercise and training. Let's swim, we want to do the most, everyone! Your muscle and brain gene can be activated.



* Contents: 2 sets of 3 hr.-swimming exercise with 45-min. rest in between

Research Findings

Nutritional Status of Pregnant and Lactating Women in Japan

Hidemi Takimoto
Center for Collaborative Research

Duration of the pregnancy and the lactation is the most important period of nutrition intake for women. All nutrition that fetus needs to develop is delivered from mother body via the placenta. And breast milk is the important nutrient supply source for unweaned infant. But nutritional status of women during pregnancy or lactation at national level is rarely reported in our country. So we utilized data of the National Nutrition Survey which represent Japanese, and examined epidemiologically about nutrient and food intake and hemoglobin (Hb) level during pregnancy or lactation in our country.

Object is 330 pregnant and 388 lactating women from data of the National Nutrition Survey in 1995-99, and non-pregnant and non-lactating women (controls) which match one-on-one to each group on age, survey year, region, and with or without blood test. Average age of pregnant group and lactating group were 29.2 and 32.1 respectively.

Proportion of smokers, drinkers, and drivers in a pregnant and a lactating group was significantly low, compared to each control group ($p < 0.01$). Compared with nutritional status between pregnant women and non-pregnant controls (Table 1), no significant differences were shown in energy intake. Lactating women were significantly low in energy intake compared to controls ($p < 0.01$). Each woman in both pregnant and lactating were significantly high in carbohydrates, calcium, and vitamin B2 intake compared to each control ($p < 0.05$), milk and daily

products intake were significantly high ($p < 0.05$), and alcohol intake were resulted low ($p < 0.01$). Average intake of iron from meals in pregnant women was as low as 11.0mg/day.

22.9% of pregnant women were anemia (if less than 11g/dl of Hb level was anemia). Proportion of anemia in lactating women and non-pregnant/non-lactating women (if less than 12g/dl of Hb level was anemia) were 11.1% and 15.7% respectively. Ratio of women, whose Hb level were less than 10g/dl, were 5.7% in pregnant, 2.0% in lactating, 1.7% in non-pregnant controls, and 3.3% in non-lactating controls. Comparing nutritional status between women who were anemia and non-anemia in each group, no differences were shown in iron intake.

It was revealed that pregnant and lactating women in Japan concerned about their lifestyle and meals by refraining from drinking and smoking, and taking more daily products compared to non-pregnant/non-lactating women. Contrary to our existing expectations, pregnant women didn't consume much energy compared to controls. In the National Nutritional Survey, pregnant women are classified either less than 19 weeks or more than 19 weeks pregnant. It's interesting to get these results despite 223 out of 330 objects at this time were more than 19 weeks pregnant, and about 2/3 passed morning sickness. In addition, while rate of anemia in pregnant are high, it was mostly mild anemia that was associated with physiological increase in blood circulation during pregnancy.

Table 1. Nutritional Status

	<i>Pregnant</i> N=330		<i>Non-Pregnant</i> N=330		<i>Lactating</i> N=388		<i>Non-Lactating</i> N=388	
	Average±SD.	Allowances [†]	Average±SD	Allowances [†]	Average±SD	Allowances [†]	Average±SD	Allowances [†]
Energy (kcal)	1869±498	2153	1813±536	1919	2072±558*	2589	1893±511	1917
Protein (g)	73.7±22.8	76.9	72.6±25.1	60.7	80.4±25.1**	80.3	73.8±23.4	60.8
Fat (g)	60.4±22.7		58.9±27.5		65.7±25.9*		61.2±23.9	
Carbohydrate (g)	254.7±73.5*		241.7±73.3		282.6±81.7**		253.8±71.7	
Calcium (mg)	597.7±296.8*	923.3	499.6±250.4	600	609.4±308.8*	1100	499.1±249.9	600
Fe (mg)	11.0±4.6	18.4	10.6±4.5	12	11.5±4.6**	20	10.3±3.9	12
Vitamin A (IU)	3442±6593*	1935	2431±2550	1800	3200±4443**	3200	2643±4297	1800
Vitamin B ₁ (mg)	1.20±0.47	0.90	1.08±0.50	0.80	1.20±0.50*	1.10	1.07±0.42	0.80
Vitamin B ₂ (mg)	1.42±0.6**	1.2	1.26±0.6	1.1	1.5±0.6**	1.5	1.3±0.6	1.1

** $p < 0.01$, * $p < 0.05$: Significant differences in a comparison with controls

[†] : Average allowances of objects in each group

Research Findings

Tumor-Suppressive Effect of Connexin 32 in Renal Cell Carcinoma from Maintenance Hemodialysis Patients

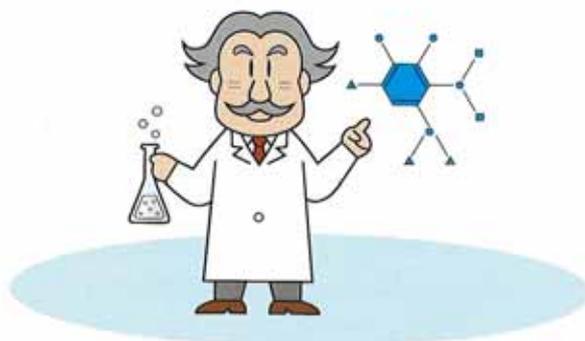
Tomohiro Yano
Laboratory of Nutrient Research for Labeling

Today in Japan, 200,000 patients are newly forced to be undergone kidney dialysis by increase in diabetic renal failure or others each year, and kidney transplantation which is the only treatment of renal failure has not been going well because of donor problems and so forth. As a result, patients of renal failure are forced to undergo kidney dialysis for long term. As a matter of fact, hemodialysis patients whose dialytic history is more than 10 years account for more than 20% of a whole. Recently, several complications associated with these hemodialysis patients become an issue. A particular problem of those is associating with acquired cystic disease of kidney as a result of hemodialysis, and associating with renal cell carcinoma by mixing in many cysts of all sizes. Recent survey reported that incidence rate of renal cell carcinoma on 88,534 hemodialysis patients in Japan was 41 times more than normal healthy subjects. Thus, it is thought to be important in both prevention and treatment for renal cell carcinoma by analyzing development processes of this renal cancer from maintenance hemodialysis patients, identifying tumor-suppressive gene that involves in preventing outbreak, and finding out its' mechanism.

Renal cell carcinoma from hemodialysis patients is most often associated with acquired cystic disease of kidney which is thought of as precancerous change in more than 3-4 years of hemodialysis. And longer a period of hemodialysis, more of cancerous catabolic cyst will be recognized. Thus, we suspected that

gene involved in suppression of this catabolic cyst outbreak, works as tumor-suppressive effect in renal cell carcinoma. We analyzed renal cancerous tissue of hemodialysis patients that surgically removed in detail by gaining cooperation of Tokyo Women's Medical University. As a result, connexin (Cx) 32 were identified as cancer inhibition gene specifically suppressive in early stages of cancer. In addition, we established and examined cancer cell line that developed expression vector in which implanting human Cx 32 into cancer cell line acquired from human renal cell carcinoma to verify tumor-suppressive effect of Cx 32 in renal cell carcinoma. As a result, Cx 32 was verified as tumor-suppressive gene in human renal cell carcinoma by significantly controlling cell growth, oncogenesis ability, and cellular infiltrate ability in vitro, and oncogenesis ability, angiogenesis ability, and examined all parameter related to oncogenesis ability in vivo.

This gene is known in forming gap junction (GJ), and less than 1200 molecular weight of hydrophilic molecule are exchanged among cells through this GJ as an important signal, and maintain a relative constancy of intracellular circumstances nearby. It is reported that Cx induces cytodifferentiation through this function, and works as tumor-suppressive gene. Therefore, from now, identifying an inhibition mechanism of Cx 32 manifestation in early stages of renal cell carcinoma from hemodialysis patients will reduce the risk of developing renal cell carcinoma.



Research Findings

Interactions between Health Foods and Medications ~ Does Overconsumption of Ginkgo Biloba Extract Lose Effectiveness of Medicines? ~

Keizo Umegaki
Laboratory of Nutrient Research for Labeling

While consumption of so-called health foods is increasing worldwide, safety issues or complaints are reported increasingly. Many of health foods consumers are on medication with worry about health, and influences on treatment or unexpected side effect may be expressed by taking both medicines and health foods. Since most of medicines are decomposed by drug-metabolizing enzyme mainly in liver, changes of drug-metabolizing enzyme directly influence on medical effect. Thus, we are examining effects of health foods materials on drug-metabolizing enzyme to predict interactions between health foods and medications. In the past animal testing, we verified that overconsumption of ginkgo biloba extract induced hepatic drug metabolizing enzymes, and increased its activity. As just described, taking medicines under circumstances where increasing activity of drug-metabolizing enzyme hastens metabolism (decomposition) of medicines, and loses effectiveness of medicines. So, long-term overconsumption of ginkgo biloba extract may be possibly discourage medical treatment.

Then, how should one do if one intake ginkgo biloba extract for long term? We tested

in an animal study whether enzyme activity recovers in a normal level after excessive ingestion of ginkgo biloba extract and increase in drug-metabolizing enzyme. When rats were fed excessive amount of ginkgo biloba extract, hepatic drug metabolizing enzymes increased four times of normal amount. Next, we stopped giving them ginkgo biloba extract, fed them normal food, and measured metabolizing active enzyme. Then, enzyme activity was immediately restored to a normal level, in other words, recovered as same as before ingestion of ginkgo biloba extract. This result indicated that stop taking ginkgo biloba extract when medical treatment was necessary would be able to avoid interactions between them.

While induction of drug-metabolizing enzyme for human has never been reported when taking recommended amount of ginkgo biloba extract, it may have a possibility of interactions with medicines if one intake it more than needed. If you take health food, you need to avoid taking more than you needed. While you are on medication, you may need to consult your doctor, not by solving all by yourself, and care about your medical condition.