CRI/ICEIT
NEWSLETTER

VOL. 26 NO. 1 – January 2016
ISSN 0858-2793
BANGKOK, THAILAND

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 and WHO Co-Host Meeting of the WHO Chemical Risk Assessment Sub-network of Developing Countries in Bangkok, Thailand (December 2 - 4, 2015)

The three-day meeting was attended by 36 participants from 21 developing countries*. Six experts from WHO, HQ, SEARO, OECD and UNEP also joined the discussions.

The meeting presented a forum in which Chemical Risk Assessment (CRA) Network members and candidate members could collaborate on topics of mutual interest. Promoting tools for chemical risk assessment in developing countries was an important objective of the meeting.

After introducing the CRA Network and reporting on a WHO survey of risk assessment capacities in developing countries, participants learned about tools available for chemical risk assessment, including the WHO Human Health Risk Assessment Toolkit, the Inter-Organization Programme for the Sound Management of Chemicals (IOMC) Toolbox for decision-making in chemicals management, International Safety Cards, and a toolkit for registration of pesticides. An electronic distance learning tool for risk assessment and risk management of chemicals was also demonstrated.

For the next Network meeting and beyond, a number of collaborative activities for the CRA sub-network were proposed. One working group was asked to help make the existing CRA Network training database more interactive and useful for developing countries. A fellowship program was also proposed which would allow representatives of sub-network institutions to attend the annual CRI training course on risk assessment and management in Bangkok. CRI will conduct face-to-face training in chemical risk assessment in selected developing countries.

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* Bhutan, Botswana, Brazil, Costa Rica, Egypt, Georgia, Ghana, India, Indonesia, Jamaica, Kazakhstan, Malaysia, Mongolia, Morocco, Myanmar, Nigeria, South Africa, Suriname, Tanzania, Thailand, Tunisia

Association of Urban Particle Numbers and Sources with Childhood Lung Function

Ambient particulate matter (PM) air pollution is a well-documented environmental and public health problem. Most studies on PM health risks have used total mass within different size ranges as exposure indicators.

There has been increasing interest in using particle number concentrations (PNC) as an alternative exposure indicator to assess air quality and associated health risks, but conclusive results are still lacking.

In estimating PM risks, data on distributions of PNC data are commonly categorized into the ultrafine particle [UFP; aerodynamic diameter (Dp) < 0.1 μm] and accumulation particle (AP; 0.1 μm < Dp < 2.5 μm) modes.

Previous risk analyses using size-segregated PNC data have suggested that respiratory and cardiovascular effects might be associated with ambient UFP and/or, AP levels, but again, no consistent and conclusive relationships have been determined.

These inconclusive findings in previous studies may result from not having accounted for the source differences in their examinations of PM health effects.

By contrast, this hypothesis has been evaluated in studies using mass data resolved from source apportionment as inputs to epidemiologic models of the effects of PM on health.

One of the most common source apportionment methods is Positive Matrix Factorization (PMF), a factor analytic approach which seeks to partition the observed PM mass to its originating sources.

Source-based studies have indicated clear associations between human health effects and specific PM sources, especially primary combustions and secondary particles.

The present study was conducted to examine the health effects of source-specific PNC. The researchers de-composed urban PNC data into source factors using PMF and explored associations between source-specific PNC exposures and spirometric indices.

The source categories identified in this study were urban dust from multiple sources (Factor 1), gasoline vehicle emissions (Factor 2), diesel vehicle emissions (Factor 3), aged vehicle emissions (Factor 4), and secondary aerosols (Factor 5).

In addition, health effects due to PNC for UFP, AP, and total particles (TP; the sum of UFP and AP) size fractions were examined in order to determine whether there were any differences in estimated risks between source-specific and size-segregated PNC impacts.

Spirometry, measured as forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and forced expiratory flow (FEF), was recorded monthly for 59 children with asthma or allergies at five schools during 2007-2008.

The results provided preliminary evidence that secondary source PNC may be more strongly associated with pediatric lung functions than other sources.

In this study, AP were not positively associated with FVC and FEV_1, even though the profile of secondary aerosols covered a considerable size range of AP.

This indicates that previous studies of PM health risks, which have relied on size-segregated PNC as an indicator without considering their multi-source nature, may underestimate the health impact of PM.

These findings also suggest that PNC of secondary origin as one most responsible for pollution-related respiratory effects among children living in urban Taipei. Studies that rely on exposure to size segregated PNC may underestimate PM health impacts.

Therefore, integrating additional information on the composition of PM with size distribution profiles would improve the identification of the sources that are most responsible these health effects.

In conclusion, the researchers observed inverse and significant associations between spirometric lung function indices and secondary particle number concentrations in urban air.

Respiratory health effects may vary among different sources of PM. Future research on PNC should incorporate source apportionment models in the examinations of PM health effects.

Source: Science of the Total Environment Part A, Vol. 54, Pages 841–844, January 2016.

Maternal Urinary Bisphenol A Levels and Infant Low Birth Weight

Low birth weight (LBW), defined as a birth weight of a liveborn infant of less than 2500 grams, is a significant public health concern, as it is a leading cause of infant morbidity and mortality and is one of the main risk factors for global disease burden.

LBW can be caused by multiple etiological factors, and accumulating evidence suggests the importance of environmental exposure to contaminants as risk factors for LBW.

Bisphenol A (BPA), an endocrine disrupting chemical, is a high production-volume chemical used in the manufacture of numerous products used in daily life such as bottles, canned food containers, medical equipment, dental materials, and receipt paper.

Concerns have been raised regarding the potential impact of BPA on fetal development as there is evidence showing that BPA may disturb hormonal balance, cause reproductive organ damage and induce malformation.

Although, findings from epidemio-logical studies about asso-ciations between prenatal BPA exposure and birth weight are inconsistent, previous studies do suggest the important of sex-based differences.

(Continued on page 3)

Dermal Exposure to Phthalates in Indoor Air: Experimental Verification

Certain phthalate esters used widely in vinyl plastics and other consumer products have been associated with impaired neurodevelopment, altered genital development, respiratory problems, obesity and the development of diabetes.

Studies of dermal absorption of phthalates have largely focused on skin contact with the chemicals, but some models predict that transdermal uptake directly from ambient air may be a potentially important route of exposure.

Fundamental physical-chemical considerations indicate, for certain phthalate esters, that dermal absorption from air is an uptake pathway that is comparable to or greater than inhalation. Yet this pathway has not been experimentally evaluated and has been largely overlooked when assessing uptake of phthalate esters.

The present study investigated transdermal uptake, directly from the air, of diethyl phthalate (DEP) and di(n-butyl) phthalate (DnBP) in humans.

DEP and DnBP are among the semivolatile organic compounds (SVOCs) predicted to have substantial dermal uptake directly from air.

DEP is used in personal care products such as cosmetics, perfumes, and shampoos; it is also used in the automotive sector and in food packaging.

DnBP is a common ingredient of adhesives and coatings and is used as a solvent for organic compounds, as an anti-foam agent, as a fiber lubricant, and as an additive in cosmetics, including nail polish.

DEP and DnBP have been identified in indoor air and dust samples from around the world. Their metabolites are often the most abundant synthetic chemicals identified in human urine.

The participants in this study, all males between the ages of 27 and 66, were exposed for 6 hr in a chamber containing deliberately elevated air concentrations of DEP and DnBP.

The participants either wore a hood and breathed air with phthalate concentrations substantially below those in the chamber in which phthalate exposure was exclusively dermal or did not wear a hood and breathed chamber air which resulted in both dermal and inhalation exposures.

All urinations were collected over the 48 hours following each exposure period. Metabolites of DEP and DnBP, including mono-ethyl phthalate (MEP), mono-n-butyl phthalate (MnBP) and 3OH-MnBP, were measured in these samples and extrapolated to parent phthalate intakes, corrected for background and hood air exposures.

For both DEP and DnBP, both the dermal and inhalation pathways resulted in similar exposures. The levels of the metabolites MEP, MnBP and 3OH-MnBP in urine samples collected over the next 2 days were roughly half those measured in urine samples following a 6-hr dermal plus inhalation exposure.

The participants stayed in the exposure chamber for just 6 hours, although the previous dermal exposure models had predicted that the concentration of chemicals in the skin would continue to increase for about 36-48 hours. The reserchers expect that dermal exposure would have been much higher relative to inhalation had the participants stayed in the chamber longer.

This apparent disparity may reflect the fact that in this study the participants were exposed to elevated levels of DEP and DnBP for only 6 hr, whereas dynamic modeling indicates that > 40 hr would be required to reach steady-state and maximal uptake via the dermal pathway in comparison to the inhalation pathway.

In conclusion, this study shows that dermal uptake directly from air can be a meaningful exposure pathway for DEP and DnBP.

For other SVOCs whose molecular weight and lipid/air partition coefficient are in the appropriate range, direct absorption from air is also anticipated to be significant.

The present study provides support for including this dermal pathway in risk assessments. Although earlier assessments of human exposure to phthalate esters have included the dermal pathway, it is only recently that dermal absorption directly from air has been part of such assessments.

Source: Environmental Health Perspectives, Vol. 123, No. 10, Pages 928–934, October 2015.

Maternal Urinary Bisphenol A Levels and Infant Low Birth Weight

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This nested case-control study in a Chinese population was designed to investigate whether maternal exposure to BPA during pregnancy was associated with an increased risk of LBW.

BPA concentrations were measured in maternal urine samples collected at delivery, and the information on birth outcomes was retrieved from medical records.

The researchers also determined whether the association between prenatal BPA exposure and LBW was modified by infant sex and maternal age.

Mothers with LBW infants had significantly higher urinary BPA levels than the control mothers. Increased risk of LBW was associated with higher maternal urinary levels of BPA.

The association was more pronounced among female infants than among male infants, with a statistical evidence of heterogeneity in risk. This suggests that females might be more susceptible to BPA exposure before birth.

In conclusion, prenatal exposure to higher levels of BPA may potentially increase the risk of delivering LBW infants, especially for female infants.

Source: Environment International, Vol. 85, Pages 96–103, December 2015.

Effects of Arsenic on Glucose Metabolism/Homeostasis in Estrogen-deficient Female Mice

Recent epidemiological evidence has supported a link between inorganic arsenic exposure and the increased prevalence of diabetes in populations exposed to arsenic in drinking water. Urine arsenic was associated with poor diabetes control in a population of American Indians from rural communities in the United States with a high burden of diabetes.

Previous study reported an association between arsenic and diabetes in participants with uncontrolled diabetes but not in participants with controlled diabetes. Thus, the detailed effects and mechanisms of arsenic-induced diabetes mellitus still remain to be clarified.

Preclinical studies have indicated that estrogen plays a role in sustaining insulin and glucose homeostasis, which underlies a healthy metabolic profile.

High estrogen and testosterone levels in post-menopausal women are related to an increased risk of developing type 2 diabetes.

However, a prospective cohort study found that menopausal hormone therapy was capable of reducing the incidence of new onset diabetes in women.

Therefore, the association of estrogen levels and diabetes mellitus after menopause is complex.

Previous epidemiological studies have reported that the prevalence of diabetes in women > 40 years of age, especially those in the post-menopausal phase, was higher than in men in areas with high levels of arsenic in drinking water.

These studies suggested that an association between arsenic exposure and diabetes might be causal for women but not men. The detailed effect of arsenic on glucose metabolism/homeostasis in the post-menopausal condition is still unclear.

In the present study, the researchers hypothesized that estrogen deficiency is an important factor for arsenic-impaired glucose metabolism/homeostasis in females.

The effects of inorganic arsenic were investigated at doses relevant to human exposure from drinking water on blood glucose and insulin, glucose tolerance, and insulin resistance on estrogen-deficient female mice in the presence or absence of estrogen (17β-estradiol) supplementation. Glucose metabolism were also performed.

Exposure of sham mice to arsenic significantly increased blood glucose, decreased plasma insulin, and impaired glucose tolerance, but did not induce insulin resistance.

Blood glucose and insulin were higher, and glucose intolerance, insulin intolerance, and insulin resistance were increased in arsenic-treated ovariectomized (OVX) mice compared with arsenic-treated sham mice.

The results indicate that estrogen-deficient female mice exposed to arsenic experience an exacerbated diabetic state that resembles type 2 diabetes.

Furthermore, liver phosphoenolpyruvate carboxykinase (PEPCK) mRNA expression was increased and liver glycogen content was decreased in arsenic-treated OVX mice compared with arsenic-treated sham mice.

PEPCK is a key rate-controlling enzyme that catalyzes the first committed step in hepatic gluconeogenesis. Lack of PEPCK gene expression may cause defective insulin signaling and induce hyperglycemia in diabetic animal models.

Glucose-stimulated insulin secretion in islets isolated from arsenic-treated OVX mice was also significantly decreased.

Estrogen supplementation significantly reversed the increased liver PEPCK expression, decreased liver glycogen content, and decreased islet insulin secretion in arsenic-treated OVX mice.

These results indicate that estrogen deficiency enhances impairments in the regulations of liver gluconeogenesis and glycogenolysis and islet insulin secretion in arsenic-treated mice.

Arsenic treatment significantly decreased plasma adiponectin levels in sham and OVX mice. Adiponectin is an adipokine that is released from adipose tissue and directly sensitizes the body to insulin.

These results suggest that reduced adiponectin may play a causal role in arsenic-induced impairment of glucose homeostasis. However, the detailed mechanism remains to be clarified.

Moreover, the researchers found that the regulation of liver gluconeogenesis and glycogenolysis and islet insulin secretion were markedly impaired by arsenic exposure in estrogen-deficient female mice, which could be effectively reversed by estrogen supplementation.

In conclusion, the results in an estrogen-deficient female mouse model and the findings of previous epidemiological studies support the possibility that estrogen deficiency is an important risk factor in arsenic-induced glucose metabolism / homeostasis damage.

The changes in arsenic metabolism in arsenic-treated estrogen-deficient mice remain to be fully investigated.

Source: Environmental Health Perspectives, Vol. 123, No. 11, Pages 1138–1144, November 2015.

IARC Announced the Carcinogenicity of Lindane, DDT, and 2,4-D

On June 23rd, 2015, after convening a meeting of 26 cancer experts from 13 countries, the International Agency for Research on Cancer (IARC; Lyon, France) announced its assessment of the carcinogenicity of the insecticides lindane and 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (DDT), and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D).

The results of the IARC evaluations are as follows:

1. The insecticide Lindane:

Lindane was classified as ***carcinogenic to humans (Group 1).***

There was sufficient evidence in humans for the carcinogenicity of lindane for non-Hodgkin lymphoma (NHL).

Lindane has been used extensively for insect control, including in agriculture and for treatment of human lice and scabies.

High exposures have occurred among agricultural workers and pesticide applicators; however, the use of lindane is now banned or restricted in most countries.

Large epidemiological studies of agricultural exposures in the USA and Canada showed a 60% increased risk of NHL in those exposed to lindane.

2. The insecticide DDT:

DDT was classified as ***probably carcinogenic to humans (Group 2A)***, based on sufficient evidence that DDT causes cancer in experimental animals and limited evidence of its carcinogenicity in humans.

Epidemiological studies found positive associations between exposure to DDT and NHL, testicular cancer, and liver cancer. There was also strong experimental evidence that DDT can suppress the immune system and disrupt sex hormones. However, overall there was no association between breast cancer and DDT levels measured in samples of blood or fat.

DDT was introduced for the control of insect-borne diseases during the Second World War and was later applied widely to eradicate malaria and in agriculture. Although most uses of DDT were banned from the 1970s, DDT and its breakdown products are highly persistent and can be found in the environment and in animal and human tissues throughout the world.

Exposure to DDT still occurs, mainly through diet. The remaining and essential use of DDT is for disease vector control, mainly for malaria. This use is strictly restricted under the Stockholm Convention.

3. The herbicide 2,4-D :

2,4-D was classified as ***possibly carcinogenic to humans (Group 2B)***, based on inadequate evidence in humans and limited evidence in experimental animals. There is strong evidence that 2,4-D induces oxidative stress, a mechanism that can operate in humans, and moderate evidence that 2,4-D causes immunosuppression, based on *in vivo* and *in vitro* studies.

However, epidemiological studies did not find strong or consistent increases in risk of NHL or other cancers in relation to 2,4-D exposure.

Since its introduction in 1945, 2,4-D has been widely used to control weeds in agriculture, forestry, and urban and residential settings. Occupational exposures to 2,4-D can occur during manufacturing and application, and the general population can be exposed through food, water, dust, or residential application, and during spraying.

Detailed assessments will be published in Volume 113 of the IARC Monographs: Some Organochlorine Insecticides and Some Chlorphenoxy Herbicides (in Press).

Source: The Lancet Oncology, Volume 16, Issue 8, Pages 891-892, August 2015.

Role of Epigenetics in the Latent Effects of Early Life Exposure to Obesogenic Endocrine Disrupting Chemicals

The current global epidemic of obesity poses a serious threat to human health. The main contributing factors to this epidemic include high caloric intake, a sedentary lifestyle, and genetic predisposition.

Recent research also points to the role in this global epidemic of exposure to endocrine-disrupting chemicals (EDCs).

Obesogenic EDCs have the potential to inappropriately stimulate adipogenesis and fat storage, influence metabolism and energy balance and increase susceptibility to obesity.

In particular, early life exposure to obesogenic EDCs has been linked to latent effects on obesity-related outcomes in epidemiological and animal studies.

Developmental exposure to obesogenic EDCs may interfere with epigenetic programming of gene regulation, partly by activation of nuclear receptors, thereby influencing the risk of obesity later in life.

This minireview briefly describes the epigenetic mechanisms underlying developmental plasticity. It also assesses the evidence of a mechanistic link between altered epigenetic gene regulation by early life EDC exposure and latent onset of obesity.

The results of recent *in vitro, in vivo*, and transgenerational studies summarized here clearly show that the obesogenic effects of EDCs such as tributyltin, brominated diphenyl ether 47, and polycyclic aromatic hydrocarbons are mediated by the activation and associated altered methylation of peroxisome proliferator-activated receptor-γ (PPARγ), the master regulator of adipogenesis, or its target genes.

The studies published so far tend to focus on PPARγ, but this provides an undeniably narrow interpretation of the multiple mechanisms that could be altered when considering a complex disorder as obesity.

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Biomarkers of Pesticide Exposure in Non-invasive Human Specimens

The potentially adverse effects of exposure to pesticides on the general population, and specifically on the more susceptible groups such as infants and children, are a public health concern.

Apart from the conventional approach of assessing external exposure to pesticides (environmental monitoring), there is a growing interest in evaluating integrated exposure to environmental chemicals using human biomonitoring, defined as the measurement of chemicals or their metabolites in human tissues or specimens.

Human biomonitoring has been used in many types of investigations to explore the occurrence of biomarkers of pesticide exposure in the general population or relevant groups.

Ideally a valid biomarker of exposure should be sensitive. That is, it should allow the measurement of the contaminant after exposure and should vary accordingly. To be valid, the biomarker should be specific to the chemical of interest, and also biologically relevant.

In an ideal matrix for biomonitoring studies, the chemicals or their metabolites in human tissues or specimens should be accessible in sufficient amounts without a risk for the donor. These elements should reflect the body burden, should contain detectable levels of the biomarker in terms of the analytical methods available, and should be easy to collect (non-invasive) and store.

The main objective of this review is to present the most recent data (i.e. within the last six years) on the occurrence of currently used biomarkers of pesticide exposure in non-invasive matrices, namely urine, breast milk, hair and meconium.

Specific and non-specific metabolites of organophosphate and pyrethroid insecticides have been widely investigated in urine, where some of the suitable biomarkers present rates of detection higher than 80%. Such high levels reflect ongoing chronic exposure to traces of these chemicals.

More health-related human biomonitoring values are needed for the most frequently used and most toxic pesticides, if we are going to better interpret biomonitoring data, better evaluate temporal trends, or more quickly detect highly-expsoed populations.

Human milk can be used to evaluate the exposure of lactating women and their breast-feeding children to environmental chemicals. Breast milk can provide useful information about time trends of legacy pesticides and other lipophilic pollutants.

Hair is another promising matrix for assessing exposures to both persistent and currently used pesticides, but some issues on its sensitivity and capability for measuring internal dose and its biological relevance require further research.

Meconium is an appropriate matrix for measuring prenatal exposure to pesticides. Chemicals accumulate in meconium from the third month of gestation until birth, so its analysis reflects any long-term exposure of the fetus. It can be collected straightforwardly, and in large amount. Despite this, there are not many studies using meconium to evaluate these prenatal exposures.

Although both specific and group biomarkers are relevant for biomonitoring studies, the development of non-specific group biomarkers is particularly relevant, given the frequent changes in the regulation of pesticides, with ongoing restrictions and bans of specific substances.

In order to share findings and compare results, the importance of analytical methods, and of inter-laboratory quality assurance/quality controls should be highlighted. More efforts are needed to bring all the various research efforts in this field into greater harmony and to help us communicate the results more effectively.

Source: Chemosphere, Vol. 139, Pages 91-108, November 2015.

Role of Epigenetics in the Latent Effects of Early Life Exposure to Obesogenic Endocrine Disrupting Chemicals

(Continued from page 5)

It is also clear that the complex interplay of DNA methylation, histone modifications, and noncoding RNA has not been studied yet in the context of obesogenic EDCs, because most studies in this field have focused on DNA methylation.

A combination of changes in histone marks and DNA methylation to key genes involved in mitochondrial metabolism underlie the effects of perinatal BPA exposure and latent onset of steatosis. More studies of this type are needed to better understand chromatin conformational changes by EDCs.

Importantly, studies are emerging that assess the effects of EDCs on the interplay between DNA methylation and histone modifications in altered chromatin structure.

Genome-wide epigenetic analysis is clearly the way forward to provide a more unbiased identification of regulated genes and sites of epigenetic modification.

These types of studies coupled with genome-wide rather than gene-specific analyses are needed to improve mechanistic understanding of epigenetic changes by EDC exposure.

Current advances in the field of epigenomics have led to the first potential epigenetic markers for obesity that can be detected at birth, providing an important basis to determine the effects of developmental exposure to obesogenic EDCs in humans.

Epidemiological studies which link EDC exposure, epigenetic gene regulation, and obesity outcomes are needed to understand the effects of developmental exposure to EDCs and to identify epigenetic biomarkers of latent onset of obesity in humans.

Source: Endocrinology, Vol. 156, Issue 10, Pages 3466–3472, October 2015.

Developmental Neurotoxic Effects of Chlorpyrifos and Carbaryl

Incidences of neurodevelopmental disorders and dysfunctions, associated with pesticide exposure have been increasing. They include, for example, autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), developmental delays, and learning disabilities.

Two of the most common insecticides currently in use worldwide are organophosphates (OPs) and carbamates, the acute neurotoxic effects of which inhibit the enzyme acetylcholine esterase (AChE) in the nervous system.

OPs are considered the more adverse of the two insecticides. The AChE inhibition caused by OPs is long lasting, sometimes even irreversible once aging has occured. By contrast AChE inhibition caused by carbamates lasts only minutes to hours. Symptoms occur when AChE inhibition surpasses ~70%.

The mammalian central nervous system goes through several distinct developmental stages before reaching full maturation. During these stages the brain is more sensitive to toxic insults.

One of these critical stages of brain development is known as the "brain growth spurt" or BGS, and is characterized by a rapid increase in brain size. This sudden expansion of biochemical processes includes, for example, synaptogenesis, neuronal proliferation and myelination.

These processes are regulated by proteins such as calcium/calmodulin-dependent kinases II (CaMKII), growth associated protein-43 (GAP-43), glutamate receptor 1 (GluR1), post-synaptic density protein-95 (PSD95), synaptophysin and tau.

The neurodevelopmental sequence is similar between human and murine animals; the primary difference is in timing. That is, the human BGS is perinatal, starting around the third trimester, peaking around birth, and extending up to the first years of life.

On the other hand, the murine BGS is neonatal, starting from birth, peaking around postnatal day 10, and continuing up to the 3rd or 4th week of life.

The present study focused on two different pesticides, chlorpyrifos (OP) and carbaryl (carbamate). Both specifically inhibit AChE in the nervous system.

The objective in this study was to investigate whether a single oral exposure to these pesticides during a period of BGS and maturation could cause neurochemical changes in the protein levels of CaMKII, GAP-43, GluR1, PSD95, synaptophysin and tau in the mouse brain and induce adult neurobehavioral disruptions.

The researchers also investigated for possible developmental neurotoxic effects linked to AChE inhibition in the brain.

The results in mice neonatally exposed to a single oral dose of chlorpyrifos or carbaryl on postnatal day 10, show that both compounds can affect protein levels in the developing brain and induce persistent impairment of cognition and behavior in adults.

The timing of the exposure was shown to be an additional factor, as a single exposure to either chlorpyrifos or carbaryl at the peak of the BGS caused developmental neurotoxic effects.

The behavioral effects may be attributed to the disturbance of normal brain development, as the levels of several important proteins were shown to be altered.

In regard to protein changes and behavioral effects, carbaryl may be as adverse developmental neurotoxicant as chlorpyrifos

Although some proteins are highly involved in learning and memory processes, it is still unlikely that a single protein could be fully responsible for all of the functional neurotoxic effects seen.

The results also indicate that the developmental neurotoxic effects induced are not related to the classical mechanism of acute cholinergic hyperstimulation, as the AChE inhibition level (8–12%) remained below the threshold for causing systemic toxicity.

Such behavioral and cognitive effects may be induced by an alternative cholinergic mechanism such as the serotonergic, dopaminergic and endocannabinoid pathways as a downstream effect, or because of oxidative stress.

However, the neurotoxic effects are more likely caused by disturbed neurodevelopment. Similar behavioral neurotoxic effects have been reported in studies with pesticides such as organochlorines, organophosphates, pyrethroids and POPs, when exposed during a critical window of neonatal brain development.

It is more plausible that several contributing mechanisms are in play. Hence, further investigations are in order, not only to identify and better understand the underlying mechanisms of developmental toxicants, but also to find prevention models.

Source: Toxicology and Applied Pharmacology, Vol. 288, Issue 3, Pages 429–438, November 2015.

CONGRESS ANNOUNCEMENT

The 8th Princess Chulabhorn International Science Congress

Congress Theme: **ENVIRONMENTAL HEALTH: INTER-LINKAGES AMONG THE ENVIRONMENT, CHEMICALS AND INFECTIOUS AGENTS**

November 13-17, 2016 at Shangri-La Hotel, Bangkok, Thailand

Chairperson of Organizing Committee: **Professor Dr. HRH Princess Chulabhorn**

Nobel Laureate Lecture: The Critical Role of the Ubiquitin Pathway in the Development of Human Disease,
Aaron Ciechanover (Nobel Laureate, Israel)

ANNOUNCEMENT AND CALL FOR ABSTRACTS

The Congress will be held **to commemorate the seventieth anniversary celebrations of His Majesty King Bhumibol's accession to the throne, His Majesty's upcoming ninetieth birthday, and the seventh cycle (84 years) birthday of Her Majesty Queen Sirikit,** auspicious occasions for the people of Thailand to celebrate and pay tribute to Their Majesties the King and Queen. The program will feature a Nobel Laureate Lecture, Keynote Lecture, Plenary Lectures, Symposia, Platform and Poster Presentations. Concurrent workshops on issues relating to the focus of the Congress are also organized.

The scientific program will cover the following areas:

- Chemical and infectious agents
- Exposure
- Diseases resulting from environmental exposure
- Mechanisms and pathways of disease development
- Modifiers of susceptibility and disease outcomes
- Tools and technologies
- New and emerging therapy

For further information, please visit the Congress Website:

https://pc8.cri.or.th

CALL FOR ABSTRACTS:

All congress participants are invited to submit abstracts for platform or poster presentations. Selection of the submissions to be presented as platform or poster presentations will be made by the Scientific Program Committee.

Deadline for Abstract Submission: **September 15, 2016**

CALENDAR OF EVENTS

International Training Course on Environmental Toxicology (June 2-10, 2016)

Course Coordinator: *Khunying* Mathuros Ruchirawat, Ph.D.

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 and pollutants. 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 of chemistry and the biological/biomedical sciences.

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

The ICEIT NEWSLETTER is published quarterly by the International Centre for Environmental and Industrial Toxicology of the Chulabhorn Research Institute. It is intended to be a source of information to create awareness of the problems caused by chemicals. However, the contents and views expressed in this newsletter do not necessarily represent the policies of ICEIT.

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