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ABSTRACT

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Changes in Neutrophil Immune Functions under Different Exercise Stresses

Nippon Eiseigaku Zasshi, 66, 533–542 (2011)
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The aim of this review is to provide a summary of the known effects of exercise on neutrophil immune functions of athletes. We measured three neutrophil immune functions (i.e., phagocytic activity (PA), reactive oxygen species (ROS) production, and serum opsonic activity (SOA)) in various types of exercise.

The following is our recent findings.

(1) A regular exercise increases ROS production and decreases PA. We call this change a normal pattern, and an abnormal pattern except this change.

(2) A prolonged, strenuous activity (e.g., rugby match and marathon) decreases both ROS production and PA. This is one of the abnormal patterns.

(3) The exercise loading performed after camp training decreases ROS production whereas PA does not change. This is another abnormal pattern.

(4) When judoists who had stopped judo training for 6 months restarted their training, the exercise loading at the beginning of their training decreases PA whereas ROS production does not change. This is another abnormal pattern.

(5) A regular exercise 2 months after the beginning of their training increases ROS production and decreases PA. This change is a normal pattern.

SOA showed a similar pattern of changes to ROS under all conditions.

The changes in neutrophil immune functions after performing various exercises might result from the balance between external factors (intensity and style of exercise) and internal factors (e.g., fatigue and physical pain). Therefore, the changes in three neutrophil immune functions after exercise might be an index of athletes' condition.

Archives of "Comprehensive Approach on Asbestos-Related Diseases" Supported by the "Special Coordination funds for Promoting Science and Technology (H18-1-3-3-1)" —Overview of Group Research Project, Case and Specimen Registration, Cellular Characteristics of Mesothelioma and Immunological Effects of Asbestos—

Nippon Eiseigaku Zasshi, 66, 543–552 (2011)
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The research project entitled "Comprehensive approach on asbestos-related diseases" supported by the "Special Coordination Funds for Promoting Science and Technology (H18-1-3-3-1)" began in 2006 and was completed at the end of the Japanese fiscal year of 2010. This project included four parts: (1) malignant mesothelioma (MM) cases and specimen registration, (2) development of procedures for the early diagnosis of MM, (3) commencement of clinical investigations including multimodal approaches, and (4) basic research comprising three components: (1) cellular and molecular characterization of mesothelioma cells, (2) immunological effects of asbestos, and (3)

elucidation of asbestos-induced carcinogenesis using animal models. In this special issue of the Japanese Journal of Hygiene, we briefly introduce the achievements of our project. The second and third parts and the third component of the fourth part are described in other manuscripts written by Professors Fukuoka, Hasegawa, and Toyokuni. In this manuscript, we introduce a brief summary of the first part "MM cases and specimen registration", the first component of the fourth part "Cellular and molecular characterization of mesothelioma cells" and the second component of the fourth part "Immunological effects of asbestos". In addition, a previous special issue presented by the Study Group of Fibrous and Particulate Substances (SGFPS) (chaired by Professor Otsuki, Kawasaki Medical School, Japan) for the Japanese Society of Hygiene and published in Environmental Health and Preventive Medicine Volume 13, 2008, included reviews of the aforementioned first component of the fourth part of the project. Taken together, our project led medical investigations regarding asbestos and MM progress and contributed towards the care and examination of patients with asbestos-related diseases during these 5 years. Further investigations are required to facilitate the development of preventive measures and the cure of asbestos-related diseases, particularly in Japan, where asbestos-related diseases are predicted to increase in the next 10–20 years.

Exploratory Study on the Detection of Markers for Diagnosing Early Stage Malignant Mesothelioma

Nippon Eiseigaku Zasshi, 66, 553–557 (2011)
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Malignant mesothelioma (MM) is a highly aggressive, incurable neoplasm associated with asbestos exposure. Early detection of MM is not easy and radiological surveillance is imperfect. The use of blood-based biomarkers might solve this difficulty and allow detection of MM at an early stage when combined treatment involving surgery, chemotherapy and radiotherapy might be effective. In the research project entitled "Comprehensive approach on asbestos-related diseases" supported by the "Special Coordination Funds for Promoting Science and Technology (H18-1-3-3-1)", we conducted an exploratory study on the detection of markers for diagnosing early stage MM. In this study, we have shown that serum soluble mesothelin-related peptide (SMRP) is a highly specific and moderately sensitive biomarker for diagnosing MM. SMRP levels in pleural effusion were elevated not only in advanced-stage malignant pleural mesothelioma (MPM), but also in early stage disease. SMRP in pleural effusion can be an MPM-specific biomarker with greater sensitivity than in serum, especially for the early stage of the disease. Circulating tumor cells (CTCs) and circulating endothelial cells (CECs) were considered to be useful surrogate markers of disease progression in MPM, although the lack of sensitivity for early stage disease remains to be improved. Cytological analysis with gene expression profiling has been more effective in detecting early-stage MPM with pleural effusion.

In conclusion, blood or effusion-based biomarkers, possibly in combination with other new modalities, such as a thoracoscopy combined with the advanced imaging systems consisting of autofluorescence imaging (AFI) and narrow band imaging (NBI), will show some promise for curing MPM if the disease is detected at an early stage.

Current Status and Future Direction of Japan's Clinical Trial for Malignant Pleural Mesothelioma

Nippon Eiseigaku Zasshi, 66, 558–561 (2011)
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The feasibility and efficacy of trimodality therapy for malignant pleural mesothelioma (MPM) are still controversial mainly due to the lack of clinical evidence. Although three major clinical trials on this therapy have been recently reported from North America and Europe, it remains unclear whether results in Caucasian populations may be directly applicable to Asian populations. In this context, as a project of the "Comprehensive approach on asbestos-related diseases" supported by the "Special Coordination Fund for Promoting Science and Technology of MEXT, Japan", a prospective multi-institutional study has been planned to evaluate the feasibility of induction chemotherapy using pemetrexed plus cisplatin, followed by extrapleural pneumonectomy (EPP) and postoperative hemithoracic radiation in patients with resectable MPM. Primary endpoints are macroscopic complete resection rate by EPP and treatment-related mortality for trimodality therapy. The study was initiated in May 2008 and patient enrollment was finished in November 2010.

Mechanisms of Asbestos-Induced Carcinogenesis

Nippon Eiseigaku Zasshi, 66, 562–567 (2011)
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Several types of fibrous stone called asbestos have been an unexpected cause of human cancer in the history. This form of mineral is considered precious in that they are heat-, friction-, and acid-resistant, are obtained easily from mines, and can be modified to any form with many industrial merits. However, it became evident that the inspiration of asbestos causes a rare cancer called malignant mesothelioma. Because of the long incubation period, the peak year for malignant mesothelioma is expected to be 2025 in Japan. Thus, it is necessary to elucidate the mechanisms of asbestos-induced mesothelial carcinogenesis. In this review, we summarize the cutting edge results of our 5-year project funded by a MEXT grant, in which local iron deposition and the characteristics of mesothelial cells are the key issues.

Approach to Elucidating the Influences and Factors Affecting Circulation System in Humans in Space Environment

Nippon Eiseigaku Zasshi, 66, 568–572 (2011)
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Many physiological changes associated with spaceflight, including decreases in orthostatic tolerance, exercise capacity and blood volume have been reported. Orthostatic intolerance is a problem affecting many astronauts immediately postspaceflight. In particular, the relationship between orthostatic intolerance and cerebral autoregulation has been the focus of study in our research group. Although impairment of cerebral autoregulation was speculated to be one of the factors resulting in reduced post flight orthostatic tolerance, a 2-week spaceflight study revealed that human cerebral autoregulation is preserved or even improved during and immediately after spaceflight in nonsymptomatic astronauts. To investigate the influences of the different kinds of reduction in central blood volume, we performed two ground-based studies. It is suggested that the mild intravascular dehydration partly explains the improved dynamic cerebral autoregulation observed during and immediately after a short-term spaceflight. Moreover, we also studied the relationship between orthostatic intolerance and cerebral autoregulation under hyperthermic conditions, because hyperthermia leads to orthostatic intolerance. Furthermore, we planned to conduct a study at the International Space Station (ISS) and ground-based studies to elucidate the influences and factors affecting the circulation system in humans in a space environment.

Effect of Lifestyle and Health Behavior on Neutrophil Function —Assessed by Nitroblue Tetrazolium Reduction Method Using Neutrophils in Elderly in Tianjin, China—

Nippon Eiseigaku Zasshi, 66, 573–581 (2011)
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Objective: In this study, we investigated the relationships of neutrophil functions with lifestyle factors (namely, subjective stress, exercise habits, smoking habits, alcohol-drinking habits, and self-perceived status health) and health behavior in the Chinese urban elderly.
Methods: We performed a health survey of the elderly aged 65 years or older living in Tianjin. The subjects were 42 males (69.1 ± 4.1 years old) and 41 females (69.1 ± 4.1 years old). Investigations of subjective stress, exercise habits, smoking habits, alcohol-drinking habits, and self-perceived health status were performed. The phagocytosis and superoxide productivity of neutrophils were measured by the nitroblue tetrazolium (NBT) reduction method. In addition, leukocyte count and serum total protein (TP) level were examined.
Results: The investigations revealed the associations of health behavior ($p < 0.05$) and self-perceived health ($p < 0.10$) with the balance between phagocytosis and subsequent superoxide production.
Conclusions: The present study revealed that there were correlations of neutrophil functions with lifestyle factors (subjective stress, exercise habits, smoking habits, alcohol-drinking habits, and self-perceived status health) and health behavior in the Chinese urban elderly.

Age-, Period-, and Birth-Cohort-Specific Effects on the Male Proportion in Japanese Newborns and Projections for Male Proportion for 20 Periods (2008–2027)

Nippon Eiseigaku Zasshi, 66, 582–588 (2011)
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Objectives: To determine the age-, period-, and cohort-specific effects on the male proportion in Japanese newborns, we performed an age-period-cohort (APC) analysis in this study. In addition, projections for the male proportion were analyzed.
Methods: We obtained data on live births of newborns for Japanese women in 1947–2007 from the National Vital Statistics. Cohort tables containing data on the male proportion were analyzed using a Bayesian APC model. Projections of the male proportion (2008–2027) were calculated.
Results: The age effect decreased when the mothers were 40–44 years old; however, the effect was relatively limited as compared with the period and cohort effects. The period effect increased from 1947 to 1969 and decreased thereafter. Analysis of the cohort effect on male proportion trends revealed a decreasing slope for birth cohorts born between 1905 and 1945 and a subsequent increase after 1958. The projections for male proportion indicated that the male proportion in 2027 would be similar to that in the 1970s.
Conclusions: The age of the mother hardly affected the male proportion. The period effect started decreasing from the latter half of the 1960s. This may be attributable to the high economic growth since 1965 that promoted industrial development that led to environmental pollution, which in turn may have lead to the deterioration of the intrauterine environment. Cohort effects changed from 1958 and exhibited trends toward increase in male proportion; this may be due to improvements in obstetric care. Our results suggest that the male proportion in Japanese newborns will increase in the future.

Variations of Indoor Environment and the Prevalence of Sick House Syndrome over Three-Year Period in Detached Houses in Sapporo

Nippon Eiseigaku Zasshi, 66, 589–599 (2011)
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Objectives: The purpose of this study was to investigate annual variations in indoor environmental chemical, fungal and dust mite

allergen levels, with regards to variations in sick house syndrome (SHS) symptoms over a three-year period.
Methods: Detached houses were randomly selected from a building plan approval application, and a questionnaire survey was conducted in 2003 in Sapporo, Japan. Indoor environmental measurements and a self-administered questionnaires survey were conducted on the selected houses in 2004, 2005 and 2006. The same protocol was used for the 3-year period to measure the levels of chemicals, fungi and dust mite allergens. A personal questionnaire to assess SHS was distributed to all inhabitants of the dwellings along with one questionnaire to assess housing characteristics.
Results: In 2004, 2005 and 2006, the owners of 104, 64 and 41 houses, respectively, agreed to participate in this study. Forty-one houses and the 127 inhabitants who participated in this 3-year survey period were included in the analysis to evaluate the associations between differences in environmental measurements and SHS. The levels of formaldehyde, acetone, toluene, *Alternaria* and *Cladosporium* tended to decrease, whereas those of limonene and *Aspergillus* tended to increase over the 3-year period. Increasing levels of *Cryptococcus* and the dampness index in individual houses correlated with increasing SHS symptom scores in the inhabitants after mutual adjustment.
Conclusions: Although the average levels of chemicals and fungi were relatively low, the results show the relationship between annual variations in indoor environmental measurements and variations in SHS symptom scores.

Fifteen Trace Elements in Eluate from Enameled Cookware Using Inductively Coupled Plasma-Mass Spectrometry

Nippon Eiseigaku Zasshi, 66, 600–607 (2011)
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Objective: The purpose of this research is to clarify the effects of the following treatments on the elution of trace elements: water settling, 2 h boiling of water, acetic acid settling, and 2 h boiling of acetic acid in prebrushed enameled cookware, and the same four treatments after brushing the surface of enameled cookware.
Method: The eluate samples from enameled cookware subjected to the above eight treatments ware obtained, and the concentrations of the 15 trace elements (B, Al, Cr, Mn, Fe, Ni, Cu, Zn, As, Se, Mo, Cd, Sb, Pb, and U) were simultaneously analyzed by inductively coupled plasma-mass spectrometry (ICP-MS).
Results: The concentrations of the 15 elements eluted from enameled cookware were low or very low after the treatments. Enameled cookware is made from iron covered with glass containing pigments. The concentrations of Al, Ni, and Sb were significantly higher ($p < 0.01$) in almost all treatments. The concentrations of Fe, which is the base element of enameled cookware, showed almost no change. The safety level for enameled cookware is standardized at 70 ng/mL Cd and 400 ng/mL Pb. The Cd and Pb concentrations in all treatment samples were below these standard levels.
Conclusion: The results of our study and other studies conducted so far suggest that the risk of acute or chronic toxicity associated with the use of enameled cookware under normal circumstances is extremely low and negligible.

An Occupational Physician-Pharmacist Cooperative Management for Hypertension by the Use of Educational Letters and Posters

Nippon Eiseigaku Zasshi, 66, 608–615 (2011)
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Objectives: To provide an occupational physician–pharmacist cooperative management for hypertension, we aimed to improve blood pressure (BP) control for workers with high-normal BP or hypertension.
Method: Health checkups were performed from May 2005 to May 2008 for male professional grooms and exercise riders aged 20–69 years working at Miho Training Center, the largest racing-horse training facility in Japan. An occupational physician-pharmacist cooperative hypertension management was performed from Jan 2007 to Mar 2008, including the use of posters at the work site and letters to employers and the subjects who were diagnosed as having high-normal BP (office systolic/diastolic BPs 130–139 and/or 85–89 mmHg) or hypertension ($\geq$140 and/or 90 mmHg) twice during 2005–2006 examinations. The observational study examined BP measurements before and after the hypertension management.
Results: We analyzed 232 participants in the 2008 Nov examination with had high-normal BP or hypertension in both of 2005 and 2006 Nov examinations. Office systolic and diastolic BP decreased after the hypertension management by the use of educational letters and posters (-3.1 mmHg; $p < 0.001$, -1.5 mmHg; $p = 0.02$). The prevalence of workers with high-normal BP and hypertension also decreased after those activities (-15 and -7%; $p < 0.001$). The subjects who started or continued the antihypertensive medication were more likely to show reductions in office BP and body mass index than those who received no treatment.
Conclusions: An occupational physician-pharmacist cooperated hypertension management by the use of educational letters and posters may improve BP control for subjects with high-normal BP or hypertension.