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Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a
"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

CRI collaborates with the National Institute of Occupational and Environmental Health (NIOEH) in organizing a training course on "Environmental and Health Risk Assessment and Management of Chemicals" in Hanoi, Vietnam (December 1-5, 2014)

A team of international training experts in the field of risk assessment and risk management of chemicals, organized by the Chulabhorn Research Institute (CRI), traveled to Vietnam to conduct in-country training on "Environmental and Health Risk Assessment and Management of Chemicals" in collaboration with Vietnam's National Institute of Occupational and Environmental Health (NIOEH) from December 1-5, 2014, with support from the Department of Technical Cooperation, Ministry of Foreign Affairs, Thailand, and CRI.

The Opening Address for this training course was delivered by H.E. Mr. Panyarak Poolthup, Ambassador of Thailand to Vietnam, Representative of Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol. Welcome statements were also made by Professor Nguyen Huy Nga, Director General of the Health Environment Management Agency, Vietnam Ministry of Health, and Dr. Doan Ngoc Hai, Director General of NIOEH.

The course was designed to provide basic scientific knowledge of the principles and concepts of risk assessment and the process involved, to illustrate by using relevant examples and case studies how risk assessment is conducted and what different issues are involved, and to introduce practical tools for the continued training of interested individuals, including WHO's IPCS Human Health Risk Assessment Toolkit and the Electronic Distance Learning Tool (eDLT) on Risk Assessment and Risk Management of Chemicals, which was developed by CRI in collaboration with WHO IPCS, the University of Ottawa (Canada) and Utrecht University (the Netherlands). The eDLT is an interactive, web-based, self-learning tool that is administered through a Learning Management System and hosted through a

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website at http://www.chemDLT.com, where interested persons can find more information about how to access the eDLT. There are a total of 8 modules: Introduction, Problem Formulation, Hazard Assessment, Exposure Assessment, Risk Characterization – Human, Risk Characterization – Ecological; Risk Management; and Risk Communication.

The teaching faculty for this training course included Professor Herman Autrup from Aarhus University (Denmark), Dr. David Russell from the WHO Collaborating Centre for Chemical Incidents/Public Health England (UK), and Professor David MacIntosh, an adjunct professor at the Harvard School of Public Health (USA), as well as Professor Mathuros Ruchirawat, CRI Vice President for Research and Academic Affairs, Dr. Jutamaad Satayavivad, CRI Associate Vice-president for Scientific Affairs, and Dr. Daam Settachan, research scientist from CRI's Laboratory of Environmental Toxicology. The teaching team has vast experience in providing training for participants within the SEA region, having trained participants from Brunei Darussalam, Cambodia, India, Indonesia, Laos, Malaysia, the Maldives, Myanmar, Nepal, the Philippines, Sri Lanka, Thailand, Timor Leste and Vietnam, amongst others. This training course was conducted as part of CRI's role as a WHO-SEARO-designated Regional Training Center for Chemical Safety in the South-East Asian Region.

CRI and the Vietnamese institutions have a close and long-standing collaboration, with the first collaborative program initiated in 1996 with the Department of Science, Technology and Environment (DOSTE) in a project aimed at capacity building in environmental and industrial toxicology, which was supported by the UNDP. In terms of research, CRI and the NIOEH have a joint-project on *in utero* arsenic exposure and its potential impact on the health of the newborns, with collaborations with Columbia University and the Massachusetts Institute of Technology, and the US National Institute of Environmental Health Sciences (NIEHS).

This training course on Environmental and Health Risk Assessment and Management of Chemicals is an important step in the bilateral cooperation, since it involves the integration of science and policy in the areas of chemical safety, public health and economic development, reflecting the shared commitment of the two countries to improve the quality of life for their people. The management of chemicals and the assessment of the risks involved in their effective and beneficial use in industry and agriculture is an area of specialization in which CRI has developed considerable expertise, both through education and research programs and through the close collaborations with eminent scientists and researchers from renowned universities in other countries, as well as from international organizations such as the WHO.

This in-country training course was attended by 61 participants from various governmental agencies and academic institutions, including: the Binh Duong Centre for Occupational Health Protection and Environment, Hanoi Medical

University, Hanoi School of Public Health, Hanoi University of Science and Technology, HCM Institute of Hygiene and Public Health, Health Environment Management Agency, Institute of Environmental Sciences and Public Health, Intel Products Vietnam, Military Medical University, Ministry of Industry and Trade, Nam Dinh Preventive Medicine Centre, National Institute of Labour Protection, the NIOEH, Pasteur Nha Trang Institute, Tay Nguyen Institute of Hygiene and Epidemiology, Training Institute for Preventive Medicine and Public Health (Hanoi Medical University), Vietnam Clean Air Partnership (VCAP), Vietnam Environment Administration, and the Vietsovpetro Medicine Centre.

In addition to attending lectures, participants worked on several different case studies, including occupational and environmental exposures to benzene, health effects of fluoride in drinking water, health risks of polychlorinated biphenyls in indoor air, health impacts of arsenic in drinking water, and accidental exposure to chlorine gas from a chemical incident, and gave presentations on the final day of training to demonstrate their understanding of the risk assessment process.

As part of its capacity building programme, CRI regularly conducts in-country training in developing countries in the Asia-Pacific region in the areas of chemical safety, environmental health, toxicology and risk assessment in response to requests made from the respective country, either directly through an agency/institution with existing collaborations with CRI, or through an international organization such as the WHO, e.g. through the respective regional office at SEARO or WPRO. For more information on CRI's capacity building programme, including a calendar of training events, please visit http://www.cri.or.th/en/envtox/default.htm.

Chronic Arsenic Exposure and Gene-Specific Differential DNA Methylation

Inorganic arsenic is one of the most common naturally occurring contaminants found in the environment. Millions of individuals worldwide are exposed to inorganic arsenic through drinking water as well as dietary sources. Arsenic is a known human carcinogen (International Agency for Research on Cancer 2012). However, the exact mechanism by which it causes cancer has not been established. Some studies have suggested that epigenetic alterations, speciafically DNA methylation, may mediate arsenic toxicity.

In addition to cancer, chronic exposure to arsenic in drinking water has been associated with an increased risk of cardiovascular disease, peripheral neuropathy, respiratory diseases, and diabetes. Previous epidemiological studies probing DNA methylation and arsenic exposure have isolated methylation patterns within specific genes of interest, and a few have begun to assess epigenome-wide changes.

The largest to date investigation of arsenic-related changes throughout the epigenome was an epigenome-wide association study conducted among 400 Bangladeshi individuals with manifest arsenical skin lesions to assess whether arsenic exposure level (as measured by blood arsenic and urinary total arsenic concentrations) is associated with differential white blood cell DNA methylation.

Four gene loci showed significant changes in methylation status in relation to urinary arsenic concentration. Three of these also showed significant changes in relation to blood arsenic concentration. These four loci, namely sites in the genes *PLA2G2C, SQSTM1, SLC4A4,* and *IGH*, had not previously been associated with arsenic exposure.

The researchers observed that several of the differentially methylated loci were associated with changes in gene expression levels in white blood cells. For instance, *PLA2G2C* encodes lipid mediators with roles in inflammation, cell growth, and cell death, making them potentially important for cancer progression. Higher arsenic exposure was associated with decreased methylation levels at a locus of the *SQSTM1* gene that has been implicated in a number of diseases, including cancer, obesity, insulin resistance, and neuro degenerative diseases.

This research indicates that epidemiological studies may be able to use DNA methylation patterns in blood as a surrogate for past exposures to arsenic. Such research, combining DNA methylation and gene expression data, is a step toward doing more integrative molecular studies

Source: Environmental Health Perspectives, Vol. 123, No. 1, Pages 64-71, January 2015.

Renal Effects from Environmental Cadmium Exposure in Thai Children

Cadmium is an important environmental pollutant of public health concern due to its toxic effects to many organs. The kidney is considered the critical target organ for chronic exposure to cadmium. Urinary excretion of cadmium is a good biomarker of long-term cadmium exposure and body burden. Many studies in adults have shown that an initial sign of cadmium-induced nephrotoxicity is tubular proteinuria, usually demonstrated by increased urinary excretion of low molecular weight proteins such as β_2-microglobulin, and calcium.

Although renal dysfunctions are well-known toxic effects of chronic cadmium exposure in adults; very few studies have shown these health effects in children. Children exposed to cadmium even at low exposure levels may have adverse effects since they may be more susceptible to toxicity than adults.

In the Mae Sot District, Tak Province, northwestern Thailand, paddy fields were irrigated from two creeks, which passed through an area where a zinc mine had been actively operated for more than 30 years. About 69.2% of 91 sediment samples from the creeks and 85.0% of 1090 paddy soil samples contained cadmium content above the maximum permissible level of 3.0 mg/kg during the surveys in 2001-2004. The majority of residents were farmers and most of them consumed rice and other crops grown locally in the areas.

The previous studies among adult residents in these contaminated areas showed high prevalence of renal dysfunctions, bone density loss in the elderly, hypertension, and urinary stone diseases.

A recent population study was conducted to examine the associations between urinary cadmium excretion, renal dysfunctions, and blood pressure in Thai children in these contaminated areas.

Renal functions, including urinary excretion of β_2-microglobulin, calcium (early renal effects), total protein (late renal effect), and blood pressure were measured in 594 primary school children.

Of the children studied, 19.0% had urinary cadmium ≥ 1 µg/g creatinine. The prevalence of urinary cadmium ≥ 1 µg/g creatinine was significantly higher in girls and in those consuming rice grown in cadmium-contaminated areas. The geometric mean levels of urinary β_2-microglobulin, calcium, and total protein significantly increased with increasing tertiles of urinary cadmium.

The analysis showed significant positive associations between urinary cadmium, urinary β_2-microglobulin, and urinary calcium, but not urinary total protein or blood pressure.

The findings provide evidence that environmental cadmium exposure can affect renal functions in children. A follow-up study is essential to assess the clinical significance and progress of renal effects in these children.

Source: Environmental Research, Vol. 136, Pages 82-87, January 2015.

Kidney Damage from Cadmium Exposure in Aged Women with Type 2 Diabetes Mellitus

Cadmium (Cd) is a toxic metal which can cause kidney and skeletal damage. The main source of cadmium is through the diet and smoking. Cadmium accumulates mainly in the kidneys and is excreted slowly in urine with a half-life of several decades. Women often have a higher cadmium uptake compared to men due to iron deficiency (causing increased intestinal cadmium uptake), which is more common in women.

Cadmium in urine (U-Cd) or blood (B-Cd) is used for biomonitoring. Adverse effects on the kidneys (e.g. increased protein excretion) have been reported also at low levels of U-Cd or B-Cd in the general population. There are, however, some concerns regarding the interpretation of associations between U-Cd and biomarkers of kidney damage, due to co-excretion of Cd and proteins caused by factors other than cadmium toxicity.

Kidney damage is a well-known long-term effect of diabetes mellitus (DM). Early stages of diabetic kidney nephropathy are characterized by hyperfiltration and proteinuria. In the long term, some people with diabetes develop end-stage renal disease with severely reduced glomerular filtration rate. Animal studies have shown that spontaneously diabetic mice are more sensitive to cadmium nephrotoxicity compared to normal mice, but few studies have examined this in humans.

A recent study was conducted to test the hypothesis that aged women (64 years old) with type 2 DM or impaired glucose tolerance (IGT) have higher risk of kidney damage from cadmium, compared to women with normal glucose tolerance (NGT). Kidney damage was assessed using estimated glomerular filtration rate (eGFR) as well as urinary excretion of albumin (Alb) and retinol-binding protein (RBP).

A significant interaction was seen between high B-Cd and DM. The effect of high B-Cd on Alb excretion was significant in women with DM, but not in women with IGT or NGT. Models with urinary Alb adjusted for creatinine showed similar results. There were no associations between B-Cd and eGFR or excretion of RBP.

The present study provides support for the hypothesis that women with DM have higher risk of renal glomerular damage from Cd exposure, compared to women without DM.

Diabetes is a common condition, and Cd exposure is widespread and causes many other detrimental health effects. The results underscore the need to monitor and reduce environmental Cd levels in order to reduce dietary Cd exposure.

Source: Environmental Research, Vol. 135, Pages 311-316, November 2014.

THE POSSIBLE ROLE OF ARSENIC AND PESTICIDES IN THE PREVALENCE OF DIABETES IN PAKISTAN

Environmental pollution has been a major health concern throughout the world for a very long time, but the risks are higher in underdeveloped countries where environmental pollution contributes about 8-9% of the total disease burden.

In Pakistan, an agricultural country, about 69-fold increase in the use of different types of pesticides has been recorded during the last two decades (from 665 tons in the year 1980 to 45,680 tons in 1999). Water pollution is a major public health threat in Pakistan, especially drinking water. Most people in Pakistan are exposed to arsenic and pesticides either in drinking water or through vegetables, fruits, and other edible items with various concentrations of pollutants above the WHO/FAO permissible limits.

Diabetes mellitus (DM) is the leading chronic disease and has emerged as a big socioeconomic burden in Pakistan. According to a WHO 2011 report, about 12.9 million people are suffering from DM, and the number is constantly increasing.

A bibliographic search of scientific databases was conducted to address the possible role of arsenic and pesticides in the prevalence of DM in Pakistan. More than 200 articles were examined.

Experimental and epidemiologic studies gathered suggest that environmental pollutants such as pesticides, arsenic, cadmium and mercury are risk factors in the incidence of DM.

Excessive arsenic presence has been reported in the water resources of many other countries, among them Argentina, China, India, Brazil, Mexico, the USA, Taiwan, and particularly Bangladesh. According to published data, arsenic exposure is considered as one of the risk factors in the incidence of DM in these countries.

This review suggests that there might be a correlation between heavy metals like arsenic and pesticide exposure and the prevalence of DM in Pakistan. There are many regions where drinking water sources are grossly contaminated with heavy metals and pesticides, but there is a complete lack of targeted epidemiologic research in the affected areas. Therefore, it is difficult to correlate the prevalence of DM in exposed populations with exposure to these pollutants.

Data obtained from such targeted research would significantly add to the growing body of evidence about the role of environmental pollutants in the occurrence of chronic diseases.

Source: Journal of Diabetes & Metabolic Disorders, Vol. 13, Issue 1, Pages 117, December 2014.

The Relationship of Urinary Pyrethroid and Chlorpyrifos Metabolite Concentrations and Indoor Residential Insecticide Levels

Since the 2001 U.S. federally mandated phase-out of residential uses of organophosphates (OPs), chlorpyrifos and diazinon, the use of and potential for human exposure to pyrethroids in indoor residential environments has increased.

Once insecticides entered the home, carpets and cushioned furniture can act as repositories for the parent compounds and their metabolites. Children have an increased risk of exposure to environmental contaminants partly because of behaviors leading to higher nondietary ingestion than adults.

Studies have shown that exposure to high levels of pyrethroids may cause significant toxicity and health effects, including acute neurotoxic effects, immunotoxic effects, and endocrine disruption which can adversely affect mammalian reproduction. Pyrethroids are possible human carcinogens, with associations seen between exposure and cutaneous melanoma, as well as childhood leukemia. The impact of chronic low or moderate level exposures in general, and on the developing fetus or child, has not been well studied.

The new study examined concentrations of common pyrethroids, pyrethroid metabolites, chlorpyrifos in floor wipes, and urinary concentrations of pyrethroid metabolites and 3,5,6-trichloro-2-pyridinol (TCPy) in samples collected in 2007−2009 from 90 northern California families (90 adults and 83 children) as part of the Study of Use of Products and Exposure Related Behavior (SUPERB).

Correlation and regression analyses examined associations between floor wipe and urine sample concentrations. The most frequently detected urinary metabolites were TCPy (the principle metabolite of chlorpyrifos) and 3-phenoxybenzoic acid (3PBA). 3PBA has been commonly used as a nonspecific biomarker for evaluating human exposure to multiple pyrethroid insecticides and has also been measured in the indoor environment.

Chlorpyrifos (98.7%), cis- and trans-permethrin (97.5%), bifenthrin (59.3%), and 3PBA (98.7%) were frequently detected in floor wipes. Floor wipe concentrations for pyrethroid insecticides were found to be significant predictors of child creatinine-adjusted urinary metabolite concentrations, suggesting that indoor residential exposure to pyrethroid insecticides is an important exposure route for children.

Results from the present study and multiple other reports for a wide range of communities support the hypothesis that data on indoor levels of pyrethroid insecticides and urinary concentrations of metabolites indicate residential insecticide use to be one of the most important contributors to pyrethroid exposures.

This is the first study evaluating correlations between floor wipe and urinary metabolite levels for pyrethroids, and it demonstrates the usefulness of floor wipe samples as indicators of pyrethroid exposure for children.

The resulting correlation provides evidence that children are being exposed to pyrethroid insecticides in their home, and thus indoor use is an important contributor to exposure.

Additionally, a comparison of measured levels in this study vs those reported for samples collected in 2001−2002 is consistent with increased use of pyrethroids and decreased use of OPs for residential applications since the 2001 Federally mandated phase-out of residential uses of chlorpyrifos and diazinon.

Further research is warranted to investigate the specific sources of these exposures to pyrethroid insecticides and to understand whether these compounds have long-term effects on child health or development.

Source: Environmental Science & Technology, Vol. 48, Issue 3, Pages 1931-1939, December 2014.

Assessment of Serum Biomarkers in Rats after Exposure to Pesticides of Different Chemical Classes

Biomarkers are becoming increasingly important as indicators of adverse outcomes in safety assessment, environmental exposure, and translational research. They help provide a basis for understanding mechanisms and adverse outcome pathways for specific manifestations of toxicity. The search for bioindicators of toxicity has also been aided by expanding technologies capable of measurements of hundreds,even thousands of analytes.

In clinical trials, there is a critical need for biomarkers of effect that can serve as predictors or surrogate endpoints for adverse outcomes, especially if such monitoring can detect toxicity at an early, preclinical stage.

Biomonitoring studies such as the National Health and Nutrition Examination Survey (NHANES) demonstrate that humans are routinely exposed to large numbers of pesticides, which represent a number of different chemical classes, including organophosphates, carbamates, pyrethroids, and others.

Insecticides in particular often target the nervous system. While children are especially at risk, there are many in the general population who are also sensitive or vulnerable to pesticide exposure, and may suffer adverse effects. However, widespread low-dose exposures may be difficult to document using biomarkers of exposure such as levels of parent chemical or metabolite in urine or blood. It was of interest, therefore, to investigate changes in biomarker patterns following exposure to a wider range of acutely neurotoxic pesticides.

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Neonatal Exposure to Low-dose Diethylstilbestrol in Female Mice

A previous study found that early life exposure to low-dose diethyl stilbestrol (DES) induced early onset of spontaneous abnormalities in estrus cycle and shortened survival in female Sprague-Dawley (SD) rats, suggesting the importance of observing the estrous cycle over along period in research on endocrine disrupting chemicals (EDCs).

Although SD rats are generally used in toxicological studies, it is known to be easy to disturb the estrous cycle of SD rats in middle age. Also, pituitary and mammary tumors occur spontaneously in SD rats.

In order to confirm the repeatability of the previous study in SD rats, a one-lifespan test was designed. It was devised as a definitive test protocol for EDCs focusing mainly on early onset of spontaneous abnormalities in the estrous cycles of female offspring. It was conducted in C57BL/6J mice by neonatal oral exposure to DES. Aging of their reproductive function and their survival was observed.

The researchers found that early life exposure to low-dose DES induced early onset of spontaneous abnormalities in estrus cycle, not only in female rats but also in female mice.

Neonatal period is characterized by very low estrogen levels to induce an early onset of menopause, delayed or precocious puberty, adult obesity and increased pituitary tumors in females. Therefore, EDCs exposure must be avoided during this critical period in humans. It is necessary to observe for a long enough period the reproductive functions of animals exposed to substances on the candidate list for their endocrine-disrupting properties during this important phase.

This study also revealed that long-term observation throughout the neonatal and aging periods made it possible to clarify what changes occurred in mice treated with DES during the neonatal period. Some of these changes included early onset of spontaneous abnormalities of estrous cycles, increased body weight, decreased antibody production, shortened survival, and accelerated occurrence of pituitary tumors. These parameters are necessary to confirm whether the chemicals are endocrine disruptors or not.

There were different results between mice and rats for some items, so it is important in a one-lifespan test to select parameters that are appropriate for the kind of animal used.

Source: Reproductive Toxicology, Vol. 50, Pages 145-151, December 2014.

Incense Use and Cardiovascular Mortality among Chinese in Singapore

It has been widely acknowledged that ambient air pollution is a significant risk factor for cardiovascular morbidity and mortality. Many studies focused mainly on solid fuel use but not on other sources of indoor air pollutants. Very few studies have investigated incense burning as a source of indoor air pollution and a risk factor for coronary heart disease (CHD). Incense burning at home for ritual or religious purpose is a common practice in many parts of the world. Airborne particles and associated organic components of the composition of particulate matter (PM) were identified from incense burning. These are potential air pollutants deleterious to health. However, there is no epidemiologic evidence linking domestic exposure to cardiovascular mortality.

In a previous study using data from the Singapore Chinese Health Study, it was found that incense use was significantly associated with an increased risk of upper respiratory tract cancer in a population-based cohort of middle-aged and elderly people in Singapore.

In the present study, the researchers examined the association between incense use and cardiovascular mortality risk using the same cohort. Differentiation between mortality due to CHD and stroke was identified, given the potential differences in the patho-physiology of these two diseases.

It was found that long-term exposure to incense burning at home on a daily basis for ≥ 20 years was associated with increased risk of cardiovascular mortality. Incense use was associated with both CHD and stroke mortality. The association between current incense use and cardiovascular mortality appeared to be limited to participants without a history of cardiovascular disease at baseline but not linked to those with a history. In addition, the association was stronger in never-smokers and former smokers than in current smokers.

This cohort provides an opportunity to evaluate the association in a population in which incense use is very common for many households, but the prevalence of outdoor air pollution and indoor solid fuel use is very low.

This study is the first to provide epidemiologic evidence that long-term exposure to daily incense burning in the home environment may increase the risk of cardiovascular mortality. It is estimated that approximately 8% of CHD deaths and 12% of stroke deaths in the study population could be attributed to incense use. Considering the worldwide prevalence of incense burning, findings of this study have significant public health implications.

It is important to educate users on approaches to limit adverse health effects. Future studies should be undertaken to identify the least harmful types of incense as well as strategies to reduce exposure and improve indoor air quality when using incense.

Source: Environmental Health Perspectives, Vol. 122, No. 12, page 1279-1284, December 2014.

Exposure to Traffic-Related Air Pollution and the Risk of Developing Breast Cancer

Exposure to traffic-related air pollution is ubiquitous and has been linked to a wide range of chronic diseases, including asthma, decreased lung function, cardiovascular disease, diabetes, and lung cancer. Vehicular emissions contain a number of well-known human carcinogens, such as benzene, 1,3-butadiene and certain polycyclic aromatic hydrocarbons (PAHs). The International Agency for Research on Cancer (IARC) has also recently classified outdoor air pollution as carcinogenic to humans.

Studies on cancer and traffic-related air pollution have focused on lung cancer due to the direct contact of inhaled air pollutants, including tobacco smoke. A few recent studies have also reported positive associations between long-term exposure to traffic-related air pollution and the incidence of breast cancer.

Although there is insufficient evidence to make any conclusions regarding the role that traffic-related pollution has in the etiology of breast cancer, there are a number of proposed mechanisms by which air pollution may increase the risk of developing breast cancer. The majority of mechanisms are related to xenoestrogens (compounds that mimic estrogen) and carcinogens such as benzene and polycyclic aromatic hydrocarbons.

Using the National Enhanced Cancer Surveillance System, a Canadian multi-site population-based case-control study was conducted to determine associations between the incidence of breast cancer and several measures of past exposure to traffic-related air pollution.

Mean exposure levels to nitrogen dioxide (NO_2) (an indicator of traffic-related air pollution) were estimated for this period using three different measures: (1) satellite-derived observations; (2) satellite-derived observations scaled with historical fixed-site measurements of NO_2; and (3) a national land-use regression (LUR) model.

The researchers found positive associations between breast cancer incidence and several measures of long-term exposure to ambient NO_2 in this large, Canadian population-based case-control study. This study supports the hypothesis that traffic-related air pollution may be associated with the development of breast cancer, with larger associations among pre-menopausal women.

Considering the widespread exposure of young women to traffic-related air pollution and the large population health burden from breast cancer, the limited information on this potential association, highlights the need for further research in this area.

Source: Environmental International, Vol. 74, Pages 240-248, January 2015.

Assessment of Serum Biomarkers in Rats after Exposure to Pesticides of Different Chemical Classes

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In a recent study, researchers evaluated serum biomarkers and targeted metabolite profiles in adult male Long-Evans rats after a single exposure to pesticides (permethrin, deltamethrin, imidacloprid, carbaryl, triadimefon, fipronil) with different neurotoxic actions.

The goal was to assess the experimental approach (proof of concept) and provide preliminary data on potential biomarker patterns associated with pesticides having different mechanisms of toxicity. Distinct patterns could result from pesticide-specific biological actions, whereas a generalized stress response could present a similar pattern across chemicals.

The patterns of serum biomarkers and metabolites were explored using targeted panels of cytokines, hormones, enzymes, and metabolites, in addition to *in vivo* neurophysiological measures such as changes in electro-encephalography (EEG).

Single and 14-day exposures to fipronil were also evaluated to compare changes in relation to exposure duration, and to link serum biomarkers and EEG measures with standard indicators of toxicity and exposure.

The results of the study demonstrate differential biomarker profiles of circulating cytokines, proteins, hormones, and metabolites following acute exposure to pesticides with different modes of neurological action.

For fipronil, these profiles differed between single- and repeated-dose exposures. Repeated dosing with fipronil produced lower thyroid hormones and altered proportions of the parent and sulfone metabolite.

Major biological processes linked to these changes include inflammation, mitochondrial metabolism, membrane lipid dynamics, hormone homeostasis, and tissue maintenance. Changes in cytokines in particular could reflect the action of some of these pesticides on different neurotransmitter systems involved in neuroimmunomodulation.

These patterns of biomarker change may provide a basis for gene mining and follow-up studies of adverse outcomes that may or may not be related to the specific central nervous system targets. Serum biomarkers also hold promise for screening approaches. However, further validation of appropriate biomarkers is necessary. These findings may suggest directions for additional studies to understand biomarker patterns and pathways.

Source: Toxicology and Applied Pharmacology, Vol. 282, Issue 2, Pages 161–174, January 2015.

CALENDAR OF EVENTS

International Training Courses in Environmental Toxicology at Chulabhorn Research Institute, scheduled for 2015

	Training Course	Date	Duration	Closing Date
1.	Environmental Toxicology	May 7-15, 2015	2 weeks	February 24, 2015
2.	Occupational and Environmental Medicine	To be announced	2 weeks	To be announced
3.	Environmental and Health Risk Assessment and Management of Toxic Chemicals	December 2015	2 weeks	September 24, 2015

1. International Training Course on "Environmental Toxicology" (May 7-15, 2015)

The course provides students and participants with a background of the major groups of toxic substances encountered by man and animals through food and the environment, and also through exposure at the workplace. These toxicants include mycotoxins, naturally occurring plant and animal toxins, toxic substances in air, water and soil, N-nitroso compounds, solvents, plastics, pesticides, pollutants and radiation (UV, electromagnetic, ionizing). The course focuses on the chemistry, fate and distribution in the environment, mechanisms of their action, toxic manifestation in living organisms, as well as toxic syndrome in human beings.

Requirement: Participants should have some basic knowledge in chemistry, biological sciences and medicine.

2. International Training Course on "Occupational and Environmental Medicine" (To be announced)

The course is intended to be a basic introductory course in occupational and environmental medicine and is designed for medical students, physicians, nurses and other healthcare workers. It will review the major occupational and environmental hazards and the associated diseases. It will emphasize the importance of the occupational/environmental exposure history as a critical tool for proper diagnosis of occupational and environmental disease, and will discuss the multidisciplinary nature of occupational and environmental medicine and underscore that treatment, prevention and control of occupational and environmental diseases requires a team approach that includes physicians, nurses, industrial hygienists, environmental scientists, engineers and policy makers.

Requirement: Participants should have some background in the health sciences and will become part of a network of professionals involving physicians, nurses and other healthcare insurance.

Fellowships: A limited number of fellowships are available that will cover roundtrip airfare, accommodation (on site) and meals, training materials, and health insurance.

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More information and application:
please visit - http://www.cri.or.th/en/ac_actcalendar.php

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