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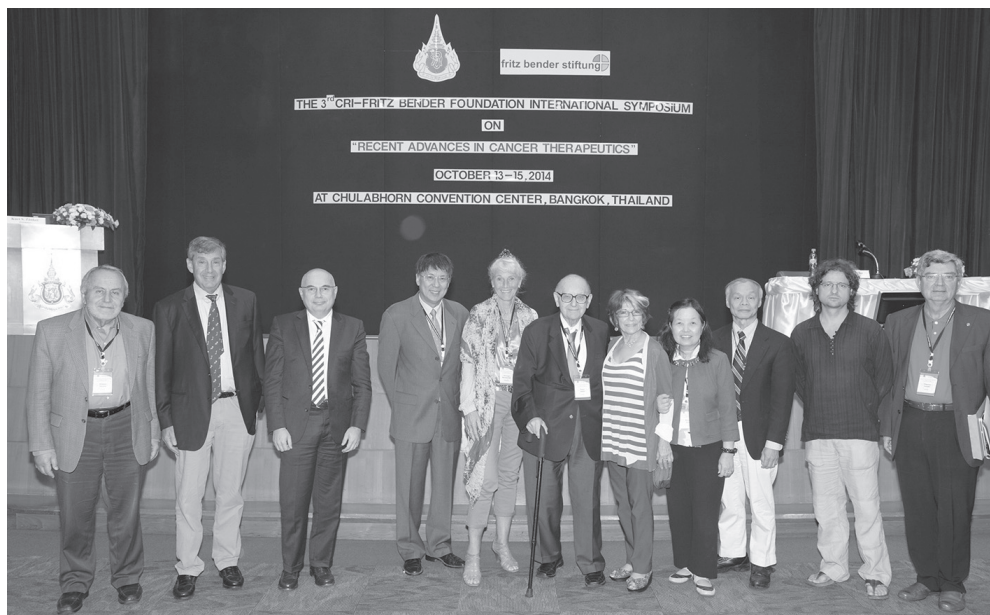
Chulabhorn Research Institute

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".

The 3rd CRI-Fritz Bender Foundation International Symposium on "Recent Advances in Cancer Therapeutics"

October 13-15, 2014 at CRI Convention Center, Bangkok, Thailand



The Chulabhorn Research Institute (CRI) co-hosted a symposium on "Recent Advances in Cancer Therapeutics" with the Fritz Bender Foundation at the CRI convention center between October 13-15, 2014.

This symposium was organized as a platform for sharing information and expertise on cancer research, thereby fostering cooperation with other academic and research institutions, both nationally and internationally. Such cooperation is needed to bring together experts in oncology, as well as other scientists, post-doctoral fellows, physicians, pharmacists, nurses, and health care professionals directly involved in the fight against cancer. Participants in the symposium had the opportunity to interact

with experts, and to keep abreast of the most recent development in research leading towards more effective cancer treatment and therapy. Professors Enrico Mihich (Dana-Farber Cancer Institute, USA), Kurt S. Zänker (University of Witten/Herdecke, Germany), and Mr. Hans-Peter Huber (Fritz Bender Foundation, Germany) played key roles in helping to organize and fund various aspects of the symposium.

The opening address delivered by Mr. Chawat Arthayukti, Representative of Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, emphasized the goal of the symposium: to inspire and carry forward greater collaboration among cancer researchers.

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The 3rd CRI-Fritz Bender Foundation International Symposium on “Recent Advances in Cancer Therapeutics”

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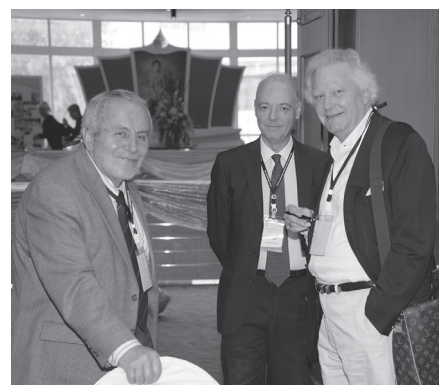
Guest speakers included 21 distinguished academics and cancer researchers from 11 countries, who conduct studies at the basic, translational and clinical levels in various international research centers. They gave presentations on five different areas of cancer research: Genetic Profiles of Cancer, Therapeutic Targets and Drugs, Experimental Therapeutics, Tumor-Host Relationships, and Translational Investigations. The presentations outlined the advances being made in cancer research and included descriptions of the latest technology available in the field. Researchers from various Thai research and academic institutions, including from CRI and the Chulabhorn Hospital (CCC), attended the symposium to learn about the latest

advances in the treatment of cancer, to share their experience, and to hear about progress in areas where breakthroughs are most urgently needed. This was the third such event co-hosted by the two institutions, and the 18th academic meeting under the auspices of the Fritz Bender Foundation.

Professor Dr. Her Royal Highness Princess Chulabhorn, President of the Chulabhorn Research Institute, is well aware of the challenges posed by cancer. It is now one of the leading causes of death in developed and developing countries, including in Thailand, where liver cancer and cholangiocarcinoma occur more commonly than anywhere else in the world. More people die from cancer nowadays than from AIDS, tuberculosis and malaria combined, and the death toll will likely climb dramatically over the coming decades. It has been predicted that, over the next ten years, as many as 84 million people will die of cancer, and more than 70% of them will be in the developing countries.

There is therefore an urgent need for collaborative research to combat this

devastating disease. There have been encouraging recent developments, but much more work still needs to be done in all areas of basic, translational and clinical research. Research and studies of the etiology of various kinds of cancer are leading to improvements in our understanding of the disease and are providing the basis for the development of exciting new cancer therapeutics. However, there is still much work to be done. Collaborations to pool resources and expertise is crucial in efficiently addressing this very important public health threat for the peoples of the developed and developing countries.



Exposure to Ambient Air Toxics and the Risk of Leukemia in Pregnancy and Early Childhood

Leukemia is the most common cancer type in children, with 5000 new cases expected in the US in 2012. The most common type of childhood leukemia is acute lymphoblastic leukemia (ALL), which accounts for 78% of cases in childhood, followed by acute myeloid leukemia (AML) which makes up 16% of childhood leukemias. Established causes of childhood leukemia including genetic predisposition, ionizing radiation, and chemotherapeutic agents are estimated to explain <10% of cases, leaving the majority of cases with an unresolved etiology.

Less is known about whether exposure to the low levels of chemicals that pregnant mothers and children are exposed to in everyday life (“ambient exposures”) increase risk for leukemia.

Using a case-control sample of linked cancer registry and birth records, a new study has investigated associations between air toxics exposures in pregnancy and early life in relation to leukemia in young children. Risk of ALL was elevated with 3rd trimester exposure to polycyclic aromatic hydrocarbons, arsenic, benzene, and three other toxics related to fuel

combustion. Risk of AML was increased with 3rd trimester exposure to chloroform, benzene, and two other traffic-related toxics. During the child’s first year, exposure to butadiene, ortho-xylene, and toluene increased risk for AML and exposure to selenium increased risk for ALL. Benzene is an established cause of leukemia in adults; this study supports that ambient exposures to this and other chemicals in pregnancy and early life may also increase leukemia risk in children.

Only one PAH, benzo(a)pyrene, has been classified as an established

human carcinogen, based upon the results of experimental studies as well as biological plausibility. PAH exposure in ambient air is associated with chromosomal aberrations in cord blood, and immune system dysfunction is observed in mice exposed to PAHs in utero. This is thought to be the first human study to report on a potential association between childhood leukemia and PAH exposure.

Source: International Journal of Hygiene and Environmental Health, Vol. 217, Issue 6, Pages 662-668, July 2014.

ASSESSING HUMAN HEALTH RISKS ASSOCIATED WITH ANDROGEN RECEPTOR ANTAGONISTS

Although evidence for links between exposure to specific chemicals and testicular dysgenesis syndrome in humans is currently limited, support for the plausibility of an involvement of androgen receptor (AR) antagonists comes from experimental studies using a developmental toxicity model in the rat. Exposure of male rats to AR antagonists and other anti-androgens in foetal life leads to incomplete masculinisation and severe malformations of the reproductive organs, similar to some of the disorders seen in humans, such as cryptorchidisms and hypospadias. These observations have provided the stimulus to assess human health risks associated with AR antagonists.

In the present study, a combination of 30 AR antagonists was selected for testing by a reporter gene assay (MDA-Kbz), which comprised 13 pesticides (herbicides, insecticides, fungicides) and 17 non-pesticides (antioxidants, parabens, UV-filters, synthetic musks, bisphenol A (BPA),

benzo(a)pyrene, perfluorooctane sulfonate and pentabromodiphenyl ether). While human exposure to the 13 selected pesticides was inferred from their wide use in the EU, the 17 non-pesticides were selected based on their high levels in human tissues. These chemicals together covered a wide range of sources and exposure routes, including oral, dermal and inhalation. The large number of chemicals included in the mixtures provided the opportunity to assess the combined effects of AR antagonists at low concentrations, particularly at concentrations where the effects of the single components are below the detection limit of the assay. Concentration addition (CA) and independent action were used to calculate additivity expectations.

Complete suppression of dihydrotestosterone effects when chemicals were combined at individual concentrations eliciting 1%, 10% or 20% AR antagonistic effect were observed. Due to the large number of components, the combined AR antagonistic effects

occurred at very low concentrations of individual mixture components. CA slightly underestimated the combined effects at all mixture ratios. In conclusion, large numbers of AR antagonists from a wide variety of sources and exposure routes have the ability of acting together at the receptor to produce joint effects at very low concentrations. Significant mixture effects are observed when chemicals are combined at concentrations that individually do not induce observable AR antagonistic effects.

However, this study has shown that the often low levels measured for individual AR antagonists are not a reliable indicator for dismissing risks from this class of chemicals. Renewed efforts of searching for AR antagonists in human tissue will be required for cumulative risk assessment.

Source: Toxicology and Applied Pharmacology, Vol. 278, Issue 3, Pages 201-208, August 2014.

Regulations and Guidance on Particulate Matter Concentrations and Indoor Air Quality

Global climate change and increasing energy requirements have led to the development of energy-saving buildings typically characterized by low air-exchange rates. Given that people may spend more than 90% of their time in such enclosed spaces during the main activities of living, working and transportation, the investigation of indoor air quality in these micro-environments is of paramount importance.

The PM_{2.5} can be classified as outdoor and indoor sources. For example, PM_{2.5} originating from outdoor sources (i.e., traffic, industrial activities) can infiltrate into indoor environments through ventilation but indoor activities (i.e., cooking, smoking, resuspension of settled dust) may also contribute. Laser printers, photocopiers and multi-task devices are well known sources for

ultra-fine particles (diameter < 0.1 µm) in the office environment.

Fine particles are composed mainly of primary and secondary organic compounds, black and elemental carbon, sulfate, nitrate and ammonium ions as well as metal compounds. In a previous study carried out in Budapest, the trace element contribution to the PM_{2.5} mass concentration ranged between 1% and 3%. Although elemental components constitute only a small portion by mass of PM, some trace elements (e.g., Cu, Fe, Cr, V, Ni, etc.) may pose a serious threat to human health by causing oxidative stress via ROS production and antioxidant depletion.

The present study was conducted in Hungary according to the guidelines of the OFFICAIR (On the reduction of health

effects from combined exposure to indoor pollutants in modern offices) project.

Fifty samples of indoor and outdoor PM_{2.5} were collected onto quartz fiber and Teflon membrane filters in five office buildings equipped with heating, ventilation and air-conditioning (HVAC) system for 8 h daily in order to coincide with the work shift of employees. Samples were analyzed for i) mass concentration; ii) elemental concentration; and iii) oxidative potential (OP) through antioxidant depletion.

The study found that mass concentrations of indoor and outdoor PM_{2.5} correlated almost linearly. The PM_{2.5} mass concentration exceeded the 10 µg/m³ WHO annual mean guideline value in 50% of the samples. Thus, the

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PULMONARY EFFECT OF AIR POLLUTION IN THE ELDERLY

By 2030, there will be 72.1 million people \geq 65 years of age, representing 19% of the U.S. population, according to the Department of Health and Human Services. The aging process reduces physiological capacity, which makes the elderly more susceptible to many health threats. There is compelling evidence that short- and long-term exposure to ambient air pollution, especially due to traffic, adversely affect lung function. However, most of the studies have focused on children. Although research examining the effects of air pollution on forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV₁) in the elderly is warranted, however these associations have not yet been investigated.

The underlying mechanisms linking air pollution and lung function are not fully characterized. Lung function has been shown to be strongly heritable, part of which is controlled by inflammatory genes. Consistent with this observation, many studies have reported associations

between lung function and polymorphisms within genes coding for inflammatory, oxidative stress and innate immunity mediators. There is increasing evidence that epigenetic mechanisms may interact with genetic variation to influence disease pathogenesis and the inheritance of disease traits.

Methylation in CpG-rich regions within gene promoters is commonly associated with repressed gene expression, because it may impede the binding of transcription factors. Studies in humans have reported associations between blood DNA methylation and cardiovascular diseases, respiratory health, and survival.

A new study has hypothesized that short-term exposure to traffic-related air pollutants would be associated with lung function decrease in the Normative Aging Study cohort of 776 elderly men living in the Boston, Massachusetts, USA area. Subsequently,

it examined whether methylation level within or near the promoter region of selected genes related to inflammation, immunity, endothelial function, and oxidative stress may be a susceptibility factor for lung function impairment.

The results of this study suggest that methylation in inflammation- and immunity-related genes might contribute to the effect of air pollution. DNA methylation marks are established mainly during early life, and although thought to be a fairly stable measure, DNA methylation has been associated with aging. In the data, almost all associations between air pollutants and lung function remained after adjustment for DNA methylation, which suggests that pulmonary effects of air pollutants were not mediated by methylation.

The study generally observed stronger associations of air pollutants with FVC than with FEV₁, suggesting that air pollution may affect more of the smaller airways and therefore is associated with restrictive lung diseases. In the elderly, particle clearance might be less efficient or impaired by other dysfunctions. The apparently small effects of air pollution on lung function should not be underestimated because they might be well tolerated by a healthy population, but become life threatening for elderly or ill subjects. In addition, repeated occurrences of short-term decrements in lung function and accompanying inflammation may play some role in the development of long-term decrements.

Nevertheless the study adds to the growing body of literature on short- and long-term effects of traffic-related air pollutants mainly studied in children and young adults, by showing that subchronic but not acute exposure is associated with lower lung function in the elderly. As for the mechanisms, alongside previous studies on genetic variation in inflammatory and immunity genes and respiratory impairment susceptibility, the results suggest that epigenetic mechanisms related to inflammation and immunity may also be implicated in these associations.

Source: Environmental Health Perspectives, Vol. 122, No. 6, Pages 566-572, June 2014.

Prenatal Exposure to Organophosphate Pesticides and Social Behavior in Childhood

Organophosphate pesticides (OPs) are acutely neurotoxic at high doses. The primary mechanism of action at these doses is inhibition of acetylcholinesterase, which leads to an accumulation of acetylcholine at the neuronal junction. At low doses, OPs have several suspected mechanisms of action, including disruption of nuclear transcription factors, interference with neural cell development and neurotransmitter systems, and altered synaptic formation. Fetuses and babies are thought to be highly susceptible to OP exposure, due to the ready transmission of OPs through the placenta, and the immaturity of metabolic pathways required to process and excrete these compounds. OPs were removed from the USA market for most residential uses in the early 2000s, although exposure in the general population can still occur through dust reservoirs and ingestion from approved agricultural uses.

OP exposure has been negatively associated with a wide range of childhood cognitive and behavioral outcomes such as pervasive developmental disorder (PDD), an umbrella term which includes autism spectrum disorders (ASDs).

The Social Responsiveness Scale (SRS) is a parent/caregiver survey designed to quantify impairments in reciprocal social behaviors. While these impairments are useful in distinguishing ASD from other child psychiatric conditions, they are not necessarily specific to ASD, in that deficits in social reciprocity may also be found in conditions such as attention-deficit hyperactivity disorder (ADHD), language problems, maladaptive behavior, social anxiety, and mood disorders.

Thus, a new study investigated the relationship between biomarkers of

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DNA-DAMAGING EFFECT OF SYNTHETIC PYRETHROIDS

Synthetic pyrethroids are among the most common pesticides currently in use worldwide for pest control and community anti-mosquito programmes, thus a significant part of the population may be exposed to these compounds. Pyrethroids are strongly lipophilic agents that paralyze the peripheral and central nervous system of insects by interacting with sodium channels on nerve membranes. Since they play an effective, therefore extensive, role in out-break control and in protecting agricultural crops, it is essential to carefully study and analyze the hazards of pyrethroids to human health including their cytotoxic and genotoxic properties, in order to take adequate measures that prevent humans from potential mutagenic and carcinogenic effects.

Phenothrin ($C_{23}H_{26}O_3$) is a synthetic type-I non-cyano pyrethroid insecticide which was first registered by the US-EPA in 1976. It is widely used in pesticide products as a spray against agricultural and household insects, as well as in the area of public health against insect vectors that can spread communicable diseases among human populations. In addition, phenothrin has therapeutic applications, particularly in the elimination of human louse infestation, in which case it is formulated as a powder, shampoo, or lotion.

Phenothrin is an effective nerve stimulant that affects the conduction of nerve impulses by forcing the sodium channels of insects to remain open; the ensuing excessive sodium discharge eventually leads to paralysis. The sensitivity of human nerves to phenothrin is low, nevertheless studies have reported toxic effects of phenothrin generally observed in humans including symptoms such as dizziness, salivation, headache, fatigue, diarrhoea, and irritability to sound and touch. Although phenothrin was found to be non-mutagenic in *Escherichia coli* strains, data provided by mutagenicity and genotoxicity studies with higher organisms are lacking. Its carcinogenic potential was investigated by *in vivo* animal studies, in two of which phenothrin increased the incidence of liver cancer; however, this effect did not reach statistical significance. On the basis of these limited findings, phenothrin has been classified by the US-EPA as "not likely to be carcinogenic to humans".

The results of a recent study show that phenothrin induces statistically significant, dose-dependent DNA damage in the absence of marked cytotoxicity of concentrations higher than 20 μM and 50 μM in human blood peripheral lymphocytes and hepatocytes, respectively. Oxidative DNA damage could also be detected in the two cell

types, although this did not reach scientific significance.

These findings provide the first evidence that the pyrethroid insecticide phenothrin has pronounced genotoxic potential. The effective doses observed in this study are in the low micromolar range, which is close to, although higher than the internal dose of phenothrin estimated by extrapolation from the limited data on endogenous concentrations of other synthetic pyrethroids. Nevertheless, due to the stochastic nature of a genotoxic effect without a threshold of safety, the DNA-damaging potential cannot be ruled out at lower concentrations. The limited data available on the toxic effects of phenothrin and the positive results reported here, with the agent used on primary and secondary cell cultures, call for further studies to characterize the genotoxic properties of this pesticide. In the light of these findings, it is advisable to reconsider the health hazards of phenothrin, especially in regard to its DNA-damaging potential. First and foremost, in order to minimize the risk of exposure and related health effects, cautious use of phenothrin-containing products can be recommended, in particular the avoidance of direct human applications.

Source: Mutation Research, Vol. 770, Pages 1-5, August 2014.

Regulations and Guidance on Particulate Matter Concentrations and Indoor Air Quality

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target value of 25 $\mu\text{g}/\text{m}^3$ for ambient $\text{PM}_{2.5}$ annual mean mass concentration set by the European Commission may be reconsidered. On the other hand, the indoor/outdoor (I/O) $\text{PM}_{2.5}$ mass concentration ratios being – with one exception – less than the unit indicated that fine aerosol particles were more or less effectively filtered out by the HVAC systems. This finding is a good indication that the $\text{PM}_{2.5}$ was not directly affected by any substantial source indoors.

Due to the low amounts of particles collected, the non-destructive and non-preparative proton-induced X-ray emission spectrometry was used for the monitoring of 21 elements. Among these

elements, quantitative determination of Al, Si, S, Cl, K, Ca, Ti, Cr, Mn, Fe and Zn was achieved in all samples collected onto Teflon membrane filters in the ng/m^3 concentration level. Due to its filamentary structure and greater thickness, quartz fiber filters were less adequate for quantitative determination of elements than Teflon membrane filters. Taking into account the I/O ratios of the element concentrations, Ca, Cr, Zn and Ti had generally higher concentrations indoors. From the aforementioned elements, Cr and Zn should have a higher implication on human health, since they may play an important role in the oxidative stress. In terms of the OP, the I/O OP ratios calculated for GSH were

higher especially for three buildings which, in return, were also characterized by higher I/O Cr and Zn concentration ratios.

The study concluded that, OP as a metric of aerosol particle toxicity pointed out that $\text{PM}_{2.5}$ collected in offices equipped with HVAC systems may have a higher adverse effect on human health. Thus, PM chemical composition is more important than PM mass in relation to oxidative activity.

Source: Atmospheric Environment, Vol. 94, Pages 44-52, September 2014.

The Role of Endocrine Disruptors in Autism Spectrum Disorders

Autism spectrum disorders (ASDs) affect approximately 1% of U.S. children and are characterized by impaired interpersonal behavior or communication and repetitive or stereotypic behaviors that begin before 3 years of age. Two lines of evidence suggest that the endocrine system plays a role in the etiology of ASDs. First, males are four times as likely to be diagnosed with ASDs as females. Second, adrenal, gonadal, and thyroid hormones play an important role in fetal neurodevelopment.

In utero environmental exposures may increase the risk of ASDs. Specifically, it has been proposed that endocrine-disrupting chemicals (EDCs) may alter endogenous hormone axes to interfere with steroid-dependent neurodevelopment and modify the risk of ASDs.

Despite the importance of identifying modifiable risk factors for ASDs and large number of EDCs in the environment, few epidemiological studies have examined the relationship between gestational EDC exposures and ASDs. Thus, epidemiological studies with multiple EDC exposure biomarkers employing robust statistical methods are needed to screen components of the chemical mixtures humans are exposed to and identify the effect of individual EDCs from correlated co-pollutants.

To address this important research need, a new study used a semi-Bayesian hierarchical regression model to estimate associations between prenatal blood or urine concentrations of 52 suspected EDCs and autistic behaviors at 4 and 5 years of age in a prospective birth cohort of 175 mothers who were pregnant between 2003 and 2006 and their children.

At ages 4 and 5 years old, the children were rated by their mothers using the Social Responsiveness Scale (SRS), a tool that assesses behaviors typically related to ASDs.

The women's chemical exposures were similar to levels reported in the 2003–2004 iteration of the National Health and Nutrition Examination Survey and they found that higher maternal exposures to *trans*-nonachlor and PBDE-28 were associated with higher average SRS scores. *Trans*-nonachlor is a component of the highly persistent banned pesticide chlordane, and PBDE-

28 is one of the polybrominated diphenyl ether compounds used as flame retardants in commercial goods containing polyurethane foam (including furniture and mattresses) made before 2005.

The study also found negative associations between four additional chemicals and average SRS scores. These included β -hexachlorocyclohexane (β -HCH), an organochlorine pesticide; perfluorooctanoic acid, a compound used to make many industrial polymers and products including Teflon; PCB-178, one of the polychlorinated biphenyls once used in hundreds of industrial and commercial applications; and PBDE-85, another PBDE congener. These results are consistent with some earlier studies but not others; the authors suggest the apparent contradictions may result from differences in the end points studied and the timing of exposure assessment.

Most biomarkers of maternal EDC exposure during pregnancy were not clearly associated with autistic behaviors in 4- and 5-year-old children in this cohort. Although this hypothesis-generating study cannot definitely identify chemical risk factors for ASDs, these results suggest that additional studies examining the relationship between ASDs and gestational exposure to PFOA, PCB-178, PBDE-28, PBDE-85, β -HCH, and *trans*-nonachlor are warranted. Given the mixture of environmental chemicals that pregnant women are exposed to, future studies should consider statistical techniques that account for the complex mixture of potentially modifiable prenatal environmental chemical exposures that might be associated with ASDs.

Source: Environmental Health Perspectives, Vol. 122, No. 5, Pages 513-519, May 2014.

Prenatal Exposure to Organophosphate Pesticides and Social Behavior in Childhood

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prenatal OP exposure and impaired reciprocal social behavior in childhood, as measured by the SRS. Using a multi-ethnic urban prospective cohort of mother–infant pairs in New York City recruited between 1998 and 2002 the study examined the relation between third trimester maternal urinary levels of dialkylphosphate (Σ DAP) OP metabolites and SRS scores among 136 children who returned for the 7–9 year visit. Overall, there was no association between OPs and SRS scores, although in multivariate adjusted models, associations were heterogeneous by race and by sex. Among blacks, each 10-fold increase in total diethylphosphates (Σ DEP) was associated with poorer

social responsiveness. There was no association among whites or Hispanics, or for total Σ DAP or total dimethylphosphate (Σ DMP) biomarker levels. Additionally, stratum-specific models supported a stronger negative association among boys for Σ DEPs, with no notable association among girls.

The results of the study support an association of prenatal OP exposure with deficits in social functioning among blacks and among boys, although this may be in part reflective of differences in exposure patterns.

Source: Environment International, Vol. 70, Pages 125-131, September 2014.

THE EFFECT OF SUBLETHAL PESTICIDE EXPOSURE ON NATURAL FORAGING BEHAVIOR OF THE BUMBLEBEE

Understanding and mitigating the causes of global insect pollinator declines has important consequences for food security and the global economy. Multiple factors have been implicated as causes of bee declines including habitat loss, pathogens and disease, and pesticides.

Although the risks posed by a 'pesticide exposure landscape' have received a great deal of recent interest, comparatively little is known about the possible impacts that such chemicals may be having on individual bees, their colonies and populations. As current agricultural practices rely heavily on pesticides to sustain high crop yields, insect pollinators can be exposed to multiple chemicals in the environment. Bees foraging on treated crops are exposed to pesticides both when they touch flowers (topical exposure) to extract nectar or pollen and when consuming these floral rewards (oral exposure). The level of pesticide to which bees are exposed depends on the amount applied to the target crop. The objective is to provide application guidelines that kill target pests whilst avoiding lethal effects for essential insect pollinators, such as foraging bees. A growing criticism of this risk assessment procedure is that it does not consider potential sublethal effects, in spite of a growing body of evidence indicating that

pesticide exposure, at levels found in treated crops, can lead to behavioural effects in bees and/or increase their susceptibility to parasites.

Social bees rely on the cooperation of many individuals carrying out a multitude of tasks to ensure the colony functions efficiently. Foraging is a fundamental task because colony growth relies on a continuous food supply; therefore, any factors that impair foraging behaviour may have serious consequences for colony survival and reproduction. Laboratory and semi-field studies of honeybees indicate that exposure to field-realistic pesticide concentrations can cause neuronal inactivation, affect motor function, learning performance, communication and also impair homing ability and foraging behaviour. However, the vast majority of studies to date have focused on the behavioural effects that follow acute exposure (i.e. within 48 hours), yet bees in the field are likely to be exposed to pesticide residues over extended

periods of time. Therefore, it is important to increase understanding of both the potential acute and chronic effects on individuals induced by prolonged exposure to field pesticide levels.

Now a new study presents a detailed analysis of the day-to-day foraging patterns of 259 *Bombus terrestris* foragers from 40 colonies over 28 days in the field. In this analysis, researchers examine how the temporal dynamics of foraging behavior are affected following prolonged exposure to either a neonicotinoid (imidacloprid), a pyrethroid (λ -cyhalothrin), or the combination of both pesticides. Colonies were exposed to these two commonly used pesticides at levels approximating field exposure over a 4-week period. The results provide new insights, showing that prolonged pesticide exposure has both acute and chronic effects on fundamental aspects of forager behavior and performance.

Source: Functional Ecology, Pages 1-13, July 2014.

Autism Spectrum Disorders and Prenatal Early-life Exposures to Mercury

Various environmental exposures have been suggested as possible risk factors for autism spectrum disorders (ASD), including mercury, which is a known neurotoxin. Methylmercury, the most common form of organic mercury in the environment, is lipophilic and thus distributes throughout the body, but is preferentially stored in the brain and central nervous system. Methylmercury can cross the placenta and blood brain barrier and is thus a potential contributor to neuro-developmental disorders such as autism.

Previous studies have demonstrated adverse neurodevelopmental outcomes including microcephaly, seizures, and mental retardation, associated with consumption of fish and

bread highly contaminated with methylmercury. These studies determined that the prenatal period was the most susceptible period to neurotoxic exposure.

Now a new study has investigated the association between ASDs and levels of total mercury measured in maternal serum from mid-pregnancy and infant blood shortly after birth.

The study sample was drawn from the Early Markers for Autism (EMA) Study. Three groups of children who were born in Orange County, CA in 2000–2001 were identified: children with ASD, intellectual disability or developmental delay (DD), and general population controls (GP). Maternal serum

specimens and newborn bloodspots were retrieved from the California Department of Public Health prenatal and newborn screening specimen archives. Blood mercury levels were measured in maternal serum samples using mass spectrometer and in infant bloodspots with a 213 nm laser.

The results indicate that levels of total mercury in serum collected from mothers during mid-pregnancy and from newborn bloodspots were not significantly associated with risk of ASD, though additional studies with greater sample size and covariate measurement are needed.

Source: Environmental Research, Vol. 133, Pages 294-303, August 2014.

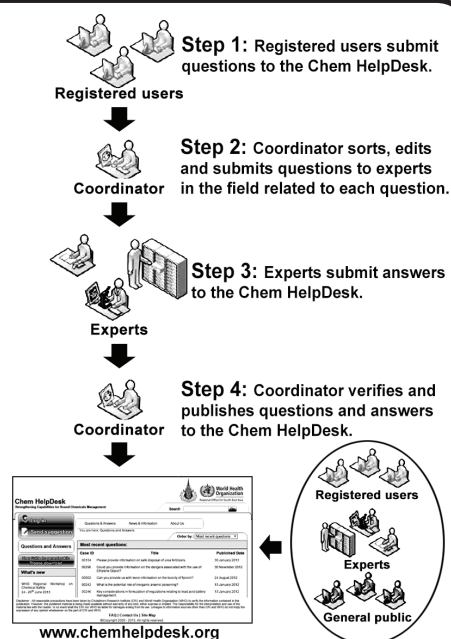
Chem HelpDesk

“Strengthening capabilities for sound chemicals management”

A joint initiative between the Chulabhorn Research Institute (CRI) and the World Health Organization Regional Office for South-East Asia (WHO/SEARO)

The regional chemical helpdesk, initiated in 2008, is a not-for-profit service that provides cost-free answers to questions submitted by registered users in the areas of chemical safety and chemicals management. These answers are provided by experts from around the world who supply technical and scientific advice as part of our Community of Practice (CoP). The aim is to address the issue of the widening gap in the field of chemical safety between developed and developing countries, and to empower countries in the South-East Asia Region to manage the import, manufacture and processing, storage, distribution, transport, use, recycling and disposal of chemicals.

In addition to the Q&A service for registered users, the website also provides information on the safe use of chemicals, as well as a comprehensive list of links to other important websites related to chemicals management in the region. General users have access to the database of questions and answers, as well as all other information on the website.



CALENDAR OF EVENTS

International Training Courses in Environmental Toxicology at Chulabhorn Research Institute, scheduled for 2014 - 2015

Training Course	Date	Duration	Closing Date
1. Environmental and Health Risk Assessment and Management of Toxic Chemicals	December 6-18, 2014	2 weeks	September 24, 2014
2. Environmental Toxicology	May 2015	2 weeks	February 24, 2015
3. Occupational and Environmental Medicine	To be announced	2 weeks	To be announced

International Training Course on

“Environmental and Health Risk Assessment and Management of Toxic Chemicals”, December 6 - 18, 2014

The course is an integration of science and policy, covering the fundamental basis of environmental and health risk assessment and management from exposure assessment and risk characterization; mode of action and human relevance framework; the relationship between risk assessment and risk management; and the need for open, transparent and participatory acceptance procedures and credible communication methods. Emphasis will be placed on human health risk assessment, although the principles of ecological risk assessment will also be covered. Importantly, the course teaches the practical application of risk assessment methods to various problems, e.g. hazardous waste site release, through the use of case studies relevant to problems faced in developing countries, and describes the policy context in which decisions to manage environmental health risks are made. Teaching and learning aids such as electronic distance learning tools and IPCS risk assessment toolkit will be introduced.

Requirement: Participants should have jobs/responsibilities related to assessment of risk from the use of chemicals.

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

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

For more information, please visit:
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