ABSTRACT

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Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and its Implementation in Japan

Nippon Eiseigaku Zasshi, 65, 5–13 (2010)
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The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) is a set of recommendations by the United Nations, first issued in 2003 as a communication tool for the sound management of chemicals, comprising harmonized classification criteria for physical, health and environmental hazards, a unified format for material safety data sheets (MSDS), and labeling elements including pictograms and hazard statements preassigned to each classification category. The GHS has been introduced into Japan and implemented in the regulatory framework for chemical safety. The Japanese Industrial Standards (JIS) adopted the GHS, and the GHS-based JIS rules have become the Japanese standards for labels and MSDS. The use of the JIS format for labels and MSDS is recommended by several competent authorities in Japan although mostly on a voluntary basis. In the workplace, however, GHS-based JIS labels and MSDS have become legal requirements by the Industrial Safety and Health Law since 2006; namely, issuing MSDS in such a format is mandatory for the 640 specified chemicals and also labeling for the 99 targeted chemicals[1]. Although the GHS provides definitions and classification criteria for ten classes of health hazards (acute toxicity, skin and eye corrosion/irritation, sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity single/repeated exposures, and aspiration hazard), it does not provide actual classification of chemicals, so that competent authorities and industries need to classify a number of chemicals and/or mixtures. Weight-of-evidence judgment and/or expert judgment would be necessary in many cases. In this paper, the outline of the GHS classification is described and problems of the GHS and its implementation are discussed.

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[1] The number of the targeted chemicals has been increased from 99 to 100 since April 2009, after acceptance of this article, due to the amendment of the Industrial Safety and Health Law.

Recent Development in Animal Testing to Predict the Skin and Respiratory Sensitizing Potential of Chemicals

Nippon Eiseigaku Zasshi, 65, 14–19 (2010)
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The identification of chemicals with skin and/or respiratory sensitizing potential is important for the prevention of allergic diseases in both living and work environments. Although a number of animal models for respiratory allergic diseases have been reported, none of these models meets the goals of broad assessments of chemical sensitizing potential. We are attempting to develop a test for predicting the respiratory sensitization of chemicals. In the evaluation of skin sensitization of chemicals, the mostly used predictive tests are the guinea pig maximization test, Buehler test, and mouse local lymph node assay (LLNA). However, only LLNA has been validated formally and independently. Recent studies have revealed that EC3 estimated by LLNA correlates well with human skin sensitizing potency and the threshold for the induction of skin sensitization in the human repeat patch test. Thus, LLNA can predict the potency of skin sensitizing potential of a chemical and its risk in humans.

Skin Sensitizers in Cosmetics and Skin Care Products

Nippon Eiseigaku Zasshi, 65, 20–29 (2010)
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Cosmetics are defined as "articles with mild action on the human body, which are intended to be applied to the human body through rubbing, sprinkling or other methods, aiming to clean, beautify and increase the attractiveness, alter the appearance or to keep the skin or hair in good condition (The Pharmaceutical Affairs Law: Article 2)." Consequently, they include personal hygiene products such as shampoos, soaps and toothpaste. In Europe, 1% of the population is

estimated to be allergic to fragrances and 2–3% to ingredients of cosmetics; 10% of outpatients patch-tested for cosmetics allergy were found to be positive. Allergenic ingredients of cosmetics can be fragrances, hair dye, preservatives, antioxidants, emollients, surfactants, UV absorbers, pigments or resins used in nail cosmetics. Among standard allergen series, eight substances are related to cosmetics; in Japan in 2003, *p*-phenylenediamine (hair dyes) induced allergic reactions with the highest rate of 7.9% in outpatients patch-tested [*n* (805)], followed by fragrance mix No. 1 (4.0%, mixture of eight fragrances frequently used), colophony (3.2%, main contents of pine resin), lanolin alcohol (2.7%, emollients), and formaldehyde, parabens, Kathon CG (2.7, 1.9 and 1.0%, respectively; preservatives). Cosmetic allergy symptoms tend to be mild except those caused by hair dye. However, the population exposed to cosmetics is huge and the number of ingredients used in cosmetics increased up to more than 6,000. Here, major cosmetic ingredient allergens, mainly reported in Japan, are reviewed and discussed.

Preventive Measures against Health Damage due to Chemicals in Household Products

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Chemicals in household products have been paid much attention as the main cause of health damage in consumers, such as allergic contact dermatitis. Preventive measures against health damage due to chemicals in fabrics, plastics and rubber products for household use, are reviewed, focusing on (1) the incidence of health damage due to household products, (2) causative product-chemical investigation, and (3) case studies on skin damage.

Toward a More Rational Field-Genetic Epidemiology

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Genetic dissection of diseases is one of the epoch-making achievements in modern medicine. Positional cloning is a key method to isolate disease-related genes. For positional cloning, there are two conventional methods: family-based studies and case–control studies. In this review, I would like to describe several family-based studies on single gene diseases which I had conducted including those of Akita diabetic mice, systemic carnitine deficiency and Hartnup disease. The study of systemic carnitine deficiency underscored a potential power of the "Carrier state." Furthermore, cultural and public health practices in Japan such as preservation of umbilical cords and mother and child passbooks enabled us to conduct linkage analysis even 20 years after the deaths of affected patients in Hartnup disease. For multifactorial diseases, I present three family-based studies: intracranial aneurysm, moyamoya and arteriovenous malformation. Finally, I discuss on theoretical issues concerning the relationship among odds ratio, phenocopy rate and penetrance by formulating a single-locus dominant association model. Analysis of the model predicted a notion that a large odds ratio facilitates familial clustering of multifactorial diseases and vice versa is the case. Furthermore, the analysis predicted that genetic markers for screening should have odds ratio ≥8 to maintain similar qualities commonly required for clinical tests. Collectively, the analysis predicted a two-

stage study design composed of linkage analysis based on a family study and subsequent replication by a case–control association study is more rational than the currently used two-independent case–control design. This newly proposed method is expected to provide polymorphisms, which have large odds ratios, requiring only minimum research budgets.

Predicting Spread of New Pandemic Swine-Origin Influenza A (H1N1) in Local Mid-Size City: Evaluation of Hospital Bed Shortage and Effectiveness of Vaccination

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Objectives: On April 24th, 2009, a new swine-origin influenza A (H1N1) was first reported in Mexico. Japan confirmed cases of the flu on May 9th, and the pandemic in Japan has become full-scale. The Ministry of Health, Labor and Welfare of Japan announced that the first peak of this pandemic was predicted to occur in October, 2009. Therefore, it is most important to predict the progress of this pandemic to be able to use medical resources effectively in Japan.
Methods: We used a modified susceptible-exposed-infected-recovered (SEIR) model to calculate the number of infected people and hospital bed shortage during this pandemic. In this model, available medical resources were investigated on the basis of four vaccination scenarios.
Results: Our model showed that it would take a further six months for the pandemic to peak than was predicted by the Ministry of Health, Labor and Welfare of Japan. Without vaccination, at the peak of the pandemic 23,689 out of 400,000 people would be infected and the hospital bed shortage would reach 7,349 in total.
Conclusions: We suggest that mathematical models are strong tools to predict the spread of infectious diseases. According to our model, it is possible to prevent hospital bed shortage by vaccination.

Estimates of Reduction in Prevalence of Diabetes Mellitus and Health Care Costs Reduced through the Intervention Program for Obese People in Japan

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Objectives: In the structural reform bill of health care, which passed the Diet in fiscal year 2006, the number of patients with lifestyle-related diseases and the number of those who will potentially develop such diseases in 2015 should be reduced by 25% from the number in 2008 through the national intervention program against obesity. We estimated the reduction in prevalence of diabetes mellitus, as a representative lifestyle-related disease, and the health care costs reduced by controlling obesity.
Methods: Firstly, we estimated the prevalence (95% confidence interval) of obese people by conducting the National Health and Nutrition Examination Survey in 2005. Secondly, we estimated the proportion of obese people that should be reduced in order to reduce

diabetes prevalence by 25% using the data from the National Diabetic Patients Survey in 2002. Thirdly, we estimated changes in prevalence of diabetes mellitus when the proportion of obese people was reduced by 20, 40, 60, 80, and 100%. Finally, we estimated how much health care costs would be reduced if the number of obese people was reduced by 20%.

Results: It is extremely difficult to reduce the prevalence of diabetes mellitus by 25% by only reducing the proportion of obese people. From our estimation of changes in the prevalence of diabetes mellitus when the proportion of obese people was reduced, the intervention for people aged from 40 to 59 years was more effective than that for people in other age groups for both male and female. The health care costs of diabetes mellitus can be reduced by ¥841,210,000,000 for male and by ¥75,930,000,000 for female.

Conclusion: It is almost impossible to reduce the prevalence of diabetes mellitus by 25% although it is cost-effective to target on people aged from 40 to 59 years against obesity to reduce the prevalence of diabetes mellitus.

Attitudes towards the Code of Conduct for Scientists among Council Members of the Japanese Society for Hygiene

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Objectives: The aim of this study was to clarify the attitudes towards the code of conduct for scientists among council members of the Japanese Society for Hygiene (JSH). We also aimed to collect information to be used as baseline data for future studies.

Methods: From November to December 2007, 439 Council members of the Japanese Society for Hygiene completed a self-administered questionnaire.

Results: The valid response rate was 43.7% [n (192/439)]. The mean ages of the subjects were 56.2 years for males [n (171)], and 53.0 years for females [n (19)]. Many council members were unfamiliar with the "Code of Conduct for Scientists" established by the Science Council of Japan, suggesting that most of the regular members were also unfamiliar with these guidelines. However, the high level of interest in the "Code of Conduct for Scientists" established by the Science Council of Japan indicated a positive attitude towards learning about research ethics. Moreover, one-half of the subjects responded that JSH should establish a code of conduct for scientists.Below are some of the reasons for requiring JSH to establish a code of conduct:

1. Private information is prevalent in the field of hygiene.
2. The overall stance as an academic society would be established and would encourage individuality in academic societies.
3. Members have various backgrounds within the field of hygiene, and they should have a code of conduct different from that of their institution of affiliation.

Conclusion: We clarified attitudes towards the Code of Conduct for Scientists among council members of the Japanese Society for Hygiene.