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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".

Professor Dr. HRH Princess Chulabhorn Mahidol Visits WHO SEARO and Signs a Memorandum of Understanding to Expand Collaboration between CRI and WHO SEARO

On February 3rd, 2012, Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, President of the Chulabhorn Research Institute (CRI), visited the World Health Organization Regional Office for South-East Asia (WHO SEARO), and signed a Memorandum of Understanding (MoU) with WHO SEARO, represented by Dr. Samlee Plianbangchang, Regional Director, to expand on the collaborations through CRI's WHO Collaborating Centre for Capacity Building and Research on Environmental Health Science and Toxicology. CRI's International Centre for Environmental Health and Toxicology (ICEHT), formerly known as the International Centre for Environmental and Industrial Toxicology (ICEIT) was first designated a WHO Collaborating Centre in 2005, and re-designated in 2010.

The Terms of Reference of the Collaborating Centre are:

- to promote and assist capacity building activities in Environmental Health, Toxicology and Risk Assessment
- to promote and conduct collaborative research in Environmental Health Science, particularly as it relates to emerging national and international problems, and in vulnerable groups such as children and the elderly, and
- to establish and maintain linkages with relevant centers, particularly in the South-East Asia and Western Pacific Regions of WHO.

Health Effects of Human Exposure to Particulate Matter

Particulate matter (PM) exposure is one of the most pressing issues in modern-day public health, particularly in relation to the effects on the cardiovascular system. Human exposure to PM has been specifically linked to a number of cardiovascular conditions including myocardial infarction, hypertension, atherosclerosis, heart rate variability, thrombosis, and coronary heart disease, all occurring due to either direct or indirect mechanisms of action.

The present study reviews the key experiments within both the direct and indirect pathways.

Many studies have examined the effects of PM on the cardiovascular system, showing a clear correlation between PM exposure and multiple cardiovascular conditions, with current research focusing on the pathology of these conditions. Many of these studies have focused on the indirect effects of PM on the cardiovascular system, while less is known of the mechanisms of the direct pathways, including reactive oxygen species, ion channel interference, and vascular dysfunction. Future studies should focus on the effects of ultrafine particles and the ability of PM to enter the bloodstream and affect cardiovascular activity directly, as the direct pathways are poorly characterized but important in triggering severe cardiovascular events. The processes involved in PM entering the bloodstream are of great importance, as the chemical concentrations and composition of PM need to be determined. Studies that examine direct cellular insult on cells are not significant unless they are treated with the correct composition and concentration of PM that is observed in the bloodstream.

Fewer studies have surveyed the time course of these indirect and direct effects of PM. Future studies should focus on the time period of response, as it is clear there is a biphasic response consisting of early and delayed responses. In particular, the response seems to continue, even 14 h post-exposure. Thus, research should monitor the response over a time period ranging from 24 h to multiple days post-exposure, determining the long term effects of PM exposure. Finally, there is an incomplete understanding of the effects of chronic or long-term exposure to PM; future studies should elucidate how the effects of long-term exposure differ, if at all, from acute exposure as well as design experiments to understand the synergistic effects of direct and indirect exposure to PM.

Research into the cardiovascular effects of PM is required in order to produce guidelines and recommendations for clinical practice. The literature, when taken as a whole, provides a useful summary of how PM can be observed in a clinical setting.

First and foremost, patients at a high risk for developing acute cardiovascular events such as myocardial infarction, stroke, and arrhythmias should avoid high levels of PM whenever possible. This includes both refraining from outdoor activities on days of particularly high pollution and avoiding living and working in areas prone to chronically high pollutant levels.

Secondly, the critical role of reactive oxygen species in PM-induced cardiovascular dysfunction suggests that antioxidant therapy holds some promise for the treatment of the deleterious effects of PM exposure. Antioxidant therapy would be especially appropriate in patients already at a high cardiovascular risk, or who are consistently exposed to high levels of pollutants, such as employees of industrial facilities. While increased dietary antioxidant intake has been shown to help prevent a number of diseases, exercise promotes the production of endogenous antioxidants in addition to its already-known benefits to cardiovascular health. On the other hand, dietary antioxidants have not yet been shown to demonstrate a clinical benefit in the treatment of cardiovascular disease. More importantly, exercise produces oxidants that may or may not be an essential step whereby exercise modulates redox regulation – dietary antioxidants could interfere with this process in ways that alter the balance between exercise's pro- and antioxidant effects. Therefore, the literature emphasizes the importance of exercise in managing cardiovascular disease, especially in patients who may be exposed to PM pollution.

Finally, antithrombotic therapy may also help prevent the onset of cardiovascular events triggered by PM-induced thrombosis. Antiplatelets may be a preventative method, as particles that enter the systemic circulation are known to promote platelet formation. Antithrombotics should be a last resort, however, as the possible side effects of such drugs could be much more severe than the side effects of any other treatment regimen or the untreated symptoms themselves.

There is no lack of epidemiological data and clinical studies to provide evidence that PM exposure causes detrimental cardiovascular dysfunction, both by direct and indirect mechanisms.

These two general mechanisms can be further divided into three main pathways: direct particle entry into the vasculature, PM deposition on the alveoli (indirect), and dysfunction of the autonomic nervous system (indirect). Further research should continue to explore the effects of PM and the corresponding response pathways, specifically the nature of the effect and time course of the response. Clinicians should be aware of the consequences of exposure to PM and should continue to proactively treat this problem since the rates of industrialization are unlikely to decrease.

Source: Toxicology Letters, Vol. 208, Issue 3, Pages 293-299, February 2012.

EXPOSURES TO PESTICIDES AND RISK OF CHILDHOOD CANCER

Childhood cancer is the second leading cause of death among children aged 5 to 14 years after accidental causes in Europe and the USA. Among the 12 major types of childhood cancer, the leukemia group has the highest incidence (40% of all cancers); cancers of the brain, lymphomas and cancers of central nervous system account for more than 25% of new cases; neuroblastoma, Wilms' tumour and sarcoma are less common. In Europe and the USA, there is concern that overall rates of childhood cancer have been increasing since 1970. The risk factors for childhood cancer are largely unknown. A few conditions such as Down's syndrome, other specific chromosomal and genetic abnormalities, and exposure to ionising radiation are known risk factors, but they explain only a small percentage of cases. Early-life exposure to environmental contaminants is suspected to be responsible for initial anomalies occurring *in utero* and leading to cancer.

Pesticides are among the suspected environmental factors, as they may promote cellular and molecular events, that is, chromosomal aberrations, oxidative stress, cell signalling disturbances or mutations, that could be linked to increased cancer risk. A review of epidemiological studies in 1997, showed that frequent occupational exposure to pesticides or use of pesticides in the home was associated with childhood leukemia, brain cancer and increased risk of Wilms' tumour, Ewing's sarcoma and germ-cell tumours. Living on a farm, a proxy for pesticide exposure, was also associated with increased risk of a number of childhood cancers in studies investigating associations between pesticide exposure and childhood cancers. Another review of epidemiological studies and childhood cancers revealed conflicting evidence across studies with regard to cancer types as well as to risk factors, and no clear data exist regarding the most critical exposure period for the occurrence of cancer.

The aim of the present study was to perform a meta-analysis of case-control and cohort studies in a comprehensive overview of all available knowledge and to clarify the possible relationships between exposure to pesticides and childhood cancers.

From the study, it appears that exposure to pesticides is significantly associated with an increased risk of leukemia, lymphoma and brain cancer in children. A strong association was found between the incidence of neuroblastoma and Ewing's sarcoma and exposure to pesticides. However, the results of the present study should be interpreted with caution because of the small number of reports analysed. These cancers are rare, and a meta-analysis was performed on only four and nine datasets respectively. No correlation was found between parental exposure to pesticides and renal cancer or germ-cell tumours in children. Conversely, the results showed that the risk of leukemia and lymphoma in children was high when their mothers were exposed during the prenatal period and when they used pesticides in the home or garden. Interestingly, the incidence of childhood brain cancer was high when the father was exposed during the prenatal period. In addition, occupational exposure of the father as well as use of pesticides in the home or in the garden was also found to influence the risk of brain cancer in the offspring. The proximity of the home to a farm or an active agricultural area was not associated with an increased risk of the cancers studied.

When assessing environmental health impacts, children, fetuses and neonates need to be distinguished from adults, as they are believed to be more vulnerable to the effects of environmental pollutants, and many routes of exposure are possible. Depending on the developmental period, children could be exposed via the placenta, maternal milk, the skin and the digestive tract. The lungs and/or air are also a potentially important source of exposure to pesticides used at home or when the home is located near farms or orchards. Paternal germ cells could also be the target of pesticides via a direct effect resulting in heritable genetic damage or in epigenetic changes that alter gene function. This could explain the strong correlation between paternal exposure and the increased incidence of brain cancer. However, several other possible mechanisms could explain this association, especially indirect mechanisms such as household contamination with substances brought home on the father's clothing.

Exposure to pesticides during fetal development is due to the capacity of these compounds to pass through the placental barrier and into the fetal bloodstream. The association between the concentration of pesticides in the biological fluid and childhood health problems is well documented. It is well established that the beginning of the initial event leading to some infant or young children cancers occurs *in utero*. Together with the positive association revealed in the meta-analyses between parental exposure and some childhood cancers, these data lead us to suggest that pesticides present in parent tissue or fluid could be responsible for the genetic modifications in the fetus or in parental germinal cells that lead to cancer.

Despite some limitations in the study, the results do provide evidence concerning the sites of childhood cancer most associated with pesticide exposure, the period and type of exposure as well as the type of pesticide that could increase the risk of developing childhood cancer. The causality of these associations is not proven, and the hypothesis of an environmental origin of some cancers requires experimental studies. Taken together with the results of previous studies, the results of the present work provide convincing evidence of the need to conduct experimental studies to confirm and explain these correlations.

Source: Occupational and Environmental Medicine, Vol. 68, Issue 9, Pages 694-702, September 2011.

Effects of Chronic Exposure to Arsenic and High-fat Diet in Mice Resulting in an Unusual Diabetes Phenotype

Type 2 diabetes is characterized by glucose intolerance and insulin resistance. Obesity is the leading cause of this type of diabetes and there is growing evidence to suggest that chronic exposure to inorganic arsenic (iAs) also produces symptoms consistent with diabetes. Thus, iAs exposure may further increase the risk of diabetes in obese individuals.

In the present study, researchers examined interactions of iAs exposure with obesity, the leading cause of diabetes worldwide. The results suggest that the key characteristics of diabetes produced in mice by an obesogenic diet combined with chronic exposure to iAs [normal fasting blood glucose and normal fasting serum insulin levels with pronounced glucose intolerance] differ from those described for type 2 diabetes. Thus, iAs exposure may target tissues or regulatory mechanisms that are not typically associated with type 2 diabetes.

The main goal of the study was to characterize the diabetogenic effects of combined exposure to iAs and high-fat diet (HFD). Specifically, the study wanted to examine whether mice fed the obesogenic HFD are more susceptible to the diabetogenic effects of chronic exposure to iAs. Type 2 diabetes results from a progressive insulin secretory defect on the background of insulin resistance. Early stages of the disease are characterized by resistance of the liver and peripheral tissues to insulin signal, resulting in hyperglycemia, hyperinsulinemia, and glucose intolerance. Characteristics of advanced disease are failure of the pancreatic β-cells to keep up with the increasing demand for insulin and a gradual decay of β-cell functions.

This is the first study to show that chronic exposure to iAs suppresses diet-induced obesity in laboratory mice. Data collected here do not provide information about mechanisms underlying the antiobesogenic effects of iAs. However, previous work has shown that iAs^{III} inhibits signal transduction mechanisms that are responsible for adipocyte differentiation. Differentiated adipocytes are responsible for fat (triacylglycerol, TAG) accumulation in adipose tissues. Thus, it is plausible that the limited fat accumulation in HFD mice exposed to iAs is due to the inhibition of adipocyte differentiation by iAs or by its trivalent methylated metabolites. An alternative mechanism could be associated with impaired TAG synthesis in the liver (e.g., as a result of hepatic insulin resistance) and decreased secretion of TAG for transport to the adipose tissues. The trend for lowering hepatic TAG accumulation and the decreased plasma TAG levels in the iAs-exposed mice on HFD are consistent with this mechanism.

Taken together, the data suggest that iAs exposure may act synergistically with HFD-induced obesity, producing glucose intolerance in mice with a relatively low adiposity. Notably, the diabetic phenotype associated with the exposure of HFD mice to iAs differs from that of typical type 2 diabetes.

Source: Environmental Health Perspectives, Vol. 119, No. 8, Pages 1104-1109, August 2011.

A Study of the Efficacy of Garlic in Reducing Heavy Metal Accumulation in the Liver of Rats

Environmental pollution and occupational exposure to heavy metals such as mercury (Hg), cadmium (Cd) and lead (Pb) contribute to major chronic and malignant diseases, with effects seen in all tissues of the body. The effects observed with heavy metal poisoning include carcinogenicity, immunotoxicity and neurotoxicity and are thought to occur through the generation of oxygen radicals leading to oxidative stress and altered physiological and biochemical characteristics.

Hg poisoning is reported to result in marked distal sensory disturbances, renal and cardiovascular problems. Platelets dysfunction and anemia-inducing effect of Hg have also been reported. Human acute and chronic Cd exposures occur through food, air, water, industrial products and by occupational exposure. Toxic effects resulting from Cd ingestion include bone defects, increased blood pressure, myocardial dysfunctions, proteinuria, renal dysfunction, pulmonary edema and death. Cd stimulates and binds to various biological components such as proteins and non-protein sulfhydryl groups, macromolecules and metallothionein, inhibition of the liver enzymatic function, which results in hepatic congestion, an increase in lipid peroxidation, production of reactive radicals, oxidative tissue damage and loss of membrane functions. Pb^{2+} has been shown to have a multisystem effect seriously affecting the nervous, circulatory, skeletal, renal, hematopoietic, and endocrine systems. Long-term exposure to Pb^{2+} may also result in a nephropathy or renal adenocarcinoma. Pb toxicity is reported to occur through its affinity for proteins and for its capacity to simulate calcium and Fe^{2+} channels.

Allium sativum (garlic) is claimed to have both prophylactic and curative properties for many disease conditions like diabetes and hypertension. It contains many sulfur active principles mainly in the form of cysteine derivative, which decompose into a variety of thiosulfinates and polysulfides by the action of the enzyme allinase on extraction. Allicin is a sulfur-containing compound extracted from garlic with anti-oxidant properties. In addition to free sulfoxides in alliums there are non-volatile sulfur-containing peptides and proteins which possess

(Continued on page 5)

A Study of the Efficacy of Garlic in Reducing Heavy Metal Accumulation in the Liver of Rats

(Continued from page 4)

various activities. Such sulfur active principles are reported to contribute to the metal chelating properties of this nutrient and are a major component of most chelating drugs.

Thus the present study was carried out to compare the effect of garlic on reducing Hg, Cd and Pb accumulation in the liver of rats.

The heavy metal accumulations in the liver were determined using atomic absorption spectroscopy. The percentage protection showed a time-dependent effect and was significantly higher for Cd compared to Hg and Pb-treated groups. Analysis between the groups showed that garlic treatment after exposure had a significantly higher percentage protection when compared with other modes.

These results suggest that raw garlic (7% w/w mixed with rat chow) offered more hepatoprotective effect to Cd followed by Hg and least protection to Pb at the selected dose of each metal (Hg = 10 ppm, Cd = 200 ppm, and Pb = 100 ppm in drinking water) in this study through the processes of uptake, assimilation and elimination of these metals.

The physiology and biological mechanisms of the animals used are similar to humans; as such the results could be extrapolated to human conditions. The major limitation of this study was the lack of quantification of actual nutrient substance taken since the animals were not fed through gavages but allowed free access to food and water. The study was also not able to measure the bioaccumulation of these metals in other tissue and the actual toxicokinetics of these metals in the presence of the nutrient substances.

Source: Food and Chemical Toxicology, Vol. 50, Issue 2, Pages 222-226, February 2012.

The Role of Immigration to California on Polybrominated Diphenyl Ether Levels in Latino Children

Elevated exposures to polybrominated diphenyl ether (PBDE) flame retardants have been linked to developmental neurotoxicity in children and endocrine disruption in adults.

Since PBDEs have been found to be higher in residents of California than other parts of the United States, the present study aimed to investigate the role of immigration to California on PBDE levels in Latino children.

Researchers compared serum PBDE concentrations in a population of 264 first-generation Mexican-American 7-year-old children who were born and raised in California, [these children were participants in the Center for Health Analysis of Mothers and Children of Salinas (CHAMACOS) cohort study], with 283 Mexican 5-year-old children, who were raised in the states in Mexico where most CHAMACOS mothers had originated.

On average, PBDE serum concentrations in the California Mexican-American children were three times higher than their mothers' levels during pregnancy and seven times higher than concentrations in the children living in Mexico. The PBDE serum concentrations were higher in the Mexican-American children regardless of length of time their mother had resided in California or the duration of the child's breast-feeding. These data suggest that PBDE serum concentrations in these children resulted primarily from postnatal exposure.

CHAMACOS comprises a unique population of Mexican-American children who have elevated serum concentrations of PBDEs by virtue of living in California and were born and breast-fed from mothers with high levels of DDT/DDE because they emigrated from Mexico. In addition, as is true of more than a quarter of Latino children living in California, the CHAMACOS participants live in poverty. Other researchers have suggested that PBDE levels may be higher in lower-income homes because of the presence of poorly manufactured furniture, deteriorated PBDE-treated furniture foam, and poorer ventilation. It has been reported that the median levels of PBDEs in dust collected from 20 homes of Mexican immigrants in Salinas and in Oakland were up to 20 times higher than those found in homes elsewhere in the United States. The maximum PBDE concentrations in the Oakland urban homes were the highest reported to date in the United States and much higher than those reported from Europe and Asia.

Given the growing evidence documenting potential health effects of PBDE exposure, the levels in young children noted in this study present a major public health challenge. Although this challenge is particularly pronounced for California children, it is also relevant to other regions in the United States, where exposures are increased through manufacturing practices seeking to achieve TB 117 compliance even in products not destined for California. This practice has resulted in the dissemination of penta-BDE-containing products throughout the United States. Some penta-BDE substitutes have recently been detected with high frequency in furniture foam and house dust collected outside of California, suggesting the potential for ongoing flame retardant exposures in homes and offices throughout the United States, due at least in part to rules developed in California over three decades ago. With the legislative ban of penta-BDE in products sold in California, other halogenated flame retardants, including chlorinated organophosphates and a variety of proprietary mixtures containing halogenated aromatic compounds, have been used instead to comply with TB 117. Thus, children's exposure to organohalogen flame retardant chemicals used in furniture will continue given current regulations and will need to be documented. In addition, the toxicology and health consequences of chemical replacements to penta-BDE should be investigated and weighed against their purported fire safety benefits.

Source: Environmental Health Perspectives, Vol. 119, No. 10, Pages 1442-1448, October 2011.

Health Risks from Shark Fin Consumption

Sharks are apex predators in virtually all marine environments and impact ecosystem structure and function through trophic cascades. However, shark populations are experiencing global declines as a result of over-fishing, largely driven to support the burgeoning shark fin trade. A minimum of 26 to 73 million sharks per year, representing a combined weight of 1.7 million tons are killed in both target and bycatch fisheries to support the high demand for fins in Asian markets. High exploitation rates continue to increase annually driven by the rising demand for highly prized fins used to make shark fin soup, an Asian delicacy and one of the world's most expensive fishery products. Shark fins consist of cartilage with fibrous protein collagens that add texture and consistency to the soup. The larger the fin and higher fin needle content (collagen fibers), the more expensive the soup. Sharks accumulate mercury and other heavy metals that pose health risks to consumers of shark products, including shark fin soup.

The neurotoxin β-*N*-methylamino-L-alanine (BMAA) is produced by diverse species of free-living cyanobacteria found in terrestrial and aquatic environments and cyano-bacterial symbionts. BMAA has been linked to the development of neurodegenerative brain diseases, such as Alzheimer's disease and Amyotrophic Lateral Sclerosis (ALS). Cyanobacteria are found in lakes, rivers, estuaries, and marine waters with bloom growth increased due to nutrient loading from agricultural and industrial runoff, farm animal wastes, sewage, groundwater inflow and atmospheric deposition. The occurrence of BMAA has been reported in isolated cyanobacteria from waters in the Baltic Sea, China, Holland, South Africa, British Isles, and Peru as well as in laboratory cultures of free-living marine cyanobacteria.

BMAA has been measured in high concentration in marine fish and invertebrates collected from South Florida coastal waters and the Baltic Sea. Given the ubiquity of cyanobacteria in marine ecosystems, BMAA could bioaccumulate up the marine food web to sharks, potentially posing health risks to consumers of shark products.

Given the increasing exploitation of sharks and the potential health hazard associated with bioaccu-mulation of BMAA in marine food webs, a recent study was conducted to determine if BMAA could be detected in shark fins. Specifically, researchers sampled fins and select organs from seven common shark species found in South Florida waters (USA) for analysis and detection of BMAA using multiple analytical techniques.

Cyanobacterial blooms in South Florida coastal waters occurred in the 1980s and have persisted ever since. Most cyanobacteria are known to produce the neurotoxin BMAA that has been linked to development of the neurodegenerative brain diseases. A study recently reported that BMAA was detected in several species of crustaceans and fish from the same South Florida coastal waters surveyed in the present study. These marine species are part of the diet of some groups of sharks. Since sharks are at the highest trophic level, they may bioaccumulate BMAA from active exposure to cyanobacterial bloom sites. All seven shark species analyzed in this study had BMAA detected in high amounts in their fins. Interestingly, high concentrations of BMAA were detected in the fins of some sharks collected in areas that had no active cyanobacteria blooms. Sharks are highly migratory, making it likely that they pass in and out of areas where cyanoblooms may have occurred over time. While planktonic cyanobacteria are abundant, benthic and cyanobacteria epiphytic on seagrass and macroalgal blades are also present, providing a source of BMAA from the lowest trophic levels to higher animals within the same marine ecosystem.

The bonnethead shark that had the highest levels of BMAA in this study are known to primarily feed on members of the benthic zone, including blue crabs and pink shrimps which reportedly have very high concentrations of BMAA (mean concentration of 2505 µg/g and 2080 µg/g, respectively). Sharks as long-lived apex predators may concentrate protein-associated BMAA over time in certain tissues. This pattern of bioaccumulation is what has been observed for mercury and other heavy metal toxins in sharks across the lifespan. The range of BMAA con-centrations measured in the different sharks surveyed most likely reflect their ecological niches, different foraging patterns, and their size and age differences.

BMAA was measured in select organ tissues including the kidney, liver, and muscle of the great hammerhead shark. The tissue uptake of BMAA has been previously reported in the brain and muscle of bottom-dwelling fishes in the Baltic Sea, muscle and tissues from fish and crustaceans in South Florida coastal waters, and in brain, muscle, skin, intestine, kidney and fur in flying foxes from Guam. Taken together, these studies suggest that BMAA may be misincorporated into proteins where it bioaccumulates with repeat exposures.

Shark fins consist of cartilage with fibrous protein collagens. Shark fin cartilage powder or capsules are marketed as dietary supplements and claimed to combat and/or prevent a variety of illnesses. However, the benefits of this supplement have not been significantly proven, nor has shark cartilage been reviewed by the US Food and Drug Administration (FDA). Recently researchers hypo-thesized that collagen abnormality in the skin of sporadic ALS patients may be caused by the misincorporation of BMAA leading to misfolding of the collagen proteins. In keeping with this hypothesis, the highest levels of BMAA found in the Guam flying fox were detected in skin tissue known to contain collagen as a major com-ponent.

The elevated level of BMAA in shark fins provides additional support that marine cyanobacteria may represent a route for human exposure to BMAA. Further studies are needed to confirm this finding and to demonstrate that widespread BMAA

(Continued on page 7)

Health Risks from Shark Fin Consumption

(Continued from page 6)

detections in sharks may occur outside of South Florida coastal waters. The recent finding that BMAA co-occurs with other cyanotoxins in contaminated water supplies raises the possibility that low-level human exposure to BMAA exists in many parts of the world. The possible link between BMAA and gene/environment interactions in progressive neurodegenerative diseases warrants concern for exposure to BMAA in human diets. In Asia, shark fin soup is considered a delicacy, which drives a high consumer demand for this product. This study indicates that human consumption of shark fins may pose a health risk for BMAA exposure especially if it occurs with mercury or other toxins.

Source: Marine Drugs, Vol. 10, Pages 509-520, February 2012.

POLYBROMINATED DIPHENYL ETHERS IN FOOD AND HUMAN DIETARY EXPOSURE

Polybrominated diphenyl ethers (PBDEs) are a class of brominated flame retardants (BFRs) used in reducing the flammability of combustible materials. A recent study reviews the scientific literature concerning the levels of PBDEs in foodstuffs and the dietary exposure to these BFRs.

PBDEs have been used for several decades providing longer escape times in case of fire and thus saving lives, as well as reducing the damage from fire. Bromine acts by reaction with the free radicals in the gas phase and thus slows down the ignition and combustion process. Therefore, PBDEs have been (and still are) widely used as non-reactive additives in textiles, polyurethane foams, thermoplastics and electronic products. There have been three major PBDE commercial formulations in the global market: penta-, octa- and deca-BDEs. PBDEs are not chemically bound to the polymers that contain them. Consequently, a fraction may escape during production, use, disposal and recycling processes. As a consequence of substantial, long term use, PBDEs have contaminated humans, wildlife, air, water, soils, and sediments, even in remote areas. In recent years, strict bans have been imposed on the worldwide use of penta- and octa-BDE formulations. The use of deca-BDE in the EU has been banned in electrical and electronic applications since July 1, 2008, while components of the penta-BDE and octa-BDE commercial mixtures have been added to the persistent organic pollutants (POPs) list of the Stockholm Convention.

With respect to the toxic effects of PBDEs, a number of experimental studies have suggested that these compounds might impact thyroid hormone levels; thyroid, liver, and kidney morphology; liver ethoxyresorufin-O-deethylase activity; neurodevelopment and behavior; reproductive success, as well as fetal toxicity/teratogenicity. However, information on the potential mechanisms of PBDE toxicity is still limited. For the non-occupationally exposed population to PBDEs (and BFRs in general), based on a number of recent studies, it seems that human exposure occurs mainly via a combination of diet, ingestion of indoor dust, and inhalation of indoor air. The exact contribution of these three pathways varies substantially on a compound-specific basis and between individuals and within national populations.

In recent years, PBDEs have become widespread environmental pollutants. As a consequence of this, the general population of industrialized countries has been (and still remains) exposed to these contaminants. With regard to human exposure through food consumption, until recently, data on the concentrations of PBDEs were only relatively abundant in fish. However, much less information has been reported on PBDE concentrations in other major food groups, or about possible differences in food concentrations between countries or regions.

It has been noted that the available information on human total daily intake through food consumption is basically limited to a number of European countries, USA, China, and Japan. In spite of the considerable methodological differences among studies, the results show notable similarities such as the important contribution to the sum of total PBDEs of some congeners such as BDEs 47, 49, 99 and 209, the comparatively high contribution of fish and seafood, and dairy products, and the probably limited human health risks derived from dietary exposure to PBDEs.

The study concludes that certain issues related to human exposure through the diet still remain to be investigated.

Thus, there is a clear need for epidemiological studies in humans to determine whether current body burden of PBDEs may be associated with adverse health effects, particularly in the domains of neurobehavioral development and reproductive effects. Also, information on other potential routes of PBDE exposure is still limited. Moreover, from a toxicological point of view, mechanistic studies would provide important information for a better assessment of the likelihood of PBDE adverse health effects. These studies should also define the toxicity of individual congeners, and should indicate whether interactions among PBDE congeners and between PBDEs and other environmental POPs may occur.

Source: Food and Chemical Toxicology, Vol. 50, Issue 2, Pages 238-249, February 2012.

TOXICOLOGICAL EFFECTS OF ACRYLAMIDE

Acrylamide (AA), a chemical widely used in industry, has been classified as a potential human carcinogen by IARC (Group 2A). It is present in starchy foods after treatment at temperatures above 120°C and has also been detected in smog.

In addition to the neurotoxicity in humans, AA may affect other species. Thus a new study has been conducted to investigate whether AA affected the male reproductive system in 3-week-old weaning male Sprague-Dawley rats treated with AA at various doses (0, 5, 15 or 30 mg/kg/day).

The model of subacute AA-treated weaning male rats was used in the study in the light of previous investigations into AA toxicology and in view of growth and development characteristics of weaning rats.

The AA residues in the treated reproductive organs of male rats, including testis, epididymis, prostate, and seminal vesicle, were determined by HPLC, and the results showed differences of AA residues in the forementioned four organs 1 h, 2 h, and 4 h after treatments with AA. These results suggested that AA could pass through blood-testis barrier and blood-epididymis barrier, enter into these important male reproductive organs, and cause toxicological damages to the reproductive system of weaning male rats. In some previous studies on the reproductive toxicology of AA, research focused on testis and epididymis as target organs. However, results in the present study showed that AA residue could also be detected in the prostate and seminal vesicle, suggesting that prostate and seminal vesicle might also be toxicological target organs for AA. Since the fluid secreted by prostate and seminal vesicle can increase sperm motility, promote sperm liquefaction, and improve sperm survival rate, the results suggest that the toxicological effects of AA on prostate and seminal vesicle may further affect the reproductive system of weaning male rats.

In the study, most weaning rats in 15 and 30 mg/kg/day groups showed decreased body weight, reduced consumption of food and water, and less activity. In addition, these animals of 30 mg/kg/day dose group exhibited distinct hind-leg splay and muscle weakness. These results could be caused by increased AA cumulative effect associated with AA exposure. Muscle weakness, hind-leg splay and paralysis, first observed in these AA-treated animals, indicate that the cumulative effect of AA to sciatic teleneurons was more obvious than to other teleneurons. The results also showed that AA treatment could decrease body weight of these animals, possibly because of the decreased consumption of food and water. Change of organ index is known to be associated with organ damaged degrees. In this study, organ indexes of four male reproductive organs of AA-treated animals were reduced. Compared to the results from studies of adult male rats, the present study found that weaning male rats might be more vulnerable to AA toxicity. AA-induced morphologic changes of testis, epididymis, prostate, and seminal vesicle demonstrated that AA treatment could induce spermatogenic cell impairment in testis and disturb the periodical development processes. Moreover, there was a dosage effect relationship between damage grade and AA dose. The damage of spermatogenic cells and Leydig cells induced by AA will affect testis reproductive function as well as spermatogenesis. This might be one of the reasons that caused sperm count decrease. The present results clearly showed that AA could result in degeneration of epithelial cells in epididymis. In particular, it could also disturb spermatogenesis and sperm morphology, and significantly reduce sperm count.

The study indicates that more attention should be paid to these findings to further confirm the risk of AA in the male reproductive system.

Source: Toxicology and Industrial Health, Vol. 27, Issue 7, Pages 617-627, August 2011.

UPCOMING EVENT:

The 8th Congress of Toxicology in Developing Countries (8CTDC)

Theme: **"Sharing Toxicological Knowledge for Healthy Life & Environment"**

September 10-13, 2012
Centara Grand at Central Ladprao, Bangkok, Thailand

Organizers
Thai Society of Toxicology (TST)
Under the auspices of the IUTOX

Important dates

- Deadline for Abstract Submission: **April 30, 2012**
- Early Bird Registration: From now until **June 1, 2012**

For more information please visit: **http://www.thaitox.org/8ctdc**

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