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CONTENTS

PREFATORY NOTE

My Expectations for NIHN . . . Osamu Igarashi

CURRENT RESEARCH PROJECTS

Division of Health Promotion and Exercise at the Moment . . . Izumi Tabata

THOUGHTS ON HEALTH AND NUTRITION RESEARCH

Ideal Research Style . . . Shigeho Tanaka

RESEARCH FINDINGS

Combined Intervention of Exercise and Genistein Prevented Androgen
Deficiency-induced Bone Loss in Mice . . . Jean Wu

Antioxidation Defense Mechanism to Protect DHA and its Application
for the Development of New Functional Food Materials . . . Kazuhiko Kubo

Which Do You Prefer, Rice or bread? . . . Satoshi Sasaki

Development of Hypertension, Diabetes and Hypercholesterolemia
by Obesity or Weight Change . . . Kazuko Ishikawa-Takada

My Expectations for NIHN

Ibaraki Christian University

Osamu Igarashi

Recently, issues related to nutrition and health became hot topics for discussion among the people. It may be because Japan became a nation of aging society and everyone wishes to live longer and healthier. Japanese mean life expectancy for both men and women has prolonged to approximately eighty years however the healthy life expectancy is few years shorter. As often said, "Ichi-byou-soku-sai," someone who has a chronic illness may take care of their health more. Even the era of human genetic analysis, we can not predict every event of life, from birth to death, of an individual person. The individual's awareness makes great difference for the state of nutrition and health. Especially, it is needless to say that while a yellow signal (or even a red signal) flashing for the national health insurance system, health promotion of individuals for disease prevention is extremely important. "Nutrition" and "Food" are very important factors. Needless to say but the healthy eating habit is one of the great preventive methods. Even if you have inherited factors related to chronic diseases, if you take care of yourself and have control over your eating habit, you may postpone developing illness and to be on medication.

From the view point of nutrition and health, NIHN concentrate on researches including effects/efficacy of foods and nutrient contents, human energy metabolism and dietary energy allowance according to amount of physical activities, effects of exercises,

action mechanism of each nutrients, data management of the National Nutrition Survey, biochemical analysis for the prevention of lifestyle-related illness and so on. These researches may not attract



people's eyes so much compare to other fashionable spectacular scientific researches however to conduct basic researches on issues as such as "Nutrition and Health" are extremely important for the promotion of health of the nation. It is quite meaningful for the Japanese government, if people are able to maintain health by basic life styles improvement related to eating and exercising. It would help suppressing the problematic present medical expenditure in great deal. However, the difficulty of nutrition researches are that they take very long time and the outcomes are not clear compare to the pharmaceutical researches. So, they may not fit for the age that seeks quick solution. It is very important for people to maintain interest for the issues related to nutrition and health in our daily life. In this sense, I also would like to expect progress on educational activities of the NIHN. Not only the tasks in front of our eyes but with longer perspectives, nutrition education and various problems related to food are the mission imposed for the National Institute of Health and Nutrition. Lastly, I expect the further advancement of the researches by the institute and sharing of the new findings from these researches for the public.

Current Research Project Introduction

Division of Health Promotion and Exercise at the Moment

Division of Health Promotion and Exercise Improvement, Izumi Tabata

We are conducting research on improvement of "metabolic power" by physical exercises. "Metabolic power" is the translated term for "metabolic fitness" which is one of the Physical Fitness Index, regarding metabolism systems in our body (for example, energy metabolism and glucose metabolism). It is known that many lifestyle-related diseases are caused by short of exercises because of the fall of this "metabolism power."

For example, the fall of glucose metabolism becomes a diabetic trigger. Moreover, the shortage of exercises cause attrition of maximum aerobic power and endurance. We would use the word "power" because of the image in the language that doing much work within a limited time. For example, we consider it "high power" for carrying heavy things quicker. Similarly, we consider the metabolism power is higher if metabolizes (making or breaking) more substances in a short time.

For example, about 80% of sugar from meals will be absorbed into muscles, the speed of sugar metabolism can be seen as a part of the metabolism power. If the speed of sugar metabolism is slow, the blood sugar level will stay high for long time after meal, i.e., a diabetic

state.

A glucose transporter called GLUT4 in muscles determines the sugar transport activity in muscles. When there are many of these carriers, the sugar in blood is carried into muscles quicker and the blood sugar level will not rise high. It was reported by the European and American researchers that GLUT-4 will increase by exercises. On the other hand, we have found out that the GLUT-4 will decrease when inactiveness continues such as lay down on the bed all day long for 20 days. However, we also detected that the GLUT-4 would increase by once-a-day muscle training even in this inactive condition. It has been said that exercises of low intensity like walking is good for diabetic prevention, however, these results show that exercise of high intensity which appears in sporting activities may also increase GLUT-4.

If you are middle-aged person, let's keep in mind and try to involve in sporting activities now on. The pleasure felt when participating in sports can be the motive to continue exercises. Of course, if you are hypertensive, since intensive exercises may raise your blood pressure, we recommend you to consult with your doctor before starting it.



Thoughts on Health and Nutrition Researches

Ideal Research Style

Division of Human Nutrition, Shigeo Tanaka

Dr. Claude Bouchard is the Executive Director of the Pennington Biomedical Research Center in Louisiana, United States. He conducted a research on effects of 1,000 kcal/day overeating for 100 days in 12 sets of identical twins. He has been conducting researches based on strict experimental design about genetic and environmental factors on phenotypes, such as body composition, physical fitness, energy metabolism, and lipid metabolism. I had an opportunity to study with him for ten months from the middle of March, 2000. In this column, I want to introduce the HERITAGE Family Study which is one of Dr. Bouchard's representative researches. This is an over 20 weeks study on genetics and environmental factors which bring individual differences to the influence of the aerobic exercise.

Because of the difficulties related to conducting exercises continuously, the number of research participants of the previous researches on influence of exercises were limited to at most several dozen people. However, analyses of genetic polymorphisms require much more research subjects. Then, a total of 742 subjects were collected as a multicenter trial at four research institutions. To avoid intercenter measurement differences, careful quality assurance and quality control was carried out by holding training sessions for the persons in charge for the measurement from each research institute. Furthermore, four persons were

assigned as experimental subjects and visited the four research institutions and their data from each institution were compared and problems were sort out. This tour was carried out twice.

After such careful preparation over one year, under strict management, with special attention to decrease the number of dropouts, experimental exercise training for 20 weeks were performed during the 1st phase of the study (five years). Valuable data on many variables, such as body composition, physical fitness, and various metabolic markers, were obtained at that time. Then, research subjects were not increased but hundreds of millions of yen were added into the budget only for the analyses (present, in the 3rd phase). In the meantime, genomic analysis, etc., using the preserved blood samples, were added and analyses from various angles are on progress. By the beginning of this year, over ten years since the research has started, the number of papers from this research exceeded even 100.

In general, when we conduct researches, data are taken separately by many research groups holding problems in experimental plans including the number of subjects, or measurement items. If data are taken like the HERITAGE Family Study based on the strict experimental plan putting time and the labor in, what are obtained should be increased dramatically. Though it is not easy, I hope to model after this approach.



CURRENT RESEARCH FINDINGS

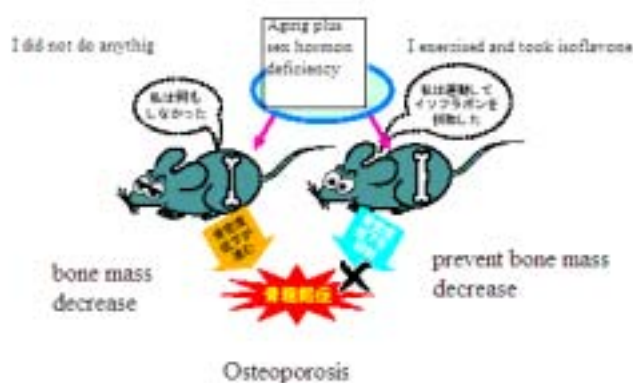
Combined Intervention of Exercise and Genistein Prevented Androgen Deficiency-induced Bone Loss in Mice

Division of Food Science, Jean Wu

There is evidence that estrogen plays an important role in skeletal tissue in males as well as females. We have reported that phytoestrogens, such as genistein, selectively act on bone and exhibit cooperative effects on bone mass when combined with exercise in ovariectomized mice. In this study, we examined whether both interventions exhibit cooperative effects on bone loss in androgen-deficient mice similar to those in estrogen-deficient mice. Male mice aged 7 wk were either sham operated or orchidectomized (ORX) and divided into six groups: 1) sham; 2) ORX; 3) ORX and treated with genistein (0.4 mg/day) subcutaneously; 4) ORX, exercised on a treadmill daily for 30 min/day at 12 m/min; 5) ORX, given genistein, and exercised (ORX+ExG); and 6) ORX and treated with 17beta-estradiol (E(2)). Four weeks after the intervention, seminal vesicle weight strikingly decreased in ORX mice, and it was not affected by administration of genistein or E(2).

Bone mineral density of whole femur was significantly reduced by ORX, and bone loss was prevented by the combined intervention. Histomorphometric analysis showed that bone volume and trabecular thickness in the distal femoral cancellous bone were significantly lower in the ORX group than in the Sham group, and they were completely restored in the ORX+ExG group, as in the ORX with E(2) group. These results indicate that the combined intervention of moderate exercise and a low dose of genistein administration shows an additive effect in preventing bone loss in ORX mice similar to that in ovariectomized mice.

Source: Jian Wu, Xin Xiang Wang, Hiroshige Chiba, Mitsuru Higuchi, Misao Takasaki, Atsutane Ohta and Yoshiko Ishimi. Combined Intervention of Exercise and Genistein Administration Prevented Androgen Deficiency-induced Bone Loss in Mice. *J Appl. Physiol.* 94:335-342; 2003



Antioxidation Defense Mechanism to Protect DHA and its Application for the Development of New Functional Food Materials

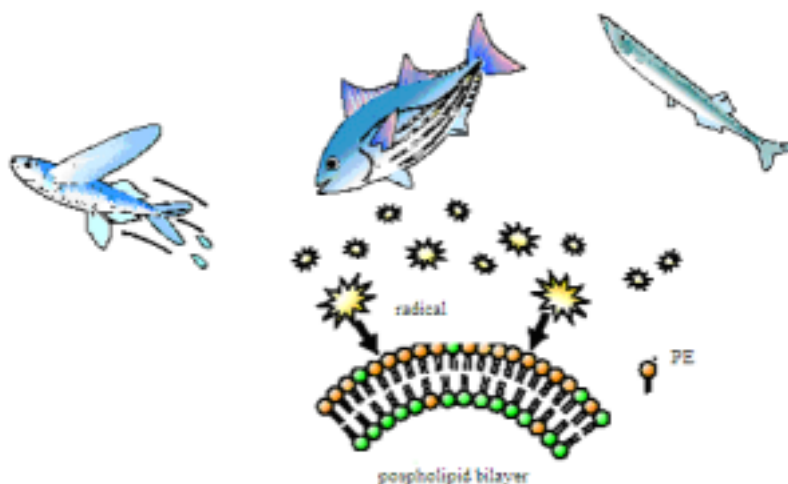
Division of Food Science, Kazuhiko Kubo

There must be quite many people who have heard the name of fatty acid called docosahexaenoic acid (DHA). DHA is one of the polyunsaturated fatty acids rich in fish oil. The consumer's attention to DHA increased rapidly in recent years and the consumption increased great deal in the form of so-called health food, general food, medical coadjuvants, dietary supplements, and also in formula milk. Today, it is almost certain that along with eicosapentaenoic acid (EPA), DHA is very effective in preventing cardiovascular diseases, one of the lifestyle-related illnesses. However, it is also a well-known fact that DHA is very easily oxidized because of its chemical structure. It tends to generate lipid peroxide and free radicals very easily, and this poses a problem in development of food products.

Recently, we discovered the anti-oxidative phospholipid membranous structure protecting DHA from oxidization. This finding is the result obtained from the research on the new anti-oxidation defense mechanism predicted to be working in our body. The distribution of DHA varies in our body and it is known that comparatively more DHA are in organs as such as the brain (hippocampus which relate to memory and learning ability), nervous system, the retina, in addition in heart muscle and in sperms, etc. Furthermore, the deviation of

DHA distribution is seen also on a molecule species level. It is typical that comparatively more DHA in aminophospholipid such as phosphatidylethanolamine (PE), one of the phospholipids composing the cell membrane. Since more PE exist in the internal layer of the membrane, we examined the oxidation stability of DHA using liposome which consists of a phospholipid bilayer, the model of a cell membrane. It turned out that DHA in the molecule became difficult to oxidize in the membrane that the polar group was directed toward the radical to come attacking. The accomplishment of this research, an oxidatively more stable material for DHA contained in functional foods, is under the patent application process being expected that this would paves the way for the possibilities for the development of DHA fortified supplement foods and medical coadjuvants for reduction of risk factors of lifestyle-related diseases, and possibility of keeping food containing DHA in normal temperature.

S o u r c e : Docosahexaenoic acid-containing phosphatidylethanolamine in the external layer of liposomes protects docosahexaenoic acid from 2,2'-azobis (2-aminopropane) dihydrochloride-mediated lipid peroxidation. Kubo K, Sekine S, Saito M. Arch Biochem Biophys 410, 141-148, 2003



Which Do You Prefer, Rice or Bread?

Project Leader of Scientific Evaluation of Dietary Reference Intake, Satoshi Sasaki

The nutritive value of rice (boiled rice) is reappraised recently. However, we are not eating rice nor bread only. When eating rice, we choose dishes to match with rice and when eating bread, we choose dishes that match with bread, unconsciously. We take nutrition from whole meals.

So, I decided to investigate the nutrient value taken in not from one particular food but from all the foods eaten every day by dividing people into Rice Group and Bread Group.

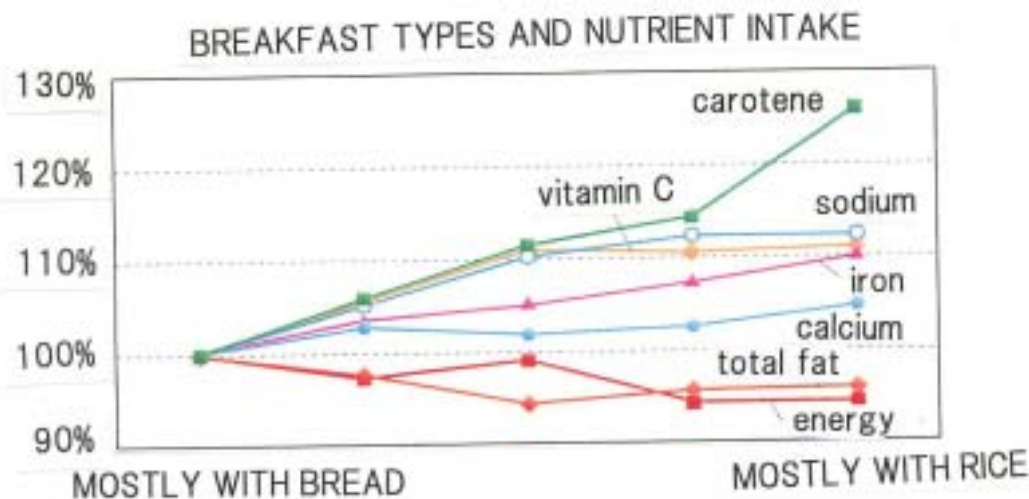
1771 female college students from 18 to 20 years old participated in this study. We asked what they have eaten in the past one month in detail, and the participants were classified into the Rice Group and the Bread Group paying attention to what they eat as staple food for breakfast. There were very few participants who ate noodles as staple food for breakfast. So, we calculated the difference between the "frequency of eating rice (times/week)" and the frequency of eating bread (times/week)" and the participants were divided into eight groups from Complete Bread Group (who had bread every morning) to Complete Rice Group (who had rice every morning).

The figure below is comparison of nutrient intake among eight groups. As frequency of eating rice increases, intake of nutrients such as n-3 polyunsaturated fatty acids, iron, sodium, protein, carotene, potassium, dietary fiber, and vitamin C

increases correspondingly. On the contrary, as the frequency of eating rice increases, intake of lipid, especially intake of saturated fatty acid among various lipids decreases. Except sodium (salt), nutrients taken more by Rice Group are considered as good nutrients for lifestyle-related illness prevention. On the other hand, excess intake of saturated fatty acid is concerned as one of the risk factors of hyperlipidemia. Even though, Rice Group people were not perfect. The sodium (salt) intake of Rice Group is a big problem because the amount of Japanese salt intake is extremely high compared with other developed countries and the necessity of salt reduction has been stressed over and over. This result showed that, in general, even though there are issue of high sodium intake, the people who prefer rice are taking more nutrients that are good for preventing lifestyle-related illnesses compare to the people who prefer bread.

This result is not indicating that you should be just eating rice, nor saying that bread is bad food. Rather, you should consider well what you eat with rice and what you eat asides with bread, and enjoy your daily meals.

Source: Sasaki S and Shimoda T, Katagiri A, and et al. Eating frequency of rice vs.bread at breakfast and nutrient and food-group intake among Japanese female college students. J Community Nutr 2002; 4: 83-9



Development of Hypertension, Diabetes and Hypercholesterolemia by Obesity or Weight Change

Division of Health Promotion and Exercise, Kazuko Ishikawa-Takada

Obesity and weight gain are known as risk factors of various lifestyle-related diseases. In this study, we examined the degree of risk increase of these diseases among people who are obese and/or experienced some weight gain.

The subjects were selected from employees of an industrial company that has 12 factories and 36 branches in various areas in Japan. The study subjects were 4,737 people among all male employees (7,560 people) who had no history of heart diseases, cancer or cerebrovascular diseases. Day-night shift workers were excluded. They must have all the measurement data obtained at the starting of the research. We followed up these candidates for a maximum of four years (or up to their retirement), and checked the frequency of developing hypertension, diabetes, and hypercholesterolemia.

For hypertension, 4,001 subjects who were not hypertensive at the beginning of the research, for diabetes, 4,385 subjects who were not diabetic at the beginning of the research, and for hypercholesterolemia, 2,995 subjects who were not hypercholesterolemic at the beginning of the research were examined. The subjects who newly developed the symptoms in four years were, for hypertension, 662 (46.7/1,000 person-year), for diabetes, 242 (14.7/1,000 person-year) and for hypercholesterolemia, 251 (22.6/1,000 person-year).

We have compared the frequency of developing these diseases in four years according to the participants' baseline BMI (value which divide weight by the square of height) score. As for the risk of hypertension, it doubled among the subjects with more than 22 kg/m² BMI score compare to the subjects with less than 18.5 kg/m² BMI score even adjusted for possible confounding factors such as age, smoking status, alcohol intake, family history and baseline value of systolic blood pressure. For the people with over 27 kg/m² BMI score, the risk of developing hypertension is almost 3 times higher. For the risks of developing diabetes and hypercholesterolemia among the people with over 29 kg/m² BMI score are even 4 to 5 times

higher.

The prevalence of hypertension, diabetes and hypercholesterolemia were compared among the groups of subjects: 1) lost weight more than 2kg in four years, 2) weight change in four years was within the range of 2kg and 3) gained weight more than 2 kg in four years. The risk of becoming hypertension was about 1.2 times more and the risk of developing hypercholesterolemia were about twice for those who had gain weight more than 2 kg compare to those whose weight change was within 2kg range. This value was consistent adjusting for possible confounding factors such as age, baseline BMI, smoking status, alcohol intake, family history, and baseline laboratory data (one of the three data: blood pressure, blood sugar, or the total cholesterol).

Compare this result with previous studies in Caucasian population; the Japanese people have higher risks of developing symptoms with rather low BMI scores. Although, the prevalence of severe obesity among Japanese is rather low, the risk increase by the weight gain is the same or is even a little higher among Japanese. As the study shows that the risks of developing symptoms increase as the BMI score increase and/or weight gain, management of the body weight is very important in preventing these diseases.

Source : Obesity, weight change and risks for hypertension, diabetes and hypercholesterolemia in Japanese men. Ishikawa-Takata K, Ohta T, Moritaki K, Gotou T, Inoue S: European Journal of Clinical Nutrition: 56: 601-607. 2002

