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"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

Health Impacts of E-waste Recycling Activities

Electronic-waste (e-waste) refers to end-of-life electronic products. It is estimated that the average lifespan of new computers has decreased 2.25 times from 1992 to 2005. As a consequence approximately 20-50 million tonnes of e-waste are generated worldwide and according to studies the amount of e-waste is increasing at a level of 3-5% per year, and the growing rate is three times faster than other individual waste streams. As the world's largest importer and recycler of e-waste, up to 80% of the world e-waste is estimated to be dumped in China, where primitive e-waste recycling activities exist.

It is known that e-waste contains numerous environmental toxicants, which may be released into the environment during the primitive e-waste recycling processes. Studies have shown that residents living in e-waste recycling and dismantling regions were at a risk of exposure to high levels of lead, antimony, mercury, cadmium, PAHs, PBDEs, PCBs and PBBs. Among these toxicants mercury and its compounds are distinguished as highly toxic material and can cause significant adverse effects on human health, particularly the developing nervous system of children.

Toxic heavy metals are released to the environment constantly from unregulated electronic waste (e-waste) recycling in Guiyu, China, and thus may contribute to the elevation of levels of mercury (Hg) and other heavy metals in human hair. Researchers therefore aimed to investigate concentrations of mercury in hair from Guiyu and potential risk factors and compare them with those from a control area, Jinping district of Shantou city, where no e-waste processing occurs.

All the volunteers were administered a questionnaire regarding socio-demographic characteristics and other possible factors contributing to hair mercury concentration.

The results suggested that hair mercury concentrations in volunteers of Guiyu were significantly higher than those of Jinping. Researchers also observed a higher over-limit ratio (> 1 μg/g according to USEPA) in Guiyu than in Jinping. Logistic regression model showed that the variables of living in a house that also served as an e-waste workshop, work related to e-waste, family income, time of residence in Guiyu, the distance between home and waste incineration, and fish intake were associated with hair mercury concentration. In the Guiyu samples, hair mercury concentration was found positively associated with the time residence in Guiyu, and frequency of shellfish intake; and negatively associated with the distance between home and waste incineration and whether homes also served as e-waste workshops.

In this study mercury levels in hair samples from Guiyu and Jinping in Shantou, China were identified. The residents from the e-waste recycling sites of Guiyu were exposed to high levels of mercury and with high over-limit ratio of hair mercury. The persistent existence of mercury in the environment and in particular the presence of mercury in humans should draw considerable public attention. Thus, the biological effects and potential risks of mercury to local residents need to be evaluated in further studies with larger samples. The finding of high levels of mercury in hair in an e-waste recycling area of a developing country highlights the need for better workplace conditions and protective measures for the workers in this type of business.

One potential limitation of the present study is that hair samples from volunteers

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Environmental Contamination and Early Life Neurodevelopment

Early life neurodevelopmental challenges and resulting disabilities due to cumulative exposure to hazardous substances begin at pregnancy and/or during the post-natal period. Exposure to environmental neurotoxic substances, per se or in combination, can burden the central nervous system (CNS) of the unborn fetus and young child.

Due to the increased pollution or environmental contamination, children nowadays are exposed to more man-made toxic agents than in the past. As a result of CNS immaturity, the unborn fetus and infant have to deal with different kinds of toxic substances co-occurring from multiple sources. Neurotoxic metals (e.g. lead – Pb, mercury – Hg, and aluminum – Al) *per se* are known to negatively affect neurodevelopment even at low doses. Indeed, developmental effects have been demonstrated in animal models and have also been observed in children. Worldwide, with the increase in manufactured goods and economic globalization, there is a high prevalence of exposure to neurotoxic chemicals *per se* or in combination.

Organic Hg compounds (methylmercury – MeHg, ethylmercury – EtHg) are comparably toxic and hazardous with demonstrable risks shown in animal and human studies. While MeHg exposure is mainly through consumption of fish and seafood, EtHg exposure occurs only through Thimerosal-containing vaccines (TCV) widely used in pediatric populations of third-world countries. Additionally, besides EtHg, TCV contains adjuvant-Al individually, these substances are below the currently assumed toxicological threshold. However, cumulative doses (during frequent immunization in infancy) can attain levels that are of concern. In the Amazon, when fish is consumed, MeHg is an obligatory dietary component driving exposure and hair Hg (HHg) concentrations in mothers and exclusively breastfed infants. During immunization with TCVs, both pregnant mothers and nursing infants are also exposed to EtHg (and adjuvant-Al). To deal with concerns about organic Hg exposure, the World Health Organization (WHO) has set guidelines to limit fish-MeHg intake during pregnancy and lactation, but considers the current exposure to multiple doses of TCV-EtHg to be safe. While eating fish during pregnancy can have neuroprotective attributes that counteract fish-MeHg effects, exposure to TCVs (during pre- and post-natal period), however, has no co-occurring counteracting substances against putative effects of EtHg (combined with adjuvant-Al).

It is known that neurotoxic chemicals (Pb, MeHg, EtHg, Al) *per se* can reach the CNS causing an adverse effect; however, neurological effects are less well known when these metals occur concomitantly. Usually, when a toxic substance does not show a measurable adverse or untoward effect, the studied level of exposure may be considered safe or without consequence. Despite the vast volume of literature about individually studied neurotoxicity of Pb, MeHg, EtHg, and Al, it is disappointing how little is known about their co-exposure and combined effects. Therefore, it is important to assess real life perinatal exposure to these metals and their effects on neurodevelopment. Furthermore, early identification of environmental toxic substances and modifying factors of neurological outcomes in children are essential for successful interventions to reduce potential hazards.

To this end a new study has been conducted of neurodevelopment in infants from two communities in Brazil.

Children living in the vicinity of tin-ore kilns and smelters (TOKS) were compared to children from a fishing village (Itapuã). Mean HHg concentrations were significantly higher in Itapuã children which received significantly less mean EtHg (88.6 µg) from TCV than the TOKS children (120 µg). Breast-milk Pb concentrations were significantly higher in the TOKS psychomotor development index (PDI) were statistically significant lower for the TOKS children only at 24 months of age. Multivariate regression analysis showed that mental development index (MDI) was negatively affected by breast-milk Pb and by HHg. PDI was positively affected by breastfeeding and negatively affected by EtHg. Milestone achievements were negatively affected by breast-milk Pb (age of walking) and by HHg (age of talking).

The two groups of young children, with distinct patterns of neurotoxic metal exposures, showed significant differences in neurodevelopmental outcomes. Children with higher exposure to maternal Pb and EtHg showed to be more sensitive to neurodevelopmental delays. The situations of multiple exposures to low doses of neurotoxic metals are complex to analyze, but show a dominant cause of neurodevelopmental delays that can lead to reversibility or aggravation.

Source: Environmental Pollution, Vol. 187, Pages 130-135, April 2014

Health Impacts of E-waste Recycling Activities

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were collected in barber shops instead of a random population sample. However, this is the first report to focus on hair mercury concentration conducted in Guiyu, China, an extremely polluted primitive e-waste recycling region. Elevated hair mercury concentrations and over-limit ratio in volunteers coming from Guiyu were found in this study. The mercury exposure in volunteers from Guiyu is related to engaging in e-waste recycling activities and environmental contamination caused by primitive e-waste recycling. Further epidemiological studies on a larger number of subjects coming from e-waste recycling and dismantling sites are needed to evaluate the effects of toxic heavy metals on human health.

Source: Environmental Research, Vol. 128, Pages 84-91, January 2014

ARSENIC METHYLATION AND LUNG AND BLADDER CANCER

Worldwide, millions of people are exposed to arsenic in their drinking water and ingested arsenic is an established cause of bladder, lung and skin cancer.

The National Research Council (NRC) has estimated that the excess cancer risk associated with lifetime exposures to arsenic at the US regulatory drinking water standard of 10 µg/L may be close to 1 in 300. This is about 30 to 300 times higher than the cancer risks estimated for exposure to all other known drinking water carcinogens at concentrations equal to their current US regulatory standards. Risks may be even higher in susceptible groups, and marked variation in susceptibility to arsenic-related disease appears to exist. Importantly, these risks are estimated based on extrapolations from studies where many people had arsenic water concentrations well above 200 µg/L. As such, the true cancer risks and the impacts of various susceptibility factors at arsenic water concentrations <200 µg/L are mostly unknown. This is important, since many people in the US and worldwide have arsenic in their water at these lower concentrations.

The primary metabolic pathway of ingested inorganic arsenic (iAs) in humans is methylation. Once ingested, iAs is methylated to monomethylarsonic acid (MMA5), which is reduced to monomethylarsonous acid (MMA3). MMA3 is then methylated to dimethylarsenic acid (DMA5), a small amount of which is then reduced to dimethylarsinous acid (DMA3).

In humans, this process is not complete, and some arsenic remains as iAs and MMA (MMA3 and MMA5). Almost all ingested arsenic is excreted through the urine and the relative distribution of arsenic metabolites in urine is commonly used as a biomarker of how well an individual can fully methylate ingested iAs. Typically, ingested iAs is excreted as 10–20% iAs, 10–15% MMA, and 60–75% DMA. However, large inter-individual variations exist.

In the past, methylation of iAs was thought to be primarily a detoxification pathway since the methylated species most commonly found in human urine, MMA5 and DMA5, are more water soluble, more readily excreted, and less acutely toxic than iAs. However, MMA3 is much more toxic *in vitro* than its pentavalent form, and may be more toxic than iAs. MMA3 is highly unstable and rapidly oxidized to MMA5 in urine, and is therefore extremely difficult to measure in field studies. However, epidemiological studies have reported associations between the proportion of total MMA (MMA3 plus MMA5) in urine (%MMA), and the risks of several arsenic-related diseases including bladder cancer, skin cancer, and arsenic-caused skin lesions. As a whole, these studies provide a highly consistent body of evidence linking methylation capacity and %MMA to arsenic-related disease risks. Currently, however, relatively little data is available for lung cancer. This is important since lung cancer is the number one cause of arsenic-related death.

In the present study, researchers investigated the association between arsenic methylation capacity and lung and bladder cancer by collecting detailed information of past arsenic exposure and potential confounders like smoking and occupation, and measuring urinary arsenic metabolites in 94 lung and 117 bladder cancer cases, and 347 population-based controls from regions in northern Chile with a wide range of arsenic drinking water concentrations. Because of its dry climate, small number of individual water sources, and availability of historic arsenic water concentration records for all cities and towns with many dating back 50 years or more, this area offers one of the best areas in the world to investigate the long-term health effects of arsenic exposure.

The assessment of methylation after cancer diagnosis raises concerns about the temporal relationship between disease and methylation capacity. That is, the effects seen in this study and in most other studies of arsenic metabolism and disease might not be due to the impact of methylation patterns on disease, but rather, due to the impact of disease or disease treatment on methylation patterns. Currently, no data are available on the impact of severe chronic non-arsenic-related diseases on arsenic metabolism. However, several of the studies linking %MMA to arsenic susceptibility involve non-melanoma skin cancer, benign skin lesions, or chromosomal aberrations, none of which would be expected to have significant systemic effects on metabolism. In addition, a few prospective cohort studies have assessed urine arsenic metabolic patterns before the disease diagnosis, and have reported associations between %MMA and heart disease and bladder cancer.

Overall, the consistency of the present findings with these studies and other data on biologic plausibility suggest the results represent the effects of %MMA on lung cancer risks, although the possibility that lung cancer affects %MMA cannot be completely ruled out. A longitudinal cohort study with accurate data on past %MMA might be better able to establish temporality, although this type of study would be incredibly difficult given the 30 to 40 year (or longer) latency of arsenic-caused cancer.

The results of the present study add to a gradually expanding body of evidence that inter-individual differences in arsenic metabolism play an important role in arsenic-related disease, including lung cancer.

The findings also add new evidence that arsenic drinking water concentrations <200 µg/L may be associated with significantly increased cancer risks, especially in people who methylate arsenic poorly. Although the design of this study does not allow confirmation of the temporal relationship between %MMA and lung cancer, the biologic plausibility of the results and their research is evidence that the findings represent a true impact of MMA on lung cancer risks. Data such as these are important in identifying susceptible subpopulations who may need specific regulatory protection. Information on the particular toxic species of ingested arsenic may also help elucidate the mechanisms of arsenic-caused disease, which are currently unknown.

Source: Toxicology and Applied Pharmacology, Vol. 274, Issue 2, Pages 225-231, January 2014

Air Pollution and Respiratory Infections during Early Childhood: *An Analysis within the ESCAPE Project*

Respiratory infections are a leading reason for outpatient physician visits and hospitalizations among children. Most infections resolve with minimal use of health care resources; however, episodes of severe or recurrent infection may require hospitalization or surgery, and the resultant burden on resources is substantial.

Young children are particularly susceptible to respiratory pathogens and also to air pollution. There is strong evidence that indoor air pollution, such as secondhand smoke and the use of biomass, is a risk factor for respiratory infections in children. Evidence is growing to support an association with outdoor air pollution as well.

The European Study of Cohorts for Air Pollution Effects (ESCAPE) is a project aimed at investigating the impacts of long-term exposure to air pollution through the development of harmonized exposure data assigned to previously established cohorts that have collected information on specific health outcomes of interest for air pollution research. A team of researchers analyzed data from 10 European birth cohorts and completed a meta-analysis of air pollution and respiratory infection during early childhood.

Urban air pollution has been associated with respiratory tract infections, pneumonia, croup, persistent cough, and otitis media during childhood. Associations have also been reported for indoor air pollution and pneumonia in developing countries where concentrations are considerably higher than in the study areas. The findings are consistent with previous studies that used similar methods to examine air pollution and otitis media and a recent meta-analysis on long-term $PM_{2.5}$ and acute lower respiratory infection in children.

Similar to secondhand smoke, air pollution is thought to increase susceptibility to respiratory infections primarily via an inflammatory response. Urban air pollution may impair defense mechanisms, and oxidant pollutants, in particular, may exacerbate virus-induced inflammation of the respiratory system.

Analyses were restricted to the first years of life to include the period of greatest age-specific incidence of respiratory infections. The findings suggested that air pollution effects may be slightly stronger during the first year. This finding could highlight a unique period of susceptibility when children are at increased risk of respiratory infections due to air pollution.

A unique strength of land use regression models is their ability to capture small-scale spatial variability in exposure; however, the measurements used to create the ESCAPE exposure models were taken after the birth year, and this may have introduced exposure misclassification. Although it is possible that overall levels of air pollution changed during this period, previous findings suggest that the spatial distribution of air pollutants within each area remained consistent. Further, the sensitivity analyses using monitoring data to back-extrapolate exposure estimates to the actual first year of life were consistent with the main findings.

The wording of parental questionnaires was similar across each cohort, and previous research has shown good agreement between maternal recall and medical records during early childhood. Geographic differences in the prevalence of outcomes across the cohorts were most pronounced for otitis media and may point to potential diagnostic biases or disease misclassification between countries.

The present meta-analysis of 10 European birth cohorts found consistent evidence for an association between traffic-related air pollution and pneumonia, and some evidence to suggest an association with otitis media. Policies aimed at reducing air pollution may be successful in reducing the overall burden of pneumonia in early childhood.

Source: Environment Health Perspectives, Vol. 122, No. 1, Pages 107-113, January 2014

Genotoxic Effect of Air Pollution: A Study of Primary School Children Exposed to Air Pollutants

Epidemiological studies indicate that in adults, there is an association between high levels of urban air pollution and increased risk of lung cancer. The biomarker-based molecular epidemiology studies may help to understand relative contribution of ambient air pollution as a risk factor of cancer and facilitate health risk assessments especially under conditions of moderate or low air pollution. Biomarkers such as DNA, protein adducts, and cytogenetic alterations (e.g., micronuclei, chromosomal aberrations) may help in identifying the exposure and revealing its early effects.

In the last 10 years, some studies have been carried out to evaluate the effect of environmental exposure to genotoxic agents in children because of the two main concerns: children may be more sensitive than adults to genotoxic agents and genetic damage appearing at younger ages may affect the lifetime risk of adverse health outcomes, e.g., cancer. These studies imply that air pollution may affect levels of genomic stability and potentially cancer in children.

Micronuclei (MN) frequencies represent both clastogenicity (chromosome breakage) and aneuploidy (chromosome loss) in cells studied, and it has been extensively used to identify potential genotoxic exposures and also chromosomal instability.

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HEALTH EFFECTS OF PERSISTENT ORGANIC POLLUTANTS

Persistent organic pollutants (POPs) are a heterogeneous group of man-made chemicals with a long half-life that accumulate in fat tissues due to their lipophilic nature. They are environmental toxicants that have been associated with cardiovascular disease (CVD) and cancers.

Although banned for more than thirty years, polychlorinated biphenyls (PCBs) still persist in the environment and in food sources such as fish, meat and dairy products. *In vitro*, these PCBs have been shown to antagonize androgen receptor activation, affect estrogen receptor activation, inhibit gap junction communication and bind to transthyretin. Organochlorine pesticides (OCPs) as well as the polybrominated diphenyl ethers (PBDEs), which are structurally similar to PCBs, are believed to be endocrine disruptors by their interference with different hormone systems. Furthermore, negative effects of POPs may be related to induction of proinflammatory pathways.

Lipoproteins are classified into three main fractions depending on their density: very low-density, low-density and high-density lipoproteins (VLDL, LDL and HDL, respectively). VLDL is synthesized in the liver and transports lipids to peripheral tissues. LDL arises from hydrolysis of VLDL and delivers cholesterol to the cells by receptor mediated endocytosis. HDL is responsible for the reversed cholesterol transport in which excess cholesterol is transported back to the liver for excretion into bile. High levels of LDL cholesterol (LDL-C) are considered a strong risk factor for future CVD, thereby being the rationale for cholesterol lowering therapies. Low levels of HDL cholesterol (HDL-C) is a risk factor for CVD. Many HDL functions are determined by the proteins in the particles. One such important protein is paraoxonase 1 (PON1), a calcium-dependent esterase associated to HDL in the circulation. PON1 has been shown to provide HDL with anti-inflammatory properties, which includes hydrolyzing lipid peroxides in LDL and preventing foam cell formation in the vascular wall. Furthermore, reduced PON1 activity has been linked to CVD diabetes mellitus and cancer.

Early reports have shown that POPs can bind to lipoproteins. However, apart from a previous study showing that a large fraction of POPs are associated to LDL/VLDL and HDL in healthy individuals, little is known about the human lipoprotein distribution of POPs *in vivo* and how this relates to disease progress.

Now a new study has been conducted that aimed to investigate the concentrations of POPs in human HDL and LDL/VLDL and the possible association with CVD and cancer occurrence in individuals living in a contaminated area.

Fourteen PCBs and 3 OCPs were detected, and especially highly chlorinated PCBs were enriched in lipoproteins. Significantly higher concentrations of POPs were found among individuals with CVD or cancer compared to controls. Principal component analyses showed that POP concentrations in HDL were more associated with CVD, while POP concentrations in LDL/VLDL were more associated with cancer. PON1 activity was negatively correlated to sumPCB and a co-variation between decreased arylesterase-activity increased PCB concentrations and CVD was found.

This study shows that POPs are present in lipoproteins and were more abundant in individuals with CVD or cancer compared to healthy controls. The results also indicate that PCB exposure is accompanied by reduced PON1 activity that could impair the HDL function to protect against oxidation.

Source: Environment International, Vol. 65, Pages 93-99, April 2014

Genotoxic Effect of Air Pollution: A Study of Primary School Children Exposed to Air Pollutants

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In a new study, researchers have investigated how exposure to air pollutants affected cytogenetic damage by measuring MN frequencies in buccal epithelial cells (BECs) from primary school children living in an urban city of Turkey.

Measured NO_2 and SO_2 concentrations did not exceed the European Union (EU) limit levels either in urban-traffic or suburban regions. Higher O_3 concentrations were measured in the suburban site especially in the summer period. Particulate matter ($PM_{2.5}$ and PM_{10}) levels which did not differ statistically between two regions were above the EU limits in general. Although BEC-MN frequencies of children living in the suburban sites were higher in general, the difference between two regions was not significant either in the summer or winter periods. BEC-MN frequencies of the urban-traffic children were found to be significantly higher in summer period when compared to winter period. On the other hand, no seasonality was observed for the suburban children. Similar results have been obtained in the BEC frequency with MN in this study. In summer, BEC-MN frequencies were significantly increased with the decrease in pulmonary function levels based on forced expiratory flow between 25 and 75% of vital capacity ($FEF_{25–75\%}$) levels.

The results of this recent study showed that increasing ozone concentrations may cause short-term impairment in lung function of school-aged children. Moreover, summer MN frequencies were significantly increased with the decrease in pulmonary function test. Considering the relationship identified between summertime O_3, which is significantly higher in the summer period, with asthma and related symptoms, an increase in O_3 may also be related with genotoxic effects.

The study concludes that children in both urban and suburban sites may be vulnerable to genotoxic damage especially in the summer season probably due to relatively high ozone concentrations.

Source: Environment Science and Pollution Research, Vol. 21, Issue 2, Pages 1197-1207, January 2014

ANTIOXIDANTS AND CANCER

Antioxidants including vitamins, carotenes, and minerals are found naturally in the diet and are added to food, cosmetic products, and pharmaceuticals. Antioxidants act as electron donors that neutralize reactive oxygen species (ROS) and other free radicals that may otherwise damage DNA and promote tumorigenesis. Consequently, popular wisdom – supported by numerous cellular and preclinical studies – holds that antioxidants protect against cancer. However, large randomized clinical trials have produced inconsistent results, and some studies indicate that antioxidants may even increase cancer risk. Moreover, recent genomic analyses of lung cancers have shown a high frequency of mutations in genes that activate an endogenous antioxidant program, suggesting that decreasing the amounts of ROS promotes tumor growth. Consistent with this notion, experimental studies show that oncogenes such as K-RAS and B-RAF promote tumor growth by stimulating NRF2-mediated transcription of endogenous antioxidant genes. Despite the striking discordance between the use of antioxidants and the lack of experimental support for their anticancer properties, no studies have yet examined their impact on tumor growth in state-of-the-art mouse models of cancer, including lung cancer – the most common form in humans.

The objective of the present study was to define the impact of antioxidant supplementation N-acetylcysteine (NAC) and vitamin E on tumor progression, severity, and lethality in mouse models of endogenous lung cancer.

This study demonstrates that antioxidant supplementation of the diet reduces ROS and DNA damage, prevents p53 activation, and markedly increases tumor cell proliferation and tumor growth in mice. The data demonstrate that tumor cells proliferate faster when oxidative stress is suppressed. This reasoning is consistent with previous studies showing that oncogenes stimulate NRF2-mediated expression of endogenous antioxidants, reduce ROS, and thereby increase tumor cell proliferation.

The antioxidants reduced the expression of genes involved in the endogenous ROS defense system. This result is consistent with the reduced amounts of ROS and oxidative DNA damage and the increased GSH/GSSG ratio. The simplest explanation for this result is that a feedback mechanism in lung cells down-regulates the endogenous ROS defense system when the amounts of ROS are suppressed by NAC or vitamin E.

The data do not support a direct role for the reduced expression of endogenous antioxidant genes in the increased tumor growth. Instead, several lines of evidence suggest that reduced amounts of p53 mediate the antioxidant-induced increase in tumor growth. First, NAC and vitamin E reduced p53 in tumors and cultured mouse and human tumor cells. Second, antioxidants increased the proliferation of human lung cancer cells with wild-type, but not mutant, p53. Third, the ability of antioxidants to increase tumor cell proliferation was abolished when p53 was inactivated or suppressed by shRNAs. One potential explanation for the reduced amounts of p53 is that the antioxidants reduced oxidative DNA damage, γH2AX, and phospho-ATM and thereby removed potent stimuli for p53 activation and stabilization.

One limitation of the study is that the K-RAS and B-RAF models only allow researchers to study the impact of antioxidants on tumor progression, and not tumor initiation or prevention. In previous studies, antioxidants were protective against chemically induced lung cancer, and it is possible that high amounts of ROS are required for tumor development in that setting. However, experimental studies and large clinical trials quite convincingly suggest that antioxidants, including isoflavones, carotenes, vitamins, and NAC, should not be recommended for the prevention of lung cancer and that their use may promote tumor growth.

This work was done in cells and in mice, but the researchers took care to make it as relevant to humans as possible. Thus, the mice were treated with types and doses of antioxidants (vitamin E and NAC) that healthy humans use, and the results were confirmed in human lung cancer cell lines. Although the current study does not show what would happen to wild-type mice or healthy people using antioxidants, it provides evidence for a procarcinogenic role of antioxidants in people who are already at a higher risk of cancer, such as smokers.

Source: Science Translational Medicine, Vol. 6, Issue 221, Pages 221ra15, January 2014

Indoor Air Pollution and the Risk of Childhood Acute Leukemia: A Study Conducted in Shanghai

Childhood acute leukemia (AL) is the most common malignant tumor in children, comprising about one-third of all childhood cancers with an average annual incidence of 40.7 per million in Shanghai. Acute lymphocytic leukemia (ALL) accounts for approximately 80% of all childhood leukemia diagnoses, with incidence reaching a peak at 2-5 years of age, indicating that exposure early in life is important. The causes of childhood AL in the majority of cases are assumed to result from complex interactions between genetic predispositions and environmental factors, including air pollution.

Indoor air pollution may have a greater impact than outdoor pollution because children spend 90% of their time indoors and they have a greater physiological susceptibility to indoor air pollutants than adults do. Home renovation as a source of indoor pollution and its impact on the health of children is an increasing concern in China.

Many indoor materials and utilities, such as paints, furnishings, carpets, and household cleaning products, contain volatile organic compounds (VOCs). The renovation of a house may significantly affect indoor VOCs concentrations. For example, the most significant sources of formaldehyde (HCHO) at home are wood products using adhesives that contain urea-HCHO resins. Among the indoor VOCs, some are carcinogenic

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Emission of Air Pollutants from Burning Candles in Indoor Environments

The increase of candle use improved the public concern about potential health effects because of the exposure to candle emissions. Burning of candles in indoor environments can release a large number of toxic chemicals, including carbon monoxide (CO), nitrogen oxides, aldehydes and unburnt hydrocarbons, such as polycyclic aromatic hydrocarbons (PAHs). It is believed that regular burning of several candles in indoor environments can expose people to harmful amounts of organic chemicals.

Few studies have been conducted concerning the emissions from burning candles; in particular emissions of lead, zinc or soot, produced by the heating of candles wick cores or by the wax combustion/evaporation were evaluated, while less research has been done on the presence of volatile organic compounds (VOCs) in candle emissions. The purity of the raw materials and additives used can play a key role because raw materials which have not been adequately refined can contain some precursors which promote the formation of pollutants once the candle wax is burnt. Paraffin waxes constitute the major bulk of crude oil based crystalline waxes and are really important for industrial applications; more than 50 % of the worldwide wax production is used for candles manufacturing.

Consequently, the aim of this present study has been to investigate the presence of several pollutants both in raw materials and in exhaust gases from the burning of different container candles using a test chamber. In particular, emission factors for some PAHs, aromatic species (BTEX), short-chain aldehydes and particulate matter (PM) have been determined for container candles constituted by paraffin waxes with different degrees of refinement. Among the various pollutants, several EU priority chemicals, such as formaldehyde, benzene, toluene and naphthalene, have been monitored into the raw materials and within the candles exhausts. Then, the obtained results have been compared to identify the possible role of the raw materials composition on the pollutants emissions.

Almost no emissions of aldehydes have been found for all the candles, leading to the conclusion that such emissions could be mainly related to the presence of a fragrance rather than to the other candle parameters, in agreement with previous findings concerning scented candles.

Conversely, it has been found that CO, SO_2, BTEX, PAHs and PM emissions are more related to the corresponding wax quality rather than to the wax additives. Moreover, for the container candles investigated it has been highlighted that the presence of oil into the candle wax influences not only PM emission factors but also the particles size formation and growth mechanisms.

Several pollutants emission factors for three different wax-based container candles have been determined in a laboratory-scale test chamber. Such results could be used, at least at a first glance, to foresee the expected pollutant concentration in a given indoor environment with respect to health safety standards, while the test chamber used for performing the reported measurements could be useful to measure the emission factors of any other candle in an easy-to-build standardized environment.

Source: Environment Science and Pollution Research, Vol. 21, Issue 6, Pages 4320-4330, March 2014

Indoor Air Pollution and the Risk of Childhood Acute Leukemia: A Study Conducted in Shanghai

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such as HCHO, benzene and 1,3-butadiene.

The previous studies suggested that living close to heavy-traffic roads, living next to a gas station, and exposure to tobacco smoking were associated with increased risks of both childhood ALL and acute myeloid leukemia (AML). Most previous studies depended on representative modeled air pollutant levels rather than the actual measured concentrations, and even less research has been conducted on the exposure to indoor air pollution.

A major methodological improvement in the current study over previous studies was the direct measurement of air pollutants in children's bedrooms, which allowed a better appraisal of individual exposure compared to indirect methods such as indoor source recording or questionnaires. The study included a broad range of VOCs quantitatively assessed by diffusive sampling. Because the diffusive sampler is small, light and noiseless, it is suitable for a large-scale field study and for determining indoor air pollution. The study showed the feasibility of measuring air pollutant levels in the bedrooms of children by diffusive sampling.

Researchers found that higher concentrations of indoor air pollutants were related to an elevated risk of childhood AL. Indoor behavioral factors and outdoor pollution might affect indoor air pollution, and synthetic materials might generate more indoor air pollutants than that of natural wood material.

Given the potential implications of the study, the association between indoor air pollutants and risk of childhood AL must be interpreted cautiously. Nevertheless, both questionnaire-based responses and quantitative measurements all indicated that indoor air pollutants were associated with increased risk of childhood AL. The substantially different levels of indoor air pollutants between cases and controls may not be due to chance. This research underscores the importance of further investigation of the link between exposure to indoor air pollution and childhood AL with repeated measurements of indoor air pollutants, detailed exposure classifications and expansion of the study population.

Source: Environment Pollution Research, Vol. 187, Pages 81-89, April 2014

ANNOUNCEMENT

International Symposium on "RECENT ADVANCES IN CANCER THERAPEUTICS"
October 13-15, 2014, Chulabhorn Convention Center, Bangkok, Thailand

Organized by Chulabhorn Research Institute in collaboration with Fritz Bender Foundation

Chairpersons: - Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol (CRI, Thailand)
- Enrico Mihich (Dana Farber Cancer Institute, USA)
- Kurt S. Zänker (University of Witten/Herdecke, Germany)

Keynote Lecture by Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol

PROGRAM

Session I. Genetic Profiles of Cancer:

- Trans-ethnic exploration of liver cancer genome, ***Tatsuhiro Shibata*** *(Japan)*
- Towards integrated "omics" for personalized treatment of breast cancer, ***Anne-Lise Borresen-Dale*** *(Norway)*
- Hypothesis based genomics as a tool to query clinically relevant essential biology in cancer, ***Zoltan Szallasi*** *(Denmark)*
- The new driver-based classification of breast cancer: 10 distinct molecular entities, ***Carlos Caldas*** *(UK)*

Session II. Therapeutic Targets and Drugs:

- Development of targeted cancer therapeutics, ***Axel Ullrich*** *(Germany)*
- Recent successes in targeted anti-cancer therapy, ***Alex Matter*** *(Singapore)*
- Development of small molecule kinase inhibitors as drugs, ***Michelle D. Garrett*** *(UK)*

Session III. Experimental Therapeutics:

- Regulation of self-renewal in cancer stem cells, ***Pier Giuseppe Pelicci*** *(Italy)*
- The critical role of extracellular matrix and microenvironment in metastasis and dormancy, ***Mina Bissell*** *(USA)*
- Precision medicine for colorectal cancers, ***Alberto Bardelli*** *(Italy)*
- Tackling the heterogeneity of brain tumors, ***Joan Seoane*** *(Spain)*

Session IV. Tumor-Host Relationships:

- Macrophages in tumor promoting inflammation: Therapeutic targeting in human cancer, ***Alberto Mantovani*** *(Italy)*
- Remodeling of collagen architecture can mirror immunological changes of tissue microenvironment: new insights for targeting treatments, ***Luca Vannucci*** *(Czech Republic)*
- MHC antigens and the immune escape of cancer, ***Federico Garrido*** *(Spain)*
- Effects of tumor acidity of immune microenvironment and therapeutic strategies based on pH modulation, ***Licia Rivoltini*** *(Italy)*

Session V. Translational Investigations:

- Rapid approval of new cancer drugs after Phase I, ***Bruce Chabner*** *(USA)*
- Disrupting arginine metabolism with apoptotic inducing agents: A new paradigm in treating arginine dependent tumors, ***Niramol Savaraj*** *(USA)*
- New approaches to the treatment of hepatocellular carcinoma, ***Lynn G. Feun*** *(USA)*
- Dissecting colorectal cancer in multiple targetable diseases, ***Josep Tabernero*** *(Spain)*
- PROFILE: An enterprise-level genomic testing program for research and clinical care, ***Barrett Rollins*** *(USA)*
- Cancer-related fatigue--symptoms, diagnosis and therapy, ***Kurt S. Zänker*** *(Germany)*

Reservation has to be made by registering no later than October 3, 2014.

--- Please note that places will be allocated on a first come first served basis.---

For more information, please visit: ***http://ract2014.cri.or.th***

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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 2 553 8535
Fax: +66 2 553 8536
CRI Homepage: <http://www.cri.or.th>

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