Session 4 Exposure

Studies on EDC Exposure in Malaysian Population

Mustafa Ali Mohd
University of Malaya, Malaysia

A study was conducted to assess the extent of exposure among Malaysian population to endocrine disrupters, especially from food and food based products. This includes sources from phytoestrogens and contamination of pesticides and bisphenol A. The study focuses on the fresh products for vegetables and the analysis of cord blood from pregnant mothers.

A total of seven pesticides, eight alkylphenols and five phytoestrogens were monitored to determine their trace levels in human cord blood. The pesticides are lindane, diazinon, α-endosulfan, β-endosulfan, endosulfan sulfate, chlorpyrifos and endrin; while the alkylphenols are 4-n-butylphenol, 4-n-pentylphenol, 4-n-hexylphenol, 4-t -octylphenol, 4-n-heptylphenol, nonylphenol, 4-n-octylphenol and bisphenol A. The pesticides and alkylphenols in the cord blood samples were extracted with solid phase extraction IST C18 cartridges and analyzed by selected ion monitoring mode using quadrapole detector in Shimadzu QP-5000 gas chromatograph-mass spectrometer. Trace levels of pesticide and alkylphenols in the range of non-detectable to 15.17 ng ml^{-1}, were detected in the human cord blood samples.

Phytoestrogens such as genistein, daidzein and their cojugates, which are also thought to have the highest estrogenic properties, were found in various types of food and food products consumed by the Malaysians. There is considerable variation in the phytoestrogen concentrations of different plants and food materials. This study was conducted to assess the amount and type of phytoesrogens contained in certain high phytoestrogen containing food and to assess the levels of phytoestrogens in the plasma of cord blood and in healthy adult volunteers.

A total of 35 vegetables and vegetable parts and 20 types of fruits were analysed using LCMS. The phytoestrogens daidzin, daidzein, genistin, genistein and coumesterol were monitored using Shimadzu QP8000α LCMS

From the total of 35 selected vegetables analysed, 21 samples were found to have phytoestrogens from the range of 0.4 ug/ g ? 150 ug/g dry weight. The vegetables and legumes, especially leguminosae family, have been found to contain higher phytoestrogens, compared to other families. Leguminosae family has higher levels of daidzin and genistin than the free forms compared to other families. From 21 samples of local fruits that were analysed, only 4 samples were found to have phytoestrogens from the range of 5 ng/gm -1100 ng/gm dry weight.

Another study on 30 selected soy based food products, all the samples were found to contain phytoestrogens (daidzin, genistin, genistein and daidzein) in the range of 0.043 mg/100 g - 42.62 mg/100 g dry weight. Coumesterol were found to be in the range of 0-0.46 mg/g dry weight. In a study to investigate the phytoestrogen content in the cord blood collected from various hospitals in the country, genistin and genistein were found to be the highest detected phytoestrogens in the cord blood.

Studies on the levels of bisphenol A in the cord blood were carried out using the same cord blood samples by GCMS method. The results showed that the concentration of bisphenol A detected in the cord blood ranges from non-detectable to 4.05 ng/ml. Bisphenol A were detected in more than 80% of the samples analysed.

(Acknowledgement: The author would like to acknowledge the following bodies for their contribution in one way or another in the conduct of this research: Shimadzu Corporation, Japan; Japan Chemical Industries Association; The United Nations University, Tokyo.)

Current Situation of Human Fetal Exposure to Multiple Chemicals in Japan

Hideki Fukata and Chisato Mori

Graduate School of Medicine, Chiba University, Japan

Ministry of the Environment of Japan has been conducting the investigation regarding to the exposure of humans to the endocrine disrupting chemicals. The investigation includes the data concerning the concentration of persistent chemicals (dioxins, PCBs, organochlorine pesticides, phytoestrogens, etc.) in umbilical cords, cord serums and maternal serums. In this presentation, we will summarize the results the past few years. Sample numbers are as follows; 63 umbilical cords for dioxins, 63 umbilical cords, 20 umbilical cord serums and 52 maternal serums for PCBs, and 72 umbilical cords, 20 umbilical cord serums and 40 maternal serums for organochlorine pesticides, 41 umbilical cord serum and 41 maternal serums for phytoestrogens. (This study has been approved by the "Congress of Medical Bioethics" of Chiba University.)

1) Persistent chemicals

Several persistent chemicals have been detected from mothers and fetuses, including dioxins (PCDDs, PCDFs and co-PCBs), PCBs, organochlorine pesticides such as DDTs, drins, hexachlorocyclohexane (HCH), hexachlorobenzene (HCB), chlordanes, etc.. They included the chemicals that were ceased to use in Japan more than 30 years ago. A correlation among accumulative chemicals, when the concentration level of one chemical was high, others also tend to be high, has been confirmed. Also, the concentration level in the umbilical cord tended to rise along with the maternal age at which she bears her first child. This analysis suggests that there are fetuses that are highly exposed to multiple persistent chemicals in Japan, and it has become clear that various types of chemicals and toxicants have been transplacentally transferred from mothers to their fetuses. There were chemicals that easily transfer from mothers to fetuses. They were PCBs, DDTs, HCH, and so on. On the other hand, those chemicals such as drins, HCB, etc. showed the opposite pattern. Regarding to PCBs, each isomer showed different pattern of transfer depending on the numbers of chloride.

2) Phytoestrogens

Phytoestrogens, estrogenic substances from plants were also detected from mothers and fetuses. In Japan, soy bean is often used for traditional food, so phytoestrogens from soy beans were detected frequently. Among phytoestrogens, genistein and daidzein were detected at higher concentration level from fetuses than mothers, while equol, daidzein metabolite, was detected at higher level from mothers than fetuses.

Mechanistic Biomarkers and Adverse Effect Endpoints in Fish Reproductive Toxicity Testing: Practical Recommendations for addressing the Risk of Aquatic Exposure

Thomas H. Hutchinson

AstraZeneca Global Safety, UK

During the six years since Japan hosted the successful first international symposium on environmental endocrine disrupters (EEDs), together with other key workshops around the world, there has been significant progress in basic scientific knowledge of exposures of EEDs and their potential effects (hazard) in aquatic organisms. Recognising the complementary need for on-going basic research, this presentation will take focus on: [1] practical techniques that can be used today for fish screening and testing and [2] the use of data for environmental risk assessment (the holistic assessment of exposure and hazard). Given current knowledge and global expertise, it is argued that a 3-tier scheme for fish screening (Tier 1), partial life-cycle testing (Tier 2) and full life-cycle testing (Tier 3) is optimal since allows cost-effective identification of an endocrine mechanism and will provide flexible tools for use in different risk assessment scenarios (see Hutchinson et al (2000) Environmental Health Perspectives 108: 1007-1014). This screening phase of this approach will be illustrated by the evaluation of (anti)androgens, (anti-)oestrogens and aromatase inhibitors in a 21 day non-spawning fish screening assay currently undergoing pre-validation by the OECD. At the testing level, examples will be given from the published literature for a range of weak versus potent EEDs (eg alkylphenols and steroidal oestrogens). Emphasising the need to maintain focus on ecologically relevant endpoints in environmental risk assessment (for example, as specified in the EU Technical Guidance Document and recommended by Kendall et al (1998) In: Principles and Processes for Evaluating Endocrine Disruption in Wildlife, SETAC Press), it is argued that fish screening data should not be used to calculate Predicted No-Effect Concentration (PNEC) values since the purpose of screening is to measure biomarker responses. Positive biomarker responses from such screens should be used to help decide on the need for (and guide the design of) higher tier fish chronic tests. These fish chronic tests should address population relevant endpoints (namely development, growth, hatching, reproduction and survival) and it is these adverse effect endpoints that should be used to derive PNEC values. In view of the significant timescale involved in developing OECD test guideline, from a pragmatist's perspective, it should be recognized that there are a number standard protocols already available for fish partial and full life-cycle testing and these should be used to test chemicals detected in the aquatic environment. In terms of new chemicals and the need to address the predicted Exposure Concentration (PEC) and PNEC values, it is argued that more rapid progress can be made if risk assessors make greater use of existing fish chronic testing methods which incorporate adverse effects endpoints.

GIS-based Environmental Fate Model and the Exposure Assessment of Endocrine Disrupting Chemicals

Noriyuki Suzuki

National Institute for Environmental Studies, Japan

Risk management framework of chemicals consists of the hazard identification and assessment of chemicals, the exposure assessment, and the risk assessment for target population or ecosystem, followed by the management and countermeasures. Multimedia environmental fate models have been playing major role within the framework especially in the screening level risk assessment and management of chemicals for years. However, because of the relatively simple environmental setup of those models, the accuracy of the output of those models is generally limited, namely, a factor of 10 or larger discrepancy may exist between modeling and monitoring outputs. Models that can give more accurate output are necessary for the more realistic exposure assessment.

As majority of environmental data, such as population, industrial activities, contaminant emissions, environmental levels, biotic conditions, and resultant risk characteristics and levels, have significant geographical distribution, explicit incorporation of geographical variability of various environmental data should have key importance for more realistic exposure assessment of endocrine disrupting chemicals.

In addition to the above technical reasons, the PRTR (Pollutant Release and Transfer Register) framework is already working in many countries, which can work as emission estimation with geographical resolution. The integration of the PRTR output and geo-referenced multimedia environmental fate model can provide more realistic exposure estimation of endocrine disrupting chemicals both for humans and ecosystem.

The authors have developed the G-CIEMS (Grid-Catchment Integrated Modeling System), a GIS (geographical information system)-based environmental fate model, that works with the “Virtual World” system for the comprehensive risk assessment and management of chemicals on GIS. The G-CIEMS model consists of G-CIEMS-River, a river water quality models and G-CIEMS-Multi, a geo-referenced multimedia fate model. The model can obtain the simulation output of the environmental levels from PRTR and other spatially-resolved emission inventories. The output resolution is now 5 km by 5 km for air on terrestrial area, average 5.7 km length for river water as real river segment structure, average 9.3 km2 area for soil as catchment structure, segmented sea for sea water, and same resolution for sediments beneath the corresponding aquatic compartments. Case study for dioxins and several VOCs will be shown in the presentation. The output of case study shows that (1) the incorporation of geographical reference to the multimedia fate model significantly enhance the accuracy of the model, to a factor of 2 to 5, depending on the compounds. (2) Geographical distribution in air is apparently different among compounds. Chemicals with longer degradation half lives tend to spread over oceanic area of Japan, although the detailed distribution is also depending on the other chemical properties. (3) Emission pattern has apparent impact on the patter of environmental levels. (4) Geographical distribution of soil and river compartments can be simulated with more geographical reality.

Those outputs can be used for the more realistic exposure assessment for humans and ecosystem based on the GIS environment. Some examples of GIS-based exposure assessment methodology will be shown based on the “Virtual World” system functions.