

VOL. 22 NO. 3 — July 2012 ISSN 0858-2793 BANGKOK, THAILAND

# Chalabhorn 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".

Professor Dr. HRH Princess Chulabhorn Mahidol Attends the UN Conference on Sustainable Development (Rio+20) in Rio de Janeiro, Brazil



Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol attended the UN Conference on Sustainable Development, UNCSD (Rio+20) in Rio de Janeiro from 20-22 June 2012 as personal representative of His Majesty King Bhumibol and head of the delegation for Thailand, which also included representatives from the Royal Thai Government: Ministry of Natural Resources and Environment, Ministry of Foreign Affairs, Ministry of Public Health, Ministry of Finance, Ministry of Transport, Ministry of Tourism and Sports, Ministry of Science and Technology, Ministry of Agriculture and Cooperatives, and the Ministry of Labour.

The UNCSD was organized to mark the 20th anniversary of the 1992 UN Conference on Environment and Development (UNCED), held in Rio de Janeiro,

and the 10<sup>th</sup> anniversary of the 2002 World Summit on Sustainable Development (WSSD), held in Johannesburg. Sustainable development is the guiding principle for long-term global development and consists of 3 dimensions: economic development, social development and environmental protection. Sustainable development meets the needs of the present without compromising the ability of future generations to meet their own needs.

The UNCSD was attended by Heads of State and Governments, and high-level representatives, who renewed their commitment to sustainable development and to ensuring the promotion of an economically, socially and environmentally sustainable future for the planet and for present and future generations. The

(Continued on page 2)

### Professor Dr. HRH Princess Chulabhorn Mahidol Attends the UN Conference on Sustainable Development (Rio+20) in Rio de Janeiro, Brazil

(Continued from page 1)

conference resulted in a focused political document that aims to reduce poverty, advance social equality and ensure environmental protection. The 2 main themes of the 2012 UNCSD were: (a) a green economy in the context of sustainable development and poverty eradication, and (b) the institutional framework for sustainable development, with 7 key areas highlighted for priority attention: decent jobs, energy, sustainable cities, food security and sustainable agriculture, water, oceans, and disaster readiness.

concept of a green economy focuses primarily on the intersection between environment and economy. A green economy in the context of sustainable development and poverty eradication is one important tool for achievement of sustainable development, and the implementation of green economy policies for the transition towards sustainable development is viewed as common undertaking. It was acknowledged that a green economy context of sustainable development and poverty eradication will enhance the world's ability to manage natural resources sustainably and with lower negative impacts, increase resource efficiency, and reduce waste. It was also recognized that urgent action on unsustainable

patterns of production and consumption is fundamental in addressing environmental sustainability. The importance of technology transfer to developing countries, particularly of environmentally sound technologies and corresponding know-how, was emphasized.

The key issue with regards to the institutional framework for sustainable development is that it should integrate the 3 dimensions of sustainable development in a balanced manner, and enhance implementation by strengthening coherence, coordination, avoiding duplication of efforts and reviewing progress in implementing sustainable development at all levels: global, regional and national. At the international level, there is a need to strengthen UN system-wide coherence and coordination, while also ensuring accountability to Member States. It was decided to establish a universal intergovernmental high-level political forum, building on, and subsequently replacing the Commission on Sustainable Development. This forum would follow up on implementation of sustainable development and avoid overlap with existing structures, bodies and entities in a cost-effective manner. It was also decided that in order to promote a balanced integration of the economic, social and environmental

of sustainable dimensions development, as well as coordination within the UN system, there is a need to strengthen international environmental governance, through strengthening the role of the UN Environment Proglobal gramme as the leading authority that environmental sets global environmental agenda, procoherent implementation of environmental dimensions of sustainable development within the UN system, and serves as an authoritative advocate for the global environment

Professor Dr. Her Royal Highness Princess Chulabhorn's statement to the UNCSD plenary reaffirmed the importance of sustainable development, pointing to His Majesty King Bhumibol's Sufficiency Economy Philosophy as an important basis for attaining poverty eradication sustainable development for Thailand. The critical importance and central role of human health to sustainable development was also highlighted. Finally, Her Royal Highness urged the adoption of the Sustainable Development Goals (SDG) process and underlined the importance of alignment of the SDGs with the Millennium Development Goals by 2015 to underpin international commitment to sustainable development.

### PARAQUAT USE AND RESPIRATORY HEALTH EFFECTS AMONG FARMERS IN SOUTH KOREA

Paraquat (1,1'-dimethyl-4,4'-bipy-ridinium dichloride) is a non-selective herbicide that has been applied in more than 100 developed and developing countries throughout the world. It is extensively used for weed control both on plantations and by small-scale farmers in hundreds of different crops, including corn, rice, orchards, soybeans, vegetables and many other crops. Paraquat has been ranked as one of the most commonly used pesticides and it is the main causative agent for acute poisoning in South Korea.

Paraquat is acutely toxic and causes a great number of health

effects. Over the preceding decades, numerous fatalities from paraquat exposure have been recorded, mainly as a result of accidental or voluntary ingestion. The major cause of death from paraquat poisoning is respiratory failure due to oxidative damage to the alveolar epithelium, with subsequent pulmonary fibrosis. Pulmonary function abnormalities. especially decreased diffusing capacity, were reported among survivors of acute paraquat poisoning in Japan.

However, the occupational hazards presented by chronic paraquat exposure have been less well

characterised, and a limited number of epidemiological studies on respiratory health effects paraquat among performed. applicators have been Chronic exposure to paraguat among farmers has been reported in certain studies to show an association with respiratory symptoms, such as wheeze, shortness of breath and chronic cough, subclinical gas exchange abnormalities, but not in others. The limitations of earlier epidemiological studies include small sample sizes and exposure to multiple pesticides.

(Continued on page 3)

#### PARAQUAT USE AND RESPIRATORY HEALTH EFFECTS AMONG FARMERS IN SOUTH KOREA

(Continued from page 2)

A new study has been conducted therefore to investigate the association of occupational paraquat exposure with respiratory health effects and lung function among South Korean farmers.

A cross-sectional survey of health effects related to an oil spill was conducted in South Korea from 2008 to 2009. For this analysis, a total of 2882 full-time farmers were selected from the overall sample. Data collection included an interviewer-administered questionnaire and spirometry testing. Logistic regression analysis and linear regression analysis were performed to evaluate the relationship between paraquat exposure and respiratory

health outcomes after adjustment for potential confounders.

The risks of self-reported physician-diagnosed asthma, chronic obstructive pulmonary disease and allergic rhinitis were non-significantly paraquat-applying increased among farmers compared with non-paraguatapplying farmers. Although the results of a pulmonary function test fell within normal limits, a decline in forced vital capacity and forced expiratory volume in one second was apparent among paraguat-applying farmers compared with non-paraguat-applying farmers. Forced vital capacity and forced expiratory volume in one second significantly decreased with each unit increase in years of paraquat application. Paraquat-applying farmers showed a significant exposure-response relationship between restrictive ventilatory defects and paraquat application years or lifetime days of application.

These findings suggest a possible association between paraquat application and adverse respiratory health effects among farmers.

Source: Environmental Health Perspectives, Vol. 69, Issue 6, Pages 398-403, May 2012.

### Behavioral Effects of Sub-acute Inhalation of Toluene in Adult Rats

he he possibility of persistent neurological effects from repeated exposures to volatile organic compounds (VOCs) remains a concern for public and occupational health. For example, hearing loss, visual dysfunctions and cognitive disturbances have been measured after occupational exposure to toluene. However, improved industrial hygiene standards have lowered the concentrations to which workers are exposed. The current 8-h time-weighted average Threshold Limit Value (TLV) for toluene is 50 parts per million (ppm) in the United States, and values of 25 to 50 ppm have recently been set in Europe. As a result, more recent studies of the consequences of occupational toluene exposure have not replicated these findings.

In addition, animal models have not consistently supported the claim that VOC exposures below levels of intentional abuse, which have not been directly measured in humans but likely exceed 10,000 ppm, lead to persistent behavioral deficits. For example, persistent effects have been reported in rats exposed daily to toluene at concentrations of 40 to 80 ppm for up to 4 months, including motor and cognitive impairment. However, these reported functional effects are neither consistently dose-related nor entirely replicable; indeed, other studies in rats reported that toluene at daily 6 h exposures to 80 ppm for 4 weeks improved performance in the water

maze and continuous exposure to 600 ppm toluene for 50 days reduced reference memory errors in the radial-arm maze

In the light of these reports a study was recently undertaken to observe the effect of 13 weeks of inhaled toluene in rats. In the study, rats showed mild but persistent changes in behaviour, primarily involving acquisition of an autoshaped level-press response. More recently, an experiment has been conducted which seeks to systematically replicate these findings, using a 4-week sub-acute exposure scenario.

Adult male Long-Evans rats inhaled toluene vapor (0, 10, 100, or 1000 ppm) for 6 h/day, 5 days/week for 4 weeks. As in the subchronic study, toluene had no effect on motor activity, anxiety-related behavior in the elevated plus-maze, or acquisition of the visual discrimination. However, subacute toluene did not affect appetitivelymotivated acquisition of the lever-press response, but did reduce accuracy of signal detection at the end of training. Analysis of the deficit in accuracy in the 1000 ppm group by means of manipulations of different task parameters suggested a greater influence of attentional impairment than visual or motor dysfunction as a source for the deficit. These results confirm a pattern of subtle and inconsistent long-term effects of repeated daily exposure to

concentrations of toluene vapor of 1000 ppm and below, in contrast to robust and reliable effects of acute inhalation of the solvent at concentrations above 1000 ppm.

The results provide very little evidence for persistent effects of inhaled toluene on motor, affective, or cognitive function in rats. Four weeks of exposure to inhaled toluene slightly lowered accuracy of visual signal detection. This effect may be associated with reduced attention because it was eliminated when the attentional load of the test was reduced by increasing the brightness of the signal intensities, and it was not exacerbated by altering the motor requirements of the test. The results also contrast with the pattern of effects observed previously after 13 weeks of exposure at the same concentrations in which toluene slowed autoshaping but exerted no other significant changes in behavior, including visual signal detection. Although persistent behavioral effects of repeated toluene exposure have been previously reported, the present results do not confirm a consistent pattern of persistent adverse consequences of inhaled toluene, even at the relatively high exposure concentrations used in the reported experiment.

**Source:** Neurotoxicology and Teratology, Vol. 34, Issue 1, Pages 83-89, January-February 2012.

## THE EFFECT OF BISPHENOL A ON THE DEVELOPMENT OF THE RHESUS MONKEY MAMMARY GLAND

A recent study has been conducted to determine whether material circulating levels of unconjugated bisphenol A (BPA) similar to those found in human serum affect the development of the mammary glands of female rhesus monkey offspring.

The xenoestrogen BPA used in the manufacture of various plastics and resins used for food packaging and consumer products has been shown to produce numerous endocrine and developmental effects in rodents.

Because very little is known about the fetal and neonatal development of the mammary gland in rhesus monkeys, researchers explored the presence of markers of epithelial differentiation and hormone receptors and found that the neonate monkey mammary gland is comparable to the human in the last trimester and to the neonatal mouse. The results show that the mammary glands of nonhuman primates are sensitive to BPA exposure during fetal development, and this sensitivity is manifested as increased complexity of the ductal system compared with unexposed animals. This study is particularly valuable because it provides mammary gland data regarding fetal exposure to BPA in nonhuman primates.

BPA exposure in mothers resulted in detectable serum levels of unconjugated BPA of 0.68  $\pm$  0.312 ng/mL. These data are important for the following reasons. First, these levels of unconjugated BPA are similar to those measured in humans, i.e.,  $\approx \! \! 1$  ng/mL, making the results of this study very relevant to human exposure. Second, the oral dose given to the mother is 8 times higher than the reference dose of 50 µg/kg per

day, suggesting that humans and the monkeys in this study are routinely exposed to levels above the "safe dose." And third, similar levels of unconjugated BPA have been shown to trigger biological effects in vitro and in vivo, some of which are mediated by the classical ERs as demonstrated experiments comparing wild-type and receptor null mice. Furthermore, these levels were within the range observed in nonpregnant female rhesus monkeys and nongestating CD-1 mice, both of which had an average 24-h unconjugated BPA concentration of ≈0.5 ng/mL.

Previous studies showed that fetal exposure to BPA affected mammary morphology in a mouse model; these alterations manifested during the period of exposure and throughout postnatal life. Although the mammary glands of mice exposed subcutaneously to 250 ng of BPA per kg of body weight per day during fetal development showed increased epithelial area, ductal extension, and branching points at gestational day 18, monkeys born to mothers orally exposed to 400 µg of BPA per kg of body weight per day had a significant increase in the number of buds per ductal unit. Because buds are incipient branches, these data point to an increased epithelial area branching in the nonhuman primate gland similar to those observed in BPA-exposed Because the mice. morphological alterations observed at birth in the mammary glands of rodents and nonhuman primates are comparable, researchers conclude that BPA exposure during gestation can be detrimental to mammary gland development across species. To determine whether the mammary glands from BPA-exposed nonhuman primates follow similar altered patterns as those displayed by rodents at puberty and adulthood, such as precancerous and cancerous lesions, further studies are required.

From what is known about the role of endogenous hormones the development of mammary gland, and from previous studies in rodents showing that the effects of fetal estrogens typically manifest after puberty, the researchers also conclude that BPA affects several developmental parameters of the mammary gland of rhesus monkeys, including some that are relevant to breast cancer risk in humans, such as epithelial density. From the similarity of mammary gland alterations observed perinatally in mice and monkeys as a result of **BPA** exposure, researchers infer that BPA will have comparable effects throughout the lifespan of nonhuman primates. The current studies reinforce the concept that the rodent mammary gland is reliable model to study developmental exposures to chemicals with estrogenic activity.

Source: Proceedings of the National Academics of Sciences, Vol. 109, No. 21, Pages 8190-8195, May 2012.

## Disposal and Recovery of Plastics from Waste Electrical and Electronic Equipment

In 2008, the plastics share from European waste electrical and electronic equipment (WEEE) over all categories was estimated to amount to 20.6%. For the members of the WEEE Forum, whose members collected and treated about 1.5 million tonnes of WEEE in 2008, this corresponds to about 300,000 tonnes of plastics waste recovered or disposed of in the same year.

The disposal and recovery of plastics from WEEE are considerable significance, both from an environmental and an economic perspective. In particular, plastics from WEEE may contain hazardous substances such as cadmium, lead, or brominated flame retardants, which on the one hand are associated with risks for health and the environment and on the other hand may give rise to high processing costs, depending on the disposal or recovery route chosen.

For newly marketed electrical electronic equipment (EEE), maximum concentration values for metals heavy brominated flame retardants have been defined in the Directive 2002/ 95/EC of the European Parliament and of the Council on the restriction of the use of certain hazardous substances in EEE (Restriction of Hazardous Substances Directive). According to the Directive, the Member States are expected to make sure that from July 1, 2006, newly marketed EEE shall not contain any lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls or polybrominated diphenyl ethers (PBDE) concentrations above-defined maximum concentration values (MCVs) for homogeneous materials. This also includes DecaBDE, which had been specifically exempted from the RoHS Directive on October 15, 2005 by the European Commission, based

conclusions of risk assessments on environmental and human health. In January 2006, however, the European Parliament and Denmark launched legal proceedings against this exemption, which led to the annulation of the Commission Decision on grounds of procedural errors by the European Court of Justice.

As a consequence, the WEEE commissioned the Swiss Forum Federal Laboratories for Materials Science and Technology (Empa) to perform a study, which provides a comprehensive empirical foundation regarding the levels of substances regulated by the RoHS Directive in mixed plastics from the treatment of the quantitatively most relevant categories defined in the European WEEE Directive. In 2008 these were large household appliances (category 1, 45.4% of the total WEEE amount), small household appliances (category 2; 10.6%), IT and telecommunications equipment (category 3; 16.4%), and consumer equipment (category 4; 21.0%).

A recently published presents the results of a study investigating current concentrations of hazardous substances mixed from WEEE implications for an environmentally sound recovery. The study included 53 sampling campaigns for mixed plastics from WEEE. The samples were analyzed with regard to heavy metals (cadmium, chromium, mercury, and lead) and flame retardants (PentaBDE, OctaBDE, DecaBDE, DecaBB) regulated in the RoHS Directive. Besides these substances, other brominated flame retardants known to occur in electronics (HBCD, TBBPA) as well as the total bromine and phosphorus contents were considered. Results show that no mixed plastics fraction from WEEE is completely free from substances regulated in the RoHS Directive. The lowest number and average concentrations were found in flat screen monitors. The highest concentrations were found in mixed plastics from CRT monitors and TVs. Mixed plastics fractions with high average concentrations of heavy metals originate from the treatment of small household appliances (cadmium), ICT equipconsumer (lead), and equipment (lead). Mixed plastics fractions with high average concentrations of brominated flame retardants mainly originate from the treatment of small household appliances for high temperature applications (DecaBDE), CRT monitors (OctaBDE and DecaBDE) and consumer equipment (DecaBDE), in particular CRT TVs (DecaBDE). To avoid a dissipation of hazardous substances into plastics and the environment, it is recommended that mixed plastics from WEEE are subject to a strict quality management.

Source: Environmental Science & Technology, Vol. 46, Issue 2, Pages 628-635, January 2012.

## Relationship between Long-term Exposure to Traffic-related Air Pollution and Blood Pressure

**B**oth short-term and long-term exposure to particulate air pollution have been associated with cardiovascular morbidity and mortality in numerous epidemiological studies. The effects of long-term exposure are substantially greater than those of short-term exposure, suggesting differences in the mechanisms may be at play, or differences in how the mechanisms are impacted by longerterm exposures. A number of pathways have been proposed to explain these associations, including, at the mooxidative lecular level, increased stress. systemic inflammation and thrombotic potential. At the functional pathways potential include changes in autonomic function, which may result in changes in blood pressure (BP).

Elevated BP is an established risk factor for coronary heart disease and stroke and an important intermediate marker of cardiovascular health. The relationship between air pollution exposure and BP is still not well understood. Studies of short-term particulate matter (PM) exposure and BP show mixed results, with some studies showing an inverse association or no association and positive findings other studies. Α key understanding the mixed results in the observed health effects of PM is that PM is a complex mixture and the concentrations of its individual components vary regionally and seasonally.

Growing evidence suggests that traffic-related components of PM pollution contribute significantly to particle-related cardiovascular effects. For example, a recent chamber study examining the mechanisms of short-term effects of PM<sub>2.5</sub> on BP found that effects were much stronger for the samples collected from a high-traffic area. A study of BP and short-term exposure to a number of air pollutants found the strongest association with

organic carbon and its estimated fossil-fuel combustion fraction. More research is needed to examine the relationship between traffic-related components of PM and BP, which will also help us understand the overall relationship between BP and PM.

Less is known however about the relationship between long-term exposures to air pollution and BP. although mortality studies have found strong associations with long-term air pollution exposures. In particular, only one recent study has investigated the relationship between long-term average air pollution exposures and BP. This study in Taiwan found a strong association between BP and 1year averages of PM<sub>2.5</sub>. Since traffic components of PM have been implicated as a key component in relation to cardiovascular disease, research is needed to address longterm exposure to traffic-related air pollution and BP.

Now a team of researchers has sought to address these research gaps by examining the relationship between BP and 1-year average exposures to traffic-related air pollution in a cohort study within the greater Boston area. An important tool for studying within-city variation in air pollution is the development geographic-based exposure models. Black carbon (BC) is a traffic-related particle and a common surrogate for traffic particles in general, weighted towards diesel particles. The researchers have developed and applied a land-use regression model for traffic particles based on BC in the greater Boston metropolitan area.

They hypothesised that estimated 1-year average BC at participants' addresses would be associated with elevated BP and examined this in a longitudinal study in a closed cohort of elderly men in

the greater Boston area with repeated measurements of BP taken roughly every 4 years.

Long-term average exposures to traffic particles were created from daily predictions of BC exposure at the geocoded address of each subject, using a validated spatiotemporal model based on ambient monitoring at 82 Boston-area locations. The authors examined the association of these exposures with BP using a mixed model. The researchers included the following covariates: age, body mass smoking, alcohol. glucose, creatinine clearance, use of cardiovascular medication, education, census-level poverty, day of week and season of clinical visit. The authors of the study found significant positive associations between 1-year average BC exposure and both systolic and diastolic blood pressure. An interquartile range (IQR) increase in 1-year average BC exposure (0.32 µg/m<sup>3</sup>) was associated with a 2.64 mm Hg increase in systolic BP and a 2.41 mm Hg increase in diastolic BP.

Long-term exposure to BC is associated with increases in BP in this older population, a finding that could explain part of the association of particulate air pollution with cardiovascular mortality. More research is needed to address the relation between traffic-related air pollution exposures and BP among diverse study populations, including women, other races and younger populations. Further research is also needed to study the role of diabetes, obesity and anti-hypertensive medication use in modifying the effect and to clarify mechanisms underlying association between BC and BP.

**Source:** Occupational and Environmental Medicine, Vol. 69, Issue 6, Pages 422-427, May 2012.

#### Benefits of a Face Mask to Reduce Particulate Air Pollution in Patients with Coronary Heart Disease

Air pollution exposure is an established risk factor for cardiovascular morbidity and mortality, especially exposure derived from traffic and industrial sources. Acute exposure to combustionderived particulate matter (PM) is associated with the onset of myocardial infarction and admissions to hospital in survivors of myocardial infarction and has been proposed as a trigger for acute cardiovascular events. Although estimates vary, chronic exposure to air pollution has been estimated to increase all-cause mortality by 2-4% per 10-µg/m3 increase in PM, with most deaths due to cardiovascular disease. The World Health Organization estimates that outdoor urban air pollution results in around 800,000 deaths worldwide each year.

In controlled exposure studies, inhalation of PM air pollution affects blood pressure and causes abnormalities in vascular function, coagulation, and myocardial perfusion. These responses provide a plausible mechanism to explain the observed increase in acute cardiovascular events and cardiovascular mortality after exposure to PM air pollution. However, although acute exposure induces these adverse effects, whether improvements in cardiovascular

health can be achieved by interventions targeted to reduce exposure in those living and working in highly polluted urban environments is unclear.

Major environmental health policy interventions can have a substantial impact on the health of populations. More practical solutions to reduce individual exposure and protect susceptible persons are urgently required. Therefore, a new study investigated the effects of a simple face mask intervention to reduce PM air pollution exposure on measures of cardiovascular health in patients with coronary heart disease.

In an open randomized crossover trial, 98 patients with coronary heart disease walked on a predefined route in central Beijing, China, under different conditions: once while using a highly efficient face mask, and once while not using the mask. Symptoms, exercise, personal air pollution exposure, blood pressure, heart rate, and 12-lead electrocardiography were monitored throughout the 24-hr study period.

Ambient air pollutants were dominated by fine and ultrafine particulate matter (PM) that was present

at high levels [74  $\mu$ g/m³ for PM,  $_{s}$ ]. Consistent with traffic-derived sources, this PM contained organic carbon and polycyclic aromatic hydrocarbons and was highly oxidizing, generating large amounts of free radicals. The face mask was well tolerated, and its use was associated with decreased self-reported symptoms and reduced maximal ST segment depression over the 24-hr period. When the face mask was used during the prescribed walk, mean arterial pressure was lower and heart rate variability increased. However, mask use did not appear to influence heart rate or energy expenditure.

Reducing personal exposure to air pollution using a highly efficient face mask appeared to reduce symptoms and improve a range of cardiovascular health measures in patients with coronary heart disease. Such interventions to reduce personal exposure to PM air pollution have the potential to reduce the incidence of cardiovascular events in this highly susceptible population.

Source: Environmental Health Perspectives, Vol. 120, No. 3, Pages 367-372, March 2012.

### EFFECTS OF MATERNAL CADMIUM EXPOSURE DURING PREGNANCY ON SIZE AT BIRTH

Human exposure to the toxic metal cadmium (Cd) occurs mainly through food, such as cereals, seafood, and offal, and inhalation of tobacco smoke. Once absorbed, Cd has a long half-life in the body, especially in the kidneys. Chronic Cd exposure has been shown to adversely affect kidney and bone and to increase the risk of cancer and overall mortality. Cd also functions as an endocrine disruptor and may thus affect reproduction and child development. In general, women are more susceptible to Cd toxicity, mainly because of increased intestinal uptake of Cd given low iron stores, which are more prevalent in women than in men.

There is, however, little information on the effects of Cd exposure in early life. Cd has been shown to be both embryotoxic and teratogenic in a variety of animal species, but this has not yet been confirmed in humans. Cd accumulates in human placenta, but the placenta is not a complete barrier, and Cd concentrations in cord blood increase with

maternal exposure. There is increasing evidence of associations between maternal Cd exposure and adverse pregnancy outcomes, such as reduced size at birth and preterm delivery.

The present study took advantage of the large, population-based, longitudinal mother-child cohort in Bangladesh to assess the effects of maternal Cd exposure on size at birth. The researchers previously reported arsenic exposure is associated with reduced size at birth. Additionally, pregnant women in this rural area had elevated concentrations of Cd in their placentas, and placental inversely associated with zinc (Zn) in cord blood, suggesting a possible effect of Cd on the transfer of Zn to the fetus. Thus, it is possible that Cd has adverse effects on pregnancy outcomes as well.

Women recruited from February 2002 through January 2003 who had a singleton birth with measurements of size at birth and had donated a urine sample

in early pregnancy for Cd analyses (n = 1,616) were selected.

The study found significant inverse associations between maternal Cd exposure and birth anthropometry in girls, especially head circumference and birth weight, but no associations in boys. These findings, along with evidence from previous experimental and observational studies, suggest that there may be sex differences in both toxicokinetics (i.e., intestinal uptake) and toxicodynamics of Cd. It is essential to follow the children through childhood to clarify whether the apparent effect on growth remains and whether the early-life Cd exposure is associated with other health outcomes later in childhood. This study clearly emphasizes the need to consider early-life effects of Cd in health risk assessments and to reduce Cd pollution worldwide.

Source: Environmental Health Perspectives, Vol. 120, No. 2, Pages 284-289, February 2012.

#### High Levels of Arsenic Discovered in Infant Formulas

Arsenic (As) is an established carcinogen based on studies of populations consuming contaminated drinking water. Recently, attention has focused on As exposure from food, in particular fruit juices and rice. Rice may contain As in total concentrations up to 100-400 ng/g, including both inorganic As (As) and the organic species dimethyl arsenate (DMA), with much lower concentrations (relative to DMA) of monomethyl arsenate (MMA) also occasionally detected. Total As (As<sub>total</sub>) in rice and relative proportions of DMA and As, differ both geographically and as a function of genetic and environmental controls.

As, is more toxic than DMA or MMA, and food regulatory limits, where they exist, are based on As,. Infants fed rice cereal at least once daily may exceed the daily As exposure limit of 0.17 µg/kg body weight per day based on drinking water standards. Rice products such as cereals and crackers, and rice drinks are potentially significant dietary sources of As. Infants and young children are especially vulnerable because their dietary As exposure per kilogram of body weight is 2-3 times higher than that of adults.

DMA is a metabolite of As, Although considered less toxic than As, its toxicological potential has not studied extensively. been presence of DMA in rice is likely due to natural soil microbial processes; however, DMA was used as a pesticide before being banned by the U.S. Environmental Protection Agency (EPA) in 2009. Organic food consumers may therefore object to its presence in organic foods even in the absence of direct evidence of human health effects of DMA.

In the United States, organic brown rice syrup (OBRS) is used as a sweetener as a healthier alternative to high-fructose corn syrup in products aimed at the "organic foods" market. Added sugar is often the main ingredient in infant and toddler formula, and the addition of sucrose to a main-brand organic formula was the feature of a popular press article in relation to possible childhood obesity. Many products - including some baby milk formulas, cereal bars, and highenergy performance products for athletes - list OBRS as the major ingredient. Brown rice is usually higher in both  $\mathrm{As}_{\mathrm{total}}$  and  $\mathrm{As}_{\mathrm{i}}$  than white rice

because As, is localized to the aleurone layer, which is removed when rice is polished, whereas DMA passes into the grain. Ranges of As concentration in rice products, including OBRS, are similar to As concentrations in brown rice.

Researchers posited that consumers of organic food products are generally attempting to make educated eating choices and that this consumer group would be particularly interested to know if, and to what extent, OBRS introduces As, DMA, and MMA into products. They therefore measured As<sub>total</sub> and As speciation in three commercially available brown rice syrups, 15 infant formulas without OBRS, 2 toddler formulas with OBRS, 29 cereal bars (13 with OBRS), and three flavors of a high-energy performance product.

The researchers used inductively coupled plasma mass spectrometry (ICP-MS) and ion chromatography coupled to ICP-MS to determine total As (As<sub>total</sub>) concentrations and As speciation in products purchased via the Internet or in stores in the Hanover, New Hampshire, area.

They found that OBRS can contain high concentrations of As, and DMA. An "organic" toddler milk formula containing OBRS as the primary ingredient had As, concentrations up to six times the U.S. EPA safe drinking water limit. Cereal bars and high-energy foods containing OBRS also had higher As concentrations than equivalent products that did not contain OBRS. As, was the main As species in most food products tested in this study.

There are currently no U.S. regulations applicable to As in food,

but the findings of this study suggest that the OBRS products evaluated may introduce significant concentrations of As, into an individual's diet. The study indicates that there is an urgent need for regulatory limits on As in food.

Source: Environmental Health Perspectives, Vol. 120, No. 5, Pages 623-626, May 2012.

#### **EDITORIAL BOARD**

Skorn Mongkolsuk, Ph.D. Khunying Mathuros Ruchirawat, Ph.D. Somsak Ruchirawat, Ph.D. Jutamaad Satayavivad, Ph.D. M.R. Jisnuson Svasti, Ph.D.

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

Correspondence should be addressed to:

#### ICEIT NEWSLETTER Chulabhorn Research Institute Office of Academic Affairs

54 Kamphaeng Phet 6 Road Lak Si, Bangkok 10210, Thailand Tel: +66 2 574 0615

Tel: +66 2 574 0615 Fax: +66 2 574 0616

CRI Homepage: <a href="http://www.cri.or.th">http://www.cri.or.th</a>

For back issues of our newsletter, please visit:

http://www.cri.or.th/en/envtox/et\_newsletter.htm