

## Immunotoxicity of Beryllium

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**Abstract** The lymphocyte transformation test and the macrophage migration inhibition test are quantitative methods invaluable for examination of beryllium (hereafter referred to as Be) effects on cell-mediated immunity. We recognized that the Be sensitizing ability was related to active as well as passive cell-mediated immunity in mice subcutaneously injected with Be once a week over a 6-week period.

Be also affects B cells, and it increases the amount of immunoglobulins in sera. In the study of immunological health surveys of Be workers in a copper-beryllium casting factory, the serum complement titer tended to be lower in Be workers than in the controls. In mice, injected with Be once a week over a 12-week period, serum complement titers decreased.

Correlation coefficients of the experimental parameters showed a significant negative correlation between the complement titers and the prothrombin time or the coagulation time for factor VII, using mice injected with 5  $\mu$ g of Be. It was suggested that increases in the complement titers after Be administration may be induced by temporarily-activated plasma serin protease, which is a component of blood coagulation factor VII.

The  $\delta$ -aminolevulinic acid dehydratase and porphobilinogen deaminase activities were significantly elevated in the pregnant untreated group, compared with the nonpregnant mice (the control group). However, it was noted that these values in the pregnant mice injected with 50  $\mu$ g of Be were almost the same as the values of the controls. It suggests that Be suppressed the expected pregnancy-induced increase in hematopoietic function.

There are at least two risk factors induced in the effects of beryllium on organisms-exposure to the metal and inheritance of the genetic marker. It is necessary to reduce exposure, to give preventive education and to carry out periodic health examinations for the prevention of disease induced by Be.

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## HgCl<sub>2</sub>-induced Acute Renal Failure and its Pathophysiology

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**Abstract** Mercury chloride (HgCl<sub>2</sub>) has a potent nephrotoxic effect. Most of Hg<sup>2+</sup> existing in plasma following HgCl<sub>2</sub> exposure forms a complex with sulfhydryl-containing ligands such as albumin and glutathione (GSH). The Hg<sup>2+</sup>-GSH complex is filtered in the glomeruli of the kidney and degraded into Hg<sup>2+</sup>-cysteine in the proximal tubules by the combined action of  $\gamma$ -glutamyl transpeptidase and dipeptidase present in the epithelial cells. The degradation product is then incorporated and accumulated into the proximal tubule epithelial cells. The accumulated Hg<sup>2+</sup> in the epithelial cells finally causes acute tubular necrosis (ATN) by its cytotoxic effect. At present, it is believed that tubular obstruction resulting from ATN triggers the onset of HgCl<sub>2</sub>-induced acute renal failure (ARF).

A progressive fall in glomerular filtration rate (GFR) contributes to the progression of HgCl<sub>2</sub>-induced ARF. The fall in GFR may be caused by an increment in afferent arteriole resistance (RA) and a decrement in the ultrafiltration coefficient (Kf) due to mesangial cell contraction. These changes in RA and Kf may be attributed to the increased action of the vasoconstrictors, angiotensin II and endothelin-1 and to the decreased action of the vasodilator, nitric oxide observed at the glomerulus level of HgCl<sub>2</sub>-induced ARF. Accordingly, the imbalance between these vasoactive substances appears to play an important role in the progression of HgCl<sub>2</sub>-induced ARF due to reducing GFR. Further studies, however, remain to elucidate the mechanisms involved.

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# An Evaluation of the Biting Force, the Body Composition and the Amount of Masticatory Action in Young Females

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**Abstract** The purposes of this study were to investigate factors related to maximum biting force and to understand the characteristics of physical properties of daily ingested foods in young females. One hundred and forty subjects aged 18-23, with Angle 1 class occlusion, had not suffered from periodontitis, and had not been treated for preparation of tooth crown of first molars. Body height and weight were measured, and percentage of body fat, fat mass (FM) and lean body mass (LBM) were estimated, using the impedance analyzer. The maximum biting force was measured by the press sensation method. According to the formula on the basis of our new version of Yanagisawa's food classification, the mean value of the amount of masticatory action for one day was calculated. Subjects were divided into the normal biting force and the low biting force groups with -1SD of the maximum biting force, in order to compare body composition and backgrounds in sports activities between these two groups. Multiple linear regression analysis was carried out, employing maximum biting force (kg · f) as a dependent variable, and having a background in sports activities, FM, LBM, the number of missing teeth, the number of dental caries and the amount of masticatory action for one day as independent variables. Results were as in the following: 1) The proportion of subjects who had a background in sports activities in the low biting force group were less than that in the normal biting force group ( $p < 0.01$ ). 2) Having a background in sports activities and LBM were positively correlated to maximum biting force ( $p < 0.01$ ), while the amount of masticatory action for one day was not. 3) All subjects, especially those in the low biting force group seldom had food requiring the highest amount of masticatory action. Conclusion: Having a background in sports activities and LBM are positively correlated with the maximum biting force, while the amount of masticatory action for one day was not correlated positively nor negatively in young females.

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## Characteristics of Medical Institutions Visited by Patients with Intractable Diseases — Analyses of Patients Receiving Financial Aid for Treatment —

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**Abstract** The Research Committee of Epidemiology of Intractable Diseases (Ministry of Health and Welfare, Japan) conducted a nationwide survey of 34 intractable diseases. Each of 47 prefectural governments reported information on all patients with the diseases who received financial aid for the disease from April 1992 to March 1993. Information collected on each patient included the identification number, sex, age, the code of the municipality where the patient lived, and the medical institution and department where the patient was being treated. Out of 247, 726 patients whose information was reported by prefectural governments, we analysed data of 208, 945 patients whose medical institutions were reported.

The results can be summarized as follows:

- 1) Aged patients and children who were less than ten years old tended to visit medical institutions located in their neighborhoods and be treated in small hospitals or clinics.
- 2) The proportion of patients who visited hospitals with 200 beds or more was 77 percent.
- 3) Patients with the diseases resulting in physical disabilities such as SMON and malignant rheumatoid arthritis tended to visit clinics. Patients with skin diseases as pemphigus, epidermolysis bullosa and pustular psoriasis tended to be treated in university hospitals.

4) Many patients living in prefectures near large cities such as Tokyo and Ishikawa visited medical institutions in the large cities.

5) The proportion of patients who visited university hospitals decreased during the eight years from 1984 to 1992. However, a quarter of these patients visited university hospitals.

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## A Study on the Effects of Physical Load Placed on High School Baseball Managers during Midsummer Games.

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**Abstract** We examined the influence of physical load placed on high school baseball managers during midsummer games under extremely hot and humid conditions.

The factors used to determine physical load were the following: body weight, oral temperature, amount of walking, pedometer count, heart rate, and serum biochemical elements. These factors were measured before and after the games. Twenty-two managers participated in this study. All games were played under high temperatures of  $32.4 \pm 3.5$  (mean  $\pm$  S.D) degrees Celsius dry-bulb,  $27.1 \pm 3.0$  degrees Celsius wet-bulb,  $33.8 \pm 3.6$  degrees Celsius black-glove,  $29.1 \pm 3.3$  degrees WBGT, which are likely to cause heart-related illness.

The results were as follows.

1. After the games, significant body weight loss and oral temperature rise were found. Those findings were thought to be caused by the rise in oral temperature in a hot environment which was accompanied by hyperhidrosis.

2. The average hemoconcentration ratio based on the changes in total protein during the games was 105 percent, suggesting that hemoconcentration and dehydration were caused by sweating in a hot environment.

3. A significant increase in total protein, albumin, LDH, high density lipoprotein cholesterol, calcium, hemoglobin, and a decrease in triglyceride were observed after the games, which were thought to be influenced by sweating and by increased metabolism in a hot environment.

4. The values of triglyceride, Fe, uric nitrogen, calcium and hemoglobin after the games which were adjusted by the hemoconcentration ratio were significantly lower than those before the games.

5. A prolonged game time caused a significant increase in total protein value during the games and a decrease in hemoglobin between the level before the games and the adjusted level after the games compared with those values in the short game time group.

From the above, even though high school baseball managers join in practices in a hot environment and become accustomed to it, we found that they had a great physical load on their bodies during the games in midsummer.

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# Changes of Physiological Functions in Rats Induced by Immobilization Stress

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**Abstract** A study was conducted on the changes of physiological function in rats due to immobilization stress. Male Fischer rats (SPF) of 32 weeks of age were housed in individual cages for 4 weeks. Then all rats were immobilized by stainless wire mesh for 6 hours daily for 3 days. Blood was collected before the 1st stress, immediately after the 1st stress, immediately after the 3rd stress and the day after the 3rd stress.

The results of this experiment were as follows: (1) The total leukocyte counts in the blood of the rats after the 1st trial was significantly higher than that before the 1st trial. (2) The percentage of lymphocytes in the blood after the 1st trial was significantly lower than that before the 1st trial, whereas that of neutrophils was significantly higher. (3) Correlations between phagocytic activity and superoxide production of neutrophils by histochemical NBT reduction assay showed significantly a positive correlation before the 1st trial. However, no significant correlations were observed in immediately after the 1st trial and the 3rd trial. The day after the 3rd trial, a positive correlation was observed again. These correlations showed that an unsuitable state of the neutrophil function was induced by the immobilization stress. (4) Serum biochemical profiles were affected by the immobilization stress. Also, GOT, GPT, LDH, CK and UA were increased after the 1st trial, whereas, TG, TP, ALB and ALP were decreased after the 1st trial. T-CHO was increased only immediately after the 3rd stress.

These results suggest that immobilization stress affected blood cells and serum components, and then the host defense and physiological functions were damaged respectively.

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# Estimation of the Future Numbers of Patients with Diabetes Mellitus in Japan Based on the Results of National Patient Surveys

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**Abstract** The projected numbers of patients with diabetes mellitus (ICD 9th; 250) 15 years from now were estimated. First, the numbers of patients with the disease in 1984, 1987, 1990, and 1993 were calculated by age and sex using data from the National Patient Surveys conducted by the Ministry of Health and Welfare. Then, population prevalence for calendar years 1996, 1999, 2002, 2005, and 2008 were estimated based on the past data using linear regression models. Finally, the total numbers of patients were calculated from the estimated prevalence multiplied by the estimated population figure of the national government. The prevalence and the numbers of patients are estimated to increase, and the numbers will be 1.7 million among males and 1.5 million among females in 2008. Besides, because of the increases of both the aged population and the disease prevalence, the proportion of patients aged 65 years or over will become as large as 40% of total male patients and 60% of females.

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# Mercury Sensitization Induced by Environmental Exposure

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**Abstract** We investigated mercury sensitization in relation to urinary and hair mercury concentrations. Patch tests were performed on 215 medical students and these tests demonstrated that 28 students were mercury-sensitized (13.0%). Life-styles were studied by questionnaire in 26 of the mercury sensitized students and 46 of the non-sensitized subjects. Urinary mercury concentrations were measured in 25 sensitized and 46 non-sensitized and hair mercury concentrations were measured in 19 sensitized and 22 non-sensitized subjects.

The eating of fish was not significantly associated with mercury sensitization (one-tailed t-test). The number of teeth treated with metals in the sensitized group was significantly higher than in the control group ( $6.8 \pm 4.3$  in sensitized vs.  $4.8 \pm 4.1$  in non-sensitized, one-tailed t-test,  $p < 0.05$ ). The usage of mercurochrome was not significantly associated with mercury sensitization (chi-squared test). Urinary mercury concentrations were not significantly higher in sensitized subjects. Hair mercury concentrations were significantly higher in sensitized subjects ( $1.98 \pm 0.91 \mu\text{g/g}$  in sensitized vs.  $1.23 \pm 0.53$  in non-sensitized, one-tailed t-test  $p < 0.05$ ).

These results suggest that mercury sensitization is associated with increased hair mercury concentrations but not with urinary mercury concentrations. In this study it is confirmed that dental amalgam for treating teeth may be an important factor relating to mercury sensitization.

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## A Study of the Effects of Physical Load on Umpires During the National High School Baseball Games —The Effects of Physical Load on Umpires at the Koshien Stadium in a Summer-heat Environment—

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**Abstract** This study attempted to measure the physical load on national high school baseball umpires during games played at Koshien stadium under extremely hot and humid conditions in the summer. Thirty-one umpires participated in this study. Thirteen of them were evaluated twice while eighteen were evaluated only once. The factors used to determine physical load were the following: body weight, oral temperature, blood pressure, heart rate, and serum biochemical elements. These were measured before and after the games. Heart rate was measured at one-minute intervals.

The results were as follows.

1) All the games were played under conditions of extremely high temperatures - 32.1 degrees celsius dry-bulb, 27.0 degrees celsius wet-bulb, 36.8 degrees celsius black-globe, 29.5 degrees - WBGT which are likely to cause heat-related illnesses.

2) The physical load of baseball umpires during the game showed a 1.69 percent decrease in average body weight

due to perspiration, a 0.43°C increase in oral temperature and an increase in heart rate. An examination of the serum biochemical elements showed that muscle deviation enzymes changed due to muscular activity and blood condensed due to perspiration. The physical load levels of baseball umpires were influenced by extreme heat and physical activity during the game.

3) There were no observable differences in either the amount of physical activity or the extreme heat environment among the umpires of different field positions. But the chief umpire's physical load showed a greater decrease in body weight, more blood condensation due to perspiration as a result of the heavier equipment he wore, more muscular activity and higher energy consumption than his counterparts on the bases.

4) The umpire's heart rates were higher during games than before games. The moment they were on the playing field. Their heart rates rose to an average of 134. It remained above 115 for about two hours, apparently caused by physical activity and heart load.

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