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Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

CRI Collaborates with Mongolia's Ministry of Environment and Tourism to Organize a Training Course on "Environmental Toxicology"

in Ulaanbaatar, Mongolia from June 22 - 27, 2023

Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, President of the Chulabhorn Research Institute (CRI) and Course Director, led a team of international faculty to conduct in-country training on "Environmental Toxicology", in collaboration with Mongolia's Ministry of Environment and Tourism, from June 22 - 27, 2023 in Ulaanbaatar, Mongolia. The training was supported by the Thailand International Cooperation Agency (TICA), Ministry of Foreign Affairs, Thailand, and CRI, through the institutional program for capacity building. International experts from the University of Aarhus, Denmark, Utrecht University, the Netherlands, and the Health and Environmental Sciences Institute, USA, were involved as part of the teaching faculty.

The CRI team has a vast amount of experience with regards providing training for participants within the SEA region, having trained participants from Brunei Darussalam, Cambodia, India, Indonesia, Laos, Malaysia, the Maldives, Myanmar, Nepal, the Philippines, Sri Lanka, Thailand, Timor Leste and Vietnam, amongst others. This training course was conducted as part of CRI's role as a WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology, and a WHO-designated regional centre for training in chemical safety.

The course was designed to provide a background of the major groups of toxic substances encountered by humans and animals through food and the environment, as well as through exposure at the workplace. These toxicants include toxic substances in air, water and soil; solvents; gases; pesticides; hazardous wastes and other pollutants.

(Continued on page 2)

CRI Collaborates with Mongolia's Ministry of Environment and Tourism to Organize a Training Course on "Environmental Toxicology" in Ulaanbaatar, Mongolia from June 22 - 27, 2023

(Continued from page 1)

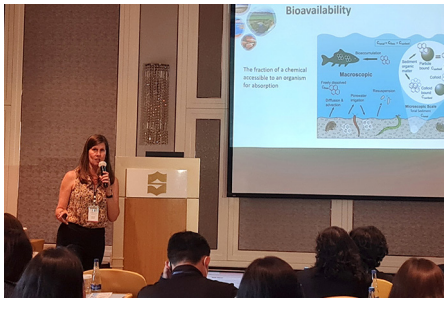
The course focused on the chemistry, fate and distribution of these toxic substances in the environment, mechanisms of their action, toxic manifestation in living organisms, as well as toxic syndrome in human beings.

The Opening Address and opening lecture entitled, "**Exposure to Chemical Hazards and Fate of Chemicals in the Body**", was delivered by Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, President of CRI and Course Director. Her Royal Highness Princess Chulabhorn Mahidol also gave a second lecture on "**Metals and Metallic Elements: Arsenic Exposure and Toxicology**" later in the course.

Participants attended lectures in 4 sessions: (1) Chemical exposure and toxicology, (2) Toxicity of environmental contaminants and industrial chemicals, (3) Air Pollution, and (4) Food safety, pesticides, and environmental carcinogens. The course also introduced modules on Hazard Assessment and Exposure Assessment through the Electronic Distance Learning Tool (eDLT) on Risk Assessment and Risk Management of Chemicals, which was developed by CRI in collaboration with WHO IPCS, the University of Ottawa (Canada), Utrecht University (the Netherlands), and the WHO Collaborating Center for Chemical Incidents (Cardiff, Wales).

The eDLT is an interactive, web-based, self-learning tool that is administered through a Learning Management System and hosted through a website at http://www.chemDLT.com, where interested persons can find more information about access and use. The participants were given access to the eDLT and went through two modules. The quizzes in the face-to-face training provided an opportunity to ask questions. Participants were also given access after the end of the face-to-face training to review the training material.

The teaching faculty for this training course included Professor Herman Autrup from Aarhus University (Denmark), Professor Martin van den Berg from Utrecht University (the Netherlands), Dr. Michelle Embry from the Health and Environmental Sciences Institute (USA), as well as Professor *Khunying* Mathuros Ruchirawat, CRI Vice-President for Research and Academic Affairs, Associate Professor Jutamaad Satayavivad, CRI Vice-President for Scientific Affairs, Associate Professor Panida Navasumrit, senior research scientist and Dr. Daam Settachan, research scientist from CRI's Laboratory of Environmental Toxicology.



The teaching team has a vast experience in providing training for participants within the South-East Asian (SEA) region, having trained participants from Bhutan, Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Sri Lanka, and Vietnam. This training course was conducted as part of CRI's role as a WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology, and a WHO-SEARO-designated Regional Training Center for Chemical Safety in the SEA Region.

The in-country training course was attended by 46 participants from various public health-related governmental agencies, as well as academic and research institutions, including the

Ministry of Environment and Tourism; National Center for Public Health of Mongolia; Central Laboratory of Environment and Metrology; National Reference Laboratory for Food Safety; Institute of Chemistry and Chemical Technology; Mongolian University of Life Sciences; and representatives of the Environmental Analysis Laboratory from various provinces.

As part of its capacity building programme, CRI regularly conducts in-country training in developing countries in the Asia-Pacific region in the areas of chemical safety, environmental health, toxicology and risk assessment in response to requests made from the respective country, either directly through an agency/institution with existing collaborations with CRI, or through an international organization, such as the WHO, e.g. through the respective regional offices at SEARO or WPRO.

For more information on CRI's capacity building programme, including a calendar of training events, please visit https://www.cri.or.th/

Arsenic Causing Gallbladder Cancer Disease

Gallbladder cancer (GBC) is one of the rarest biliary tract malignancies with high mortality rate with relatively low survivability of 5 years. India accounts for 10% of global GBC cases, about one million new cancer cases every year with mortality rate as high as 33% every year. GBC has a very unusual geographical distribution with high incidences seen in Chile, India, Japan, Poland, Israel, Bolivia, Thailand, and South Korea.

Population based data reveals that the incidences of this disease is very high (22 per 100,000) in the northern cities of India and low (0-0.7 per 100,000) in southern India. Among the total cancer patients, 8.3% and 16.9% are GBC cases in male and female, respectively.

The etiology of gallbladder cancer has generally been rather unclear, however the interplay of gallstones, genetic susceptibility, changes in the lifestyle factors and infections lead to progression of the cancer disease.

In the Gangetic plains of Bihar, a high percentage of population suffers from arsenic poisoning due to arsenic contamination of groundwater. The long duration exposure to this arsenic has magnified the toxicity by many folds causing deadly disease like cancer in human beings.

The inorganic arsenic which enters the human body is metabolized to organic arsenic (Monomethyl-arsonous acid-MMA(III), dimethyl-arsinic acid-DMA (V) and trimethyl-arsine TMA) which is still a toxic carcinogen. These organic compounds bind with DNA molecules which can influence transcription and translation leading to cancer.

Arsenic has been classified as a class I human carcinogen by International Agency of Research on Cancer (IARC), which notes that arsenic possesses the property of not only changing the configuration of the cellular activity but also modifying the gene functions at the genome level in human beings. Humans are exposed to this inorganic arsenic mainly by consumption of arsenic contaminated water and food.

The World Health Organisation (WHO) and the U.S. Environmental Protection Agency (US EPA) have recommended a threshold of 10 μg/L for inorganic arsenic concentration in drinking water.

Unfortunately, millions of people are exposed to much higher toxic levels of arsenic and some populations are unaware of its ill effects, which in long term is causing the development of malignancies. Various molecular pathways show the progression of the disease by arsenic biotransformation process, that alters the methylation pattern, which plays a key role in its carcinogenicity.

The present study was conducted to examine the association between gallbladder carcinogenesis and arsenic poisoning in the Gangetic plains of Bihar through a novel pathway.

The studied GBC patient's biological samples-gallbladder tissue, gallbladder stone, bile, blood and hair samples were collected for arsenic estimation. The blood samples from all gallbladder cancer patients were also evaluated for the presence of arsenic to understand exposure level in the population.

A significantly high arsenic concentration was detected in the blood samples with maximum concentration 389 μg/L in GBC cases in comparison to control.

Similarly, in the gallbladder cancer patients, there was significantly high arsenic concentration observed in gallbladder tissue with highest concentration of 2,166 μg/kg, in gallbladder stones 635 μg/kg, in bile samples 483 μg/L and in hair samples 6,980 μg/kg respectively.

There has been no benchmark range setup for the arsenic contamination in gall bladder tissue, bile, stones and blood, but for hair samples, the normal levels of arsenic contamination in the unexposed human populaces ranges between 20 and 200 μg/kg.

Moreover, the gallbladder cancer patient's blood samples study revealed very significant arsenic concentration in the population of Bihar with maximum arsenic concentration as 746 μg/L.

In conclusion, gallbladder cancer is prevalent in the Gangetic plains of Bihar, where the arsenic contamination in the exposed population is very high increasing the disease burden of the state.

The significantly high arsenic concentration observed in the gallbladder tissue, gallbladder stone, bile, blood and hair samples in GBC patients strongly indicates the linkage between high chronic exposure to arsenic and gallbladder carcino-genesis.

The GBC disease burden is significantly increased many folds in the arsenic exposed population. However, other confounding factors can also add to the disease burden of GBC manifolds.

The novel pathway of GBC carcinogenesis validates that arsenic is one of the important toxicants which is responsible for causing the disease in this particular area. Hence, there is an urgent need to control the disease burden by developing policies and guidelines that will alleviate arsenic exposure to the impacted populations.

Source: Scientific Report, Vol. 13, Article 4259, March 2023.

Effect of Air Pollution on Heart Failure

According to the Global Burden of Disease Study in 2019, air pollution in urban and rural areas was responsible for approximately 6.6 million premature deaths, mainly as a result of exposure to fine and ultra-fine particulate matter with an aerodynamic diameter of ≤2.5 μm ($PM_{2.5}$ and ultrafine particles (UFPs), respectively).

Observational and experimental studies have demonstrated that air pollution has a strong impact on cardiovascular diseases (CVDs) such as coronary artery disease, stroke and myocardial infarction.

Heart failure (HF) poses a significant global disease burden. The current evidence on the impact of air pollution on HF remains inconsistent.

HF is a complex syndrome caused by cardiac structural or functional impairment and is often the terminal stage of various CVDs. Although the age-standardized incidence of HF has been declining since 2000, it remains highly prevalent and contributes to considerable mortality and represents a considerable disease burden globally owing to the aging of the population.

In 2017, an estimated 63.4 million people worldwide suffered from HF, representing a 106% increase in the years of lived with disability (YLDs) compared with 1990.

In previous short-term air pollution exposure studies, air pollution was reported to be associated with HF hospitalization or death within a few days after exposure; however, most of the reports were from high-income countries (HICs) with lower concentrations of air pollutants. However, numerous studies have recently provided new evidence on the link between air pollution and HF from low-and middle-income countries (LMICs) or long-term exposures.

In addition, associations between long-term exposure to air pollution and HF have increasingly been reported. However, the results across studies have been largely inconsistent owing to variations in demographic characteristics, study design, types and concentrations of pollutants, and other factors.

The present study aimed to conduct a systematic review of the literature and meta-analysis to provide a more comprehensive and multi-perspective assessment of the associations between short- and long-term air pollution exposure and HF from epidemiological evidences.

Of 100 studies covering 20 countries worldwide, 81 were for short-term and 19 were for long-term exposure. Both short- and long-term exposure to $PM_{2.5}$, PM_{10}, and NO_2 were estimated to be significantly associated with higher risk of HF.

For short-term exposures, the results found the risk of HF increased by 1.8% and 1.6% per 10-μg/m^3 increment of $PM_{2.5}$ and PM_{10}, respectively. HF was also significantly associated with NO_2, SO_2, and CO, but not O_3. Positive associations were stronger when exposure was considered over the previous 2 days rather than on the day of exposure only.

For long-term exposures, there were significant associations between HF and several air pollutants including $PM_{2.5}$, PM_{10}, and NO_2.

Neither short- nor long-term exposure to O_3 was significantly associated with an increased risk of HF.

The adverse associations of most pollutants with HF were greater in low- and middle-income countries than in high-income countries.

Available evidence highlighted adverse associations between air pollution and HF regardless of short- and long-term exposure. The true impact of air pollution on HF hospitalization, incidence, and mortality still needs to be further explored in many aspects.

In conclusion, the present systematic review and meta-analysis provides compelling evidence for a significant association between $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO and increased risk for HF regardless of short- or long-term exposure.

The results reinforce the impact of air pollution on cardiovascular health. Sustained public and environmental policies and actions aimed at controlling air pollution are needed to reduce the burden of HF.

Source: Environmental Health Perspectives, Vol. 131, No. 7, Article 076001, July 2023.

Combined Chronic Copper Exposure and Aging Lead to Neurotoxicity

Copper, one of the most abundant transition metal ions in the human body and essential for life, participates in erythropoiesis, immune function, energy production, glucose metabolism, and neuropeptide synthesis.

Copper's involvement in physiological processes is mainly due to its function as a cofactor or structural component in diverse proteins. Alterations in copper homeostasis, either increased or decreased copper bioavailability, is related to neurodegeneration.

Increased copper levels have been reported in the cerebrospinal fluid and blood of Parkinson's disease (PD) patients, and chronic occupational exposure to copper increases the risk of developing PD.

However, a recent meta-analysis reported decreased copper levels in the substantia nigra of PD patients compared to healthy age-matched subjects.

The previous study determined the mechanisms by which copper induces dopaminergic cell death *in vitro*. However, the effect of chronic copper exposure on the neurodegenerative process has not been explored *in vivo*.

The present study aimed to elucidate whether prolonged copper treatment reproduces PD features and mechanisms during aging. Throughout 40 weeks, C57BL/6J male mice were treated with copper at 0, 100, 250, and 500 ppm in the drinking water.

(Continued on page 5)

PAH Exposure During Pregnancy and Child Anthropometry

Polycyclic aromatic hydrocarbons (PAHs) are byproducts generated during incomplete combustion or pyrolysis of organic materials and during various industrial processes.

In low- and middle-income settings, exposure occurs primarily via indoor burning of fossil fuels for heating or cooking. Other exposure sources include food, either through external pollution or because of cooking practices, contaminated drinking water, tobacco smoking, soil and household dust.

There is evidence suggesting that PAHs have endocrine disrupting properties, and that especially low-molecular weight PAHs can cross the placental barrier, raising concern for the impact on fetal development and child health.

Based on the inconclusive and very limited data available, there is a need for more large-scale prospective studies assessing the impact of maternal exposure to PAHs during pregnancy on fetal as well as continued childhood growth.

The aim of the present study was to explore associations of several different gestational urinary PAH metabolites with size at birth, and with child anthropometry from birth to 10 years in boys and girls in a longitudinal mother-child cohort in rural Bangladesh.

Researchers hypothesize that prenatal PAH exposure can increase oxidative stress and alter endocrine signaling and thereby hamper fetal and child growth.

This is the first study to measure levels of several hydroxylated PAH metabolites in pregnant women's urine in a resource limited setting in Bangladesh, with the purpose of evaluating whether levels of these metabolites impacted fetal and child growth.

Several PAH metabolites [1-hydroxyphenanthrene (1-OH-Phe), Σ2-,3-hydroxyphenanthrene (Σ2-,3-OH-Phe), 4-hydroxyphenanthrene (4-OH-Phe), 1-hydroxypyrene (1-OH-Pyr), Σ2-,3-hydroxyfluorene (Σ2-,3-OH-Flu)] were quantified in spot urine collected around gestational week 8.

The findings indicate that pregnant women residing in the rural areas were exposed to elevated levels of PAHs, mostly likely both via inhalation and ingestion.

Interestingly, in contrast to the hypothesis, increasing concentrations of gestational urinary PAH metabolites were associated with increased newborn weight and length, and associations were clearly more pronounced in boys than in girls. In boys, the strongest associations were observed with Σ2-,3-OH-Phe and Σ2-,3-OH-Flu for which each doubling increased mean birth weight and length.

Maternal urinary PAH metabolites were not associated with child anthropometry at 10 years. In longitudinal analysis, however, maternal urinary PAH metabolites were positively associated with boys' weight-for-age (WAZ) and height-for-age Z-scores (HAZ) from birth to 10 years, but only the association of 4-OH-Phe with HAZ was significant. No associations were observed with girls' WAZ or HAZ.

The study reports for the first time that positive associations of gestational urinary PAH metabolites with boys' weight and height seem to persist into childhood, but that they appear to be attenuated towards pre-pubertal age.

In conclusion, elevated gestational exposure to PAHs may increase fetal growth in male fetuses, while female fetuses seem to be less affected. The impact of gestational exposure to PAHs on boys' growth persisted during early childhood but seemed to level out at the age of 10 years.

Further epidemiological studies are needed to confirm the present findings and potential long-term effects on child health and development, especially since prenatal exposure to PAHs has previously been associated with several adverse outcomes such as obesity, metabolic risk indicators, and altered immune and cognitive function later in life. Additional experimental studies are needed to explore the underlying modes of action for the sex-specific findings.

Source: Environmental Research, Vol. 227, Article 115787, June 2023.

Combined Chronic Copper Exposure and Aging Lead to Neurotoxicity

(Continued from page 4)

The results showed that chronic copper exposure altered motor function and induced dopaminergic neuronal loss, astrocytosis, and microgliosis in a dose-dependent manner.

α-Synuclein accumulation and aggregation were increased in response to copper, and the proteasome and autophagy alterations, previously observed *in vitro*, were confirmed *in vivo*.

Protein ubiquitination, AMP-activated protein kinase (AMPK) phosphorylation, and the autophagy marker protein light chain 3-II (LC3-II) were also increased by copper exposure.

Finally, nitrosative stress was induced by copper in a concentration-dependent fashion, as evidenced by increased protein nitration. Protein tyrosine nitration can cause structural and functional changes, including protein inactivation and degradation, which are related to neuronal cell loss.

In summary, the study demonstrated that chronic exposure to copper during aging induces dopaminergic neuronal loss, astrocytosis, microgliosis, α-synuclein accumulation, the latter associated with alteration of the protein degradation pathways, the ubiquitin/proteasome system and autophagy, and finally, protein nitration.

This is the first study combining chronic copper exposure and aging, which may represent a new *in vivo* model of non-genetic PD, and help to assess potential prophylactic and therapeutic approaches.

Source: NeuroToxicology, Vol. 95, Pages 181-192, March 2023.

Ambient Black Carbon in Human Kidney Tissues

Higher levels of fine particulate matter ($PM_{2.5}$) from ambient air pollution were associated with an increased risk of adverse health outcomes, including cardiovascular disease, diabetes, and all-cause mortality.

Increased levels of $PM_{2.5}$ have been associated with an increased risk for decline in kidney function, including a lower estimated glomerular filtration rate (eGFR), a faster decline in the glomerular filtration rate, and a higher rate of chronic kidney disease and end-stage kidney disease.

Black carbon (BC) particles, being part of the ultrafine particulate mixture, are able to reach the deepest regions of the lungs and may even reach the circulatory system to spread to distant organs. The kidneys may be particularly vulnerable to the adverse effects of BC exposure due to their filtration function.

A higher exposure to $PM_{2.5}$ could be associated with increased rates of all-cause mortality, graft failure, and graft rejection in kidney transplant recipients. Indirectly, kidney transplant recipients may be more susceptible to the detrimental effects of $PM_{2.5}$ and BC, through the development of cardiovascular disease, which has already been extensively linked to elevated $PM_{2.5}$ and BC exposure levels.

In the present study, researchers hypothesized that BC particles reach the kidneys via the systemic circulation, where the particles may reside in structural components of kidney tissue and impair kidney function.

The BC particles in kidney biopsies from 25 transplant patients were visualized using white light generation under femtosecond-pulsed illumination.

Then, the kidney BC load was evaluated to see whether this depended on the long-term ambient black carbon exposure at the residence.

Furthermore, urinary kidney injury molecule-1 (KIM-1) and cystatin C (CysC) were examined in kidney transplant recipients one year post-transplant as promising a biomarker to evaluate potential tubular kidney damage in relation to BC exposure.

KIM-1 is a type 1 transmembrane protein which is distinctly upregulated in the proximal tubule after kidney damage, such as e.g., nephrotoxic injury or transplant rejection.

CysC, a protein produced by all cells that contain a nucleus, and thus can be found in almost all tissue and body fluids. CysC gets effectively filtered by the glomerulus and completely catabolized by the renal tubules. Therefore, raised plasma or urinary CysC levels correlate closely to GFR, and reflect glomerular or tubular dysfunction, respectively. Moreover, CysC is not affected by age, sex, and ethnicity, as opposed to the clinically relevant biomarker serum creatinine.

In this study, BC particles could be identified in all biopsy samples, predominantly observed in the interstitium (100 %) and tubules (80 %), followed by the blood vessels and capillaries (40 %), and the glomerulus (24 %).

The presence of the BC particles near the vascular components of the kidney suggests migration into the kidney tissue either before filtration by the glomerulus, or partial reabsorption by the tubules. In this regard, further investigation towards the biodistribution of BC particles is required.

The findings showed that elevated urinary levels of KIM-1 positively correlated with both modelled BC over the follow-up period and tissue BC in kidney biopsy tissue.

These results indicate that even low levels of BC exposure, either modelled or measured in kidney biopsy tissue, might influence urinary KIM-1 expression levels and quantifying urinary KIM-1 levels might allow early detection of cellular stress in proximal tubular cells as a result of BC exposure.

CysC is a member of the family of cysteine protease inhibitors, and its function is believed to regulate proteases secreted from lysosomes from dying and/or diseased cells. When the kidneys function appropriately, CysC is effectively filtered by the glomerulus, completely reabsorbed, and broken down by the renal tubules for recycling.

Furthermore, elevated levels of urinary CysC are associated with interstitial fibrosis and tubular atrophy in kidney transplant recipients, which are terminal consequences of chronic inflammation in the kidney.

In addition, residential proximity to a major road was inversely associated with urinary CysC and KIM-1. No significant correlations or associations could be observed for eGFR in relation to either investigated pollution exposure or residential proximity to a major road. Albeit non-significant, the results show a trend of decline in eGFR with an increase in tissue BC and modelled BC.

This is the first study to show the presence of BC particles in human kidney tissue and to investigate a direct association between these biomarkers of kidney injury and the accumulation of BC in the kidney.

In conclusion, under real-life exposure conditions, inhaled BC particles were translocated into the kidneys of kidney transplant recipients.

Urinary biomarkers, such as KIM-1, a biomarker to assess kidney damage, were linked to higher accumulation of kidney BC load, as well as with ambient BC exposure at the transplant recipients' residential address and the residential proximity to a major road.

Furthermore, urinary KIM-1 and CysC show potential as air pollution-induced kidney injury biomarkers for taking a first step in addressing the adverse effects BC might exert on kidney function.

In the future, this personalized BC exposure determination might be individualizable in a clinical setting, where tissue BC particles can be a systemic indicator of exposure to air pollution and its influence on kidney function.

More research towards the effects of accumulated BC particles on the kidney and its functioning is warranted.

Source: Environment International, Vol. 177, Article 107997, July 2023.

IARC-JECFA: Aspartame Hazard and Risk Assessment

Assessments of the health impacts of the non-sugar sweetener aspartame were released on July 14, 2023 by the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) Joint Expert Committee on Food Additives (JECFA).

Citing "limited evidence" for carcinogenicity in humans, IARC classified aspartame as possibly carcinogenic to humans (IARC Group 2B) and JECFA reaffirmed the acceptable daily intake of 40 mg/kg body weight.

The IARC and JECFA evaluations of the impact of aspartame were based on scientific data collected from a range of sources, including peer-reviewed papers, governmental reports and studies conducted for regulatory purposes. The studies have been reviewed by independent experts, and both committees have taken steps to ensure the independence and reliability of their evaluations.

Aspartame is an artificial (chemical) sweetener widely used in various food and beverage products since the 1980s, including diet drinks, chewing gum, gelatin, ice cream, dairy products such as yogurt, breakfast cereal, toothpaste and medications such as cough drops and chewable vitamins.

The two bodies conducted independent but complementary reviews to assess the potential carcinogenic hazard and other health risks associated with aspartame consumption. This was the first time that IARC has evaluated aspartame and the third time for JECFA.

IARC classified aspartame as possibly carcinogenic to humans (Group 2B) on the basis of limited evidence for cancer in humans, specifically for hepatocellular carcinoma. There was also limited evidence for cancer in experimental animals and limited evidence related to the possible mechanisms for causing cancer. These assessments will be published in Volume 134 of the IARC Monographs.

IARC's hazard identifications are the first fundamental step to understand the carcinogenicity of an agent by identifying its specific properties and its potential to cause harm, i.e. cancer.

JECFA's risk assessments determine the probability of a specific type of harm, i.e. cancer, to occur under certain conditions and levels of exposure. It is not unusual for JECFA to factor IARC classifications into its deliberations. JECFA also considered the evidence on cancer risk, in animal and human studies, and concluded that the evidence of an association between aspartame consumption and cancer in humans is not convincing.

JECFA concluded that the data evaluated indicated no sufficient reason to change the previously established acceptable daily intake (ADI) of 0-40 mg/kg body weight for aspartame. The committee therefore reaffirmed that it is safe for a person to consume within this limit per day.

The assessments of aspartame have indicated that, while safety is not a major concern at the doses which are commonly used, potential effects have been described that need to be investigated by more and better studies.

IARC and WHO will continue to monitor new evidence and encourage independent research groups to develop further studies on the potential association between aspartame exposure and consumer health effects.

More information on Summary of findings is available at URL: https://shorturl.at/lqtC9.

Source: WHO News Release, 14 July 2023.

Toxicity of Bisphenols in Pregnancy

Bisphenol analogues belong to the group of chemicals called diphenyl-methanes, which have two phenol rings connected by one carbon atom with varying substituents. Analogues of bisphenol are widely used in consumer products such as disposable dinnerware, canned food, personal care products, bottled beverages, and more, and dietary exposure is the main pathway.

Bisphenol A (BPA) is used to manufacture synthetic resins and commercial plastics in large quantities. Many epidemiological research and trials on animals have found BPA to be an endocrine disruptor that has negative effects on reproductive, immunological, and metabolic systems. Government regulations and public concerns about BPA in recent years have encouraged the production and use of bisphenol analogues as substitutes.

Bisphenol AF (BPAF), bisphenol AP (BPAP), bisphenol S (BPS), bisphenol B (BPB), and bisphenol P (BPP) are the most utilized BPA-free substitutes. These counterparts possess the same chemical structure and physical and chemical properties as BPA. Due to the absence of regulations on these BPA-free analogues, these bisphenol equivalents are currently permissible to use without limitation.

According to epidemiological and animal studies, bisphenols disrupt the reproductive, immunological, and metabolic systems. These analogues are estrogenic like Bisphenol A, although human studies are limited.

Researchers review the literature on the toxicity of bisphenol on reproductive and endocrine systems in pregnancy, focusing particularly on human studies. Three epidemiological studies and one human observational study demonstrated a substantial link between bisphenol toxicity and recurrent miscarriages.

Recurrent miscarriage (RM) is defined as two or more consecutive pregnancy losses before 20 weeks of gestation. At least 50% of women experience RM without a clear cause, often called unexplained recurrent miscarriage (URM).

(Continued on page 8)

CALENDAR OF EVENTS

International Training Courses at Chulabhorn Research Institute, Year 2023

	Training Course	Date	Duration	Closing Date
1	Fundamentals of Environmental Immunotoxicology and Reproductive Toxicology	October 2 – 6, 2023	5 work days	August 21, 2023
2	Environmental and Health Risk Assessment and Management of Toxic Chemicals	November 27 – December 2, 2023	6 work days	October 16, 2023

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

Course Description:

Environmental and Health Risk Assessment and Management of Toxic Chemicals (November 27 – December 2, 2023)

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 an electronic distance learning tool on risk assessment and risk management of chemicals and the WHO IPCS Human Health Risk Assessment toolkit will be introduced.

Requirement: Participants should have jobs/responsibilities related to the 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 materials, and health insurance.

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

Toxicity of Bisphenols in Pregnancy

(Continued from page 7)

Bisphenol analogues have been shown to mimic estrogen or progesterone and interact with the oestrogen or progesterone receptor (ER or PR) to form complexes, activating the down-stream transcription factors, which subsequently initiate estrogenic effects.

Vulnerability of the reproductive system, link between RMs and bisphenols, and effect of bisphenols on the hormonal system, embryogenesis and the genetic programming are summarized.

The effects of bisphenol analogues on URM as well as the underlying mechanisms are both in need of further investigation.

It is evident from the previous studies that bisphenol can indeed have a significantly detrimental effect on pregnancy and can lead to miscarriages.

Source: Cureus, Vol. 15, Issue 5, Article e39168, May 2023.

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

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