CRI/ICEIT
NEWSLETTER

VOL. 18 NO. 3 – July 2008
ISSN 0858-2793
BANGKOK, THAILAND

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".

HRH PRINCESS CHULABHORN PRESIDES OVER

THE SCIENCE AND STRATEGY FORUM ON ARSENIC AND HUMAN HEALTH IN VIETNAM: AN INTERNATIONAL PERSPECTIVE HANOI, JULY 17, 2008

This landmark international event was jointly organized by Vietnam's Ministry of Health and the Chulabhorn Research Institute in collaboration with Vietnam's National Institute of Occupational and Environmental Health, Center for Environmental Toxicology and Sustainable Development, Republic of Korea's International Environmental Research Center of Gwangju, Institute of Science and Technology, and the United States' National Institute of Environmental Health Sciences.

The Science and Strategy Forum aimed at raising awareness of the scale and impact of arsenic contamination on human health in water and the environment especially in Southeast Asian countries. The meeting was attended by experts in the field of environmental health from Vietnam, Thailand, Korea and the United States.

The Forum was preceded by a workshop at which experts presented their research on arsenic and public health. A field trip was made to a region in Hanam where arsenic contamination is of current concern, particularly with regard to prenatal exposure and exposure of newborns.

The Forum aimed to identify the research needs and map out preventive measures to address the public health impacts of arsenic exposure, both in short and long term.

In the opening address, HRH Princess Chulabhorn expressed the belief that many of the region's population, as well as populations in other parts of the world, would benefit from the strategies for addressing arsenic contamination that would be the outcome of this meeting of experts.

CADMIUM EXPOSURE AND DENTAL CARIES

The prevalence of dental caries exceeds 50% in 5- to 9-year-old U.S. children and increases to 78% in those 17 years of age, making this disease more common than asthma and hay fever. Dental caries have been associated with numerous adverse effects on children's health including pain, restricted dietary intake, impaired growth, and reduced body weight. Children living below the poverty line have more severe dental caries, and many remain untreated because of low dental health insurance coverage. An increasing body of evidence supports the role of environmental factors in the etiology of dental caries. Exposure to lead and environmental tobacco smoke (ETS), which has high concentrations of cadmium, has been linked with an increased risk of dental caries in children. These studies consistently reported positive associations between environmental exposures and caries in deciduous teeth (baby teeth) but not in permanent teeth, indicating that children's deciduous dentition may be particularly susceptible to environmental toxicants.

An estimated 2.3% of Americans have elevated urine cadmium concentrations, a biomarker of cumulative cadmium exposure. ETS, a known risk factor for dental caries in children, accounts for approximately 20% of urine cadmium levels in U.S. children. Other sources of cadmium include emissions from mining, smelting, fuel combustion, phosphate fertilizer use, sewage sludge application, disposal of metal wastes, and industrial uses of cadmium in manufacturing of batteries, pigments, stabilizers, and alloys. Cadmium is present in trace amounts in certain foods such as leafy vegetables, potatoes, grains and seeds, liver and kidney, and crustaceans and mollusks. Once in the body, cadmium accumulates in the kidney, liver, and bone and is excreted very slowly.

Exposure to cadmium is associated with numerous systemic health effects including renal dysfunction, skeletal disorders, and cardiovascular disease. Furthermore, the International Agency for Research on Cancer (IARC) has classified cadmium as a Group I human carcinogen. The evidence of an association between cadmium and dental caries arises from animal experiments. Studies showed that exposure to cadmium in rats during the neonatal period resulted in the development of severe dental caries, and this caries-promoting effect of cadmium was not negated by the addition of fluoride to drinking water. Administration of cadmium also disrupted salivary gland examined in rats.

Now, researchers have examined the association of environmental cadmium exposure with pediatric dental caries using data from the Third National Health and Nutrition Examination Survey (NHANES III), a nationally representative survey conducted from 1988 to 1994 in the United States. Particular emphasis has been placed on differentiating the association of cadmium exposure and dental caries from the effects of ETS, which may confound the relationship between cadmium and dental caries.

Researchers used logistic and zero-inflated negative binomial (ZINB) regression to estimate the association between urine cadmium concentrations and caries experience, adjusting these analyses for potential confounders including ETS.

The study found that urine cadmium concentrations ranged from 0.01 to 3.38 ng/mL. Approximately 56% of children had experienced caries in their deciduous teeth, and almost 30% had been affected by caries in their permanent dentition. An interquartile range (IQR) increase in creatinine-corrected cadmium concentrations (0.21 µg/g creatinine) corresponded to a 16% increase in the odds of having experienced caries in deciduous teeth [prevalence odds ratio (OR) = 1.16; 95% confidence interval (CI), 0.96-1.40]. This association was statistically significant in children with low ETS exposure (prevalence OR = 1.30; 95% CI, 1.01-1.67). The results from the ZINB regression indicated that, among children with any caries history in their deciduous teeth, an IQR increase in cadmium was associated with 17% increase in the number of decayed or filled surfaces. No association between cadmium and caries experience in permanent teeth was observed.

Overall, the study provides evidence that cadmium may be associated with an increased risk of dental caries in deciduous teeth of children. Because of numerous sources of exposure and widespread distribution of this toxicant, it is increasingly important to understand the systemic and oral health effects of cadmium, particularly in highly susceptible populations such as children. Prospective epidemiologic studies are needed to confirm these findings and to understand the mechanisms behind the observed association between cadmium and dental caries.

Source: Environmental Health Perspectives, Vol. 116, No. 6, June 2008.

Nonmalignant Respiratory Effects of Chronic Arsenic Exposure from Drinking Water

Arsenic (As) from drinking water has been associated with malignant and nonmalignant respiratory illness. However, the association with nonmalignant respiratory illness has not been well established.

In almost all of the studies published to date, assessments of respiratory illnesses are problematic for two reasons. First, most of these studies were conducted among people with visible arsenical lesions that may have biased the assessment of respiratory symptoms in the study participants. Second, respiratory symptoms were assessed either by self-report, which may be affected by recall bias, or by lung function tests, which require patient cooperation and may be subject to information bias, leading to either over- or underestimation of the true measure of association. For instance, if persons with skin lesions or high arsenic exposure are more cooperative or if they receive more attention, the measure of association would be, to some extent, overestimated. However, detection of respiratory illness can be improved and bias can be avoided by using valid biomarkers. In the present study, researchers examined the serum level of Clara cell protein CC16, a novel biomarker for detecting respiratory illnesses, in 241 nonsmokers chronically exposed to wide levels of As from drinking water. Although the clinical significance of early epithelial changes detected by serum CC16 remains to be fully determined, several studies have shown that CC16 can be used as a biomarker for detecting respiratory effects induced by environmental exposures such as air pollution and tobacco smoking.

The researchers conducted a cross-sectional study in nonsmoking individuals (n = 241) selected from a large cohort with a wide range of As exposure (0.1 – 761 µg/L) from drinking water in Bangladesh. Total urinary As, urinary As metabolites, and serum CC16 were measured in urine and serum samples collected at baseline of the parent cohort study.

An inverse association was observed between urinary As and serum CC16 among persons with skin lesions. However, in the overall study population a positive association was observed between secondary methylation index in urinary As and CC16 levels. The association was stronger among people without skin lesions, indicating that increased methylation capability may be protective against As-induced respiratory damage.

In a sub-sample of study participants undergoing spirometric measures (n = 31), inverse associations were observed between urinary As and predictive FEV_1 (forced expiratory volume measured in 1 sec).

The findings of this study suggest that serum CC16 may be a useful biomarker of epithelial lung damage in individuals with arsenical skin lesions.

Presently, invasive procedures for detecting respiratory illnesses, such as bronchoscopy or bronchoalveolar lavage techniques, are not suitable for large-scale population studies in rural areas in countries such as Bangladesh. Also, self-reported symptoms or lung function tests usually detect disease with relatively late-stage lung damage. In contrast, an appropriate biological marker such as CC16 can be used to detect respiratory illnesses at an early stage and it is easy to use, making it especially attractive for tracking respiratory damage from As or other exposure in populations in Bangladesh and other developing countries.

Source: Environmental Health Perspectives, Vol. 116, No. 2, February 2008.

FACTORS AFFECTING RISK OF ARSENIC INDUCED SKIN LESIONS IN BANGLADESHI MEN AND WOMEN

Elevated inorganic arsenic concentrations in drinking water is of major public health concern world-wide in many countries. In Bangladesh alone it has been estimated that more than 50 million inhabitants are drinking water containing arsenic above the World Health Organization guideline value of 10 µg/L, which is based on the cancer risk in skin, lungs, bladder, liver and possibly kidneys. A number of non-carcinogenic effects, such as skin lesions, vascular diseases, liver- and neurotoxicity, chronic cough, diabetes mellitus, adverse pregnancy outcomes and impaired child development may also be induced by arsenic. The earliest signs of toxicity from chronic exposure to inorganic arsenic in humans are pigmentation changes. Hyperkeratosis usually follows the initial pigmentation changes and may then proceed to skin cancer.

It is known that a high fraction of methylarsonate (MA) in urine is a risk modifying factor for several arsenic induced health effects, including skin lesions, and that men are more susceptible for developing skin lesions than women. Thus, researchers conducting a recent study aimed at elucidating the interaction between gender and arsenic metabolism for the risk of developing skin lesions. This study is part of a population-based case-referent study concerning the risk for skin lesions in relation to arsenic exposure via drinking water carried out in Matlab, a rural area 53km south-east of Dhaka, Bangladesh. Researchers randomly selected 526 from 1579 referents and all 504 cases for analysis of arsenic metabolites in urine using HPLC coupled to inductively coupled plasma mass spectrometry (HPLC-HG-ICPMS).

(Continued on page 7)

NEUROBEHAVIORAL AND COGNITIVE CONSEQUENCES OF CHILDHOOD LEAD EXPOSURE

Our understanding of the neurobehavioral and cognitive consequences of childhood lead exposure comes from observational research conducted mostly in developed nations where environmental exposure is more readily detected and containment and prevention policies are well enforced.

Children in less developed countries are both more vulnerable to neurodevelopmental delays (because of endemic disease, caloric and micronutrient deficiencies, and limited resources for early intervention) and less likely to be examined for toxic exposures, including lead. However, there is accumulating evidence that lead exposure in urban areas of developing nations is among the highest in the world. Recently, results were reported from a large population-based study in the Philippines showing that a high prevalence of elevated blood lead levels (BLLs) also exists in rural areas.

There is a paucity of information about the consequences of lead exposure on cognitive development in children in less developed countries. The few published studies available show a wide discrepancy in the strength of the association between lead and cognitive ability. A report from Shanghai demonstrated that a 0.91 point decrease in full scale IQ (95% CI, 0.68-1.1) was linked to a 1 µg/dL increase in BLL in school-age children. In contrast, a study in San Jose, Costa Rica, could not demonstrate a statistically significant association between BLL and IQ in children.

The substantial variation in reports is not surprising because of the challenge of conducting these studies in less developed countries. Optimally, studies should identify the known determinants of cognitive performance and account for the unique deprivation associated with poverty in developing settings. Four substantive problems arise when trying to accomplish this. First, obtaining a representative population is challenging. Second, variations in sample collection and measurement error must also be taken into account. Similarly, accounting for the variation in the local home environment---one of the most significant determinants of intellectual development---is critical. A third challenge is accounting for the impact of severe nutritional deficiencies (common in the Philippines and other developing countries) on cognitive function. Finally, any inferences need to take into consideration that the same factors that predispose to elevated BLL, such as lack of education, are also associated with lower intelligence.

These problems, if left unaccounted for, lead to over-estimation or underestimation of the impact of lead on IQ. Now a recent study has attempted to disentangle lead exposure from nutritional and other biologic and sociologic determinants of cognitive ability by using a population-based sample.

The study was conducted in the Visayas, the central region of the Philippines covering approximately a third of the country. Data were collected between December 2003 and September 2004.

With data from validated psychometric instruments, venous blood samples, and comprehensive survey instruments, researchers developed multi-stage models to account for BLLs and exogenous confounders of the association between BLLs and cognitive function.

Overall, the children in this population (n = 877) had a mean BLL of 7.1 µg/dL, an average hematocrit level of 11.8 g/dL, and a red cell folate concentration of 225 µg/mL. Households had an average of 5.7 members and low average annual income. The children were chronically malnourished, anemic, folate deficient, but were born to mothers who were mostly high school graduates, had breast fed their children, and were unlikely to smoke.

The data collected in the study provide direct observational evidence of an inverse association between BLL and cognitive function in poor children in a developing country with a high prevalence of anemia and folate deficiency.

Lead toxicity in this population had a greater impact on IQ than previously reported.

A 1 µg/dL increase in BLL was associated with a 3.32 point decline in cognitive functioning in children aged 6 months to 3 years and a 2.47 point decline in children aged 3 to 5 years. BLL was inversely associated with hemoglobin and folate levels. Higher folate levels mitigated the negative association between BLL and cognitive function.

These population-based data suggest greater lead toxicity on cognitive function than previously reported. The findings also suggest that folate and iron deficient children are more susceptible to the negative cognitive effects of lead. Folate supplementation may offer some protective effects against lead exposure.

The macroeconomic benefits of mitigating lead toxicity could be staggering. It is estimated that each 1 point increase in IQ raises eventual worker productivity 1.76% to 2.38%; the economic benefit for a cohort of 3.8 million 2-year-old children would be between $110 and $319 billion dollars in the US. In the Philippines and other developing countries where the cohorts are much larger and the marginal benefit seemingly much greater, the economic measurement would be even higher. With improved cognitive performance, school performance would improve and overall capabilities expand, all of which would push economic growth and poverty alleviation.

Source: The Journal of Pediatrics, Vol. 152, No. 2, February 2008.

A Study of the Latency Period for Neurotoxicity of Methylmercury

Methylmercury (MeHg) poses serious and practical concerns for human populations regarding perinatal exposure. Fish, especially large predator (carnivore) fish species, accumulate high concentrations of MeHg through the marine food chain, and exposure of pregnant women to MeHg through the consumption of fish has evoked widespread concern due to potential effects on offspring.

MeHg easily crosses the blood-brain barrier and accumulates in the central nervous system, where it is demethylated to inorganic mercury. Chronic perinatal exposure to environmentally relevant levels of MeHg is associated with the occurrence later in childhood of neurobehavioral problems such as impaired attention and fine motor function. Animal studies confirm this association, but epidemiologic evidence is mixed despite extensive study. Moreover, MeHg toxicity and the period of time before effects appear are not completely understood, as few studies have been conducted beyond the first months or years of life in either animals or humans.

Now a new study sets out to demonstrate the existence of a latency period in a rodent model in which the toxicity of perinatal MeHg exposure becomes apparent only later in life.

The study includes metallothionein (MT) knockout mice because other studies have suggested the potential susceptibility of this strain to the neurodevelopmental toxicity of MeHg.

In the study, pregnant MT-null and wild-type C57Bl/6J mice were exposed to MeHg through their diet containing 5 µg Hg/g during gestation and early lactation.

Behavioral functions of the offspring were examined using paradigms including open field behavior (OPF), passive avoidance (PA) and the Morris water maze (MM) at ages of 12-13 and 52-53 weeks.

At 12 weeks of age, the behavioral effects of MeHg were not detected, except for the OPF performance in MeHg-exposed MT-null females. At 52 weeks of age, the MeHg-exposed groups showed poorer performance both in PA and MM, and their OPF activity differed from controls. These effects of MeHg appeared exaggerated in the MT-null strain. The brain Hg concentration had leveled off by 13 weeks of age.

The results of the study suggest the existence of a long latency period after perinatal exposure to low-level MeHg in which the behavioral effects emerged long after the leveling off of brain Hg levels. This period may be influenced by genetic susceptibility, given the stronger effect of MeHg exposure in MT-null mice.

The existence of a latency period suggests that a slow process, such as aging, plays a role in MeHg toxicity, although the actual damage occurs much earlier in life.

Source: Environmental Health Perspectives, Vol. 116, No. 6, June 2008.

SUNSCREEN LINKED TO CORAL DAMAGE

Coral reefs are among the most biologically productive and diverse ecosystems in the world, representing hot spots of marine biodiversity, and directly sustaining half a billion people. Approximately 60% of coral reefs are currently threatened by several natural and anthropogenic impacts. Over the last 20 years, massive coral bleaching (i.e., loss of symbiotic zooxanthellae hosted within scleractinian corals) has increased dramatically, both in frequency and spatial extent. This phenomenon has been associated with positive temperature anomalies, excess ultraviolet (UV) radiation or altered available photosynthetic radiation, and presence of bacterial pathogens and pollutants.

Production and consumption of personal care and cosmetic sun products are increasing worldwide, reaching unexpected levels, with potentially important consequences on environmental contamination. The release of these products is also linked with the rapid expansion of tourism in marine coastal areas. Chemical compounds contained in sunscreens and other personal care products have been demonstrated to reach detectable levels in both fresh and seawater systems. These compounds are expected to be potentially harmful for the environment; hence, the use of sunscreen products is now banned in a few popular tourist destinations, for example, in marine ecoparks in Mexico, and in some semi-enclosed transitional systems. Because sunscreens are lipophilic, their UV filters can bioaccumulate in aquatic animals and cause effects similar to those reported for other xenobiotic compounds. Paraben preservatives and some UV absorbers contained in sunscreens have estrogenic activity. In addition it has been demonstrated that several sunscreen agents may undergo photodegradation, resulting in the transformation of these agents into toxic by-products.

Recently, it has also been demonstrated that sunscreens have an impact on marine bacterioplankton, but there is no scientific evidence for their impact on coral reefs.

To evaluate the potential impact of sunscreen ingredients on hard corals and their symbiotic algae, several independent *in situ* studies have been conducted with the addition of different concentrations of sunscreens to different species of *Acropora* (one of the most common hard-coral genus), *Stylophora pistillata,* and *Millepora complanata.* These studies were performed from 2003 to 2007 in different areas of the world, including the Celebes Sea (Pacific Ocean), the Caribbean Sea (Atlantic Ocean), the Andaman Sea and the Red Sea (Indian Ocean).

These studies indicate that viruses have a key role in population dynamics and in community composition and diversity of marine bacterioplankton and phytoplankton. Viruses also contribute significantly to horizontal gene transfer, and can influence the pathways of energy and material flow in aquatic ecosystems, with important implications for global biogeochemical cycles. These

(Continued on page 8)

Herbicide Disruption of Human Hormone Activity

Endocrine disrupting chemicals (EDCs) affect the reproductive health of fish and amphibious wild life, but their impact on mammals and particularly humans is less clear. Synthetic and natural endocrine disruptors fall into several chemical categories and include industrial chemicals, pesticides and herbicides. Some of these EDCs, such as the active chemical found in polycarbonate containers, bisphenol A, exhibit estrogenic effects in cultured cells by binding directly to the estrogen receptors ERα and ERβ. However, other EDCs fail to competitively bind ERs, including the widely used chlorotriazine herbicide atrazine (ATR).

The prevalent use of ATR as a broadleaf herbicide and its persistence in the environment underscores the importance of understanding the molecular impact of this EDC. Numerous studies in fish, amphibians, reptiles and mammals all suggest that ATR can alter normal endocrine, neuroendocrine and immune responses. For instance, in amphibians, low levels (0.1-25 µg/L) or short term exposure (48 hrs) to ATR, respectively, increases the number of intersex frogs, and impairs normal gonadal development. Consistent with these phenotypes, acute exposure to ATR lowers testosterone levels and impairs gonadal development in young fish, in the developing alligator, and in young peripubertal male rats. However, other studies suggest that reduced serum testosterone after ATR exposure results from a marked drop in body weight and food consumption. These latter effects are observed for both male and female rats and potentially reflect an unknown role of ATR in neuroendocrine signaling. Still others suggest that independent of body weight and hormone levels, ATR delays mammary gland development. Although there is ample literature documenting the effects of ATR in a variety of species, with the exception of aromatase (Cyp19A), other molecular targets of ATR remain poorly defined.

Maintenance of cytochrome p450 aromatase activity, which catalyzes the conversion of androgens to estrogens appears critical for preserving a balanced sex ratio in teleosts. All species lacking sex chromosomes, such as fish, are especially sensitive to environmental factors that perturb sex steroid levels. Indeed, increasing estrogen levels in a natural or laboratory setting feminized, and greatly altered normal sex ratios in fish. Conversely, treatment with aromatase inhibitors results in gonadal masculinization of female fish. This fact positions aromatase as a potentially useful target to examine the *in vivo* effects of ATR. In mammals, both ERα and the NR5A nuclear receptor, steroidogenic factor 1(SF-1) influence expression of the single Cyp19A gene encoding aromatase. In zebrafish *(Danio rerio),* regulating aromatase expression is more complex because of gene duplication. The gonadal-enriched zcyp19a1 contains an NR5A binding site and is presumably activated by the zebrafish SF-1/LRH-1 orthologs (ff1a, b, c and d), whereas the brain enriched zcyp19a2 contains an estrogen response element (ERE) and is responsive to estrogens. Both zebrafish aromatase promoters contain CREB binding sites and would therefore be responsive to cAMP signaling. Not surprisingly, studies using several fish species showed upregulation of zcyp19a2, with a notable downregulation of zcyp19a1 after exposure to estrogen, xenoestrogens and other estrogenic chemicals. While a direct link between ATR and zcyp19a1 has not been established, others have shown that at relatively low doses (0.1 µM or 22 µg/L). ATR greatly increases aromatase activity in selective mammalian cell lines and in immortalized sea turtle cells.

Recently, ATR has been proposed to bind and activate SF-1. This notion is particularly appealing given that SF-1 orthologs are found in all vertebrates including teleosts, and given the critical role of SF-1 in mammalian sexual development and steroidogenesis. Now a recent study has used mammalian cell lines and zebrafish as model systems to address the *in vivo* and *in vitro* roles of ATR in activating aromatase expression.

In the study, the results of *in vivo* and *in vitro* analyses of ATR strongly suggest that this widely used herbicide affects hormone signaling and endocrine transcriptional networks in fish and in mammalian cells. Indeed, the researchers found that acute and chronic exposure to ATR significantly increased the endogenous levels of zcyp19a1 encoding gonadal aromatase and altered the normal sex ratio in environmental conditions in a relevant vertebrate model system. Moreover, the cellular data illustrate that ATR induces a cluster of endocrine-related genes, including Cyp19A1. Endocrine-related cell types with a capacity for steroidogenesis appear to be especially sensitive to ATR, as demonstrated by the exquisite cellular specificity of the ATR response. Finally, based on the fact that many of these ATR responsive endocrine targets downstream of both SF-1 and cAMP signaling, the researchers propose that the selective effects of ATR in endocrine cell types are mediated by convergent regulation of NR5A receptors and elevated cAMP.

Although the *in vivo* analysis focused solely on Cyp19A1 expression and sex ratios in exposed zebrafish, the fact that ATR upregulates several peptide hormones and steroidogenic genes in mammalian cells suggests that the *in vivo* effects of these triazine herbicides will be much broader, extending well beyond estrogen metabolism. Further studies using model organisms, where genomic approaches are feasible, should help to determine the full extent of ATR effects on endocrine signaling and other physiological responses, including the immune response and early embryonic development. Given the current pervasive use and persistence of ATR in the environment, these findings support environmental concerns that ATR poses a potential risk to the reproductive health of young fish and other wild life. The researchers also suggest that further research is needed to determine how this non-estrogenic EDC influences the mammalian embryonic and adult endocrine system.

Source: PLoS ONE, Vol. 3, Issue 5, May 2008.

Mobile Phone Use and Brain Tumor – A Japanese Study

The exponential increase in mobile phone use in recent years has raised public concern about safety. Since only glial and meningial tissue close to the surface of the head is exposed to relatively high electro-magnetic fields (EMFs) emitted from mobile phones, brain tumors, especially glioma and meningioma, have received particular attention, together with acoustic neurinoma and salivary gland tumors.

Due to the level of general concern, the INTERPHONE study, a collaborative case-control study in 13 countries to investigate whether mobile phone users have an increased risk of brain tumors was initiated in 2000. The study is coordinated by the International Agency for Research on Cancer (IARC) and is still underway. However, some national reports have already been published, with mixed findings.

A central issue has been how precisely to estimate the actual EMF exposure, given the necessary reliance on self-reported use. Different parts of the brain are known to be exposed to EMFs of different magnitudes, related not only to which ear the phone is placed on, but also to the characteristics of different models of mobile phone. The specific absorption rate (SAR) is widely accepted as a dosimetric quantity in guidelines on EMF exposure in frequency ranges including those used for mobile phones. The SAR, representing absorbed radiofrequency (RF) power per unit mass of body tissue, is closely related to thermal effects. If non-thermal effects are involved, SAR is also relevant, since it is closely correlated with internal electric and magnetic fields in tissue near the radiation source.

A recent Japanese case-control study of brain tumors in relation to mobile phone use has employed a novel approach for estimating the SAR inside the tumor, taking into account spatial relationships between tumor localization and intracranial RF distribution. In this study, personal interviews were carried out with 88 patients with glioma, 132 with meningioma, and 102 with pituitary adenoma (322 cases in total), and with 683 individually matched controls. All maximal SAR values were below 0.1 WKg^{-1}, far lower than the level at which thermal effects may occur, the adjusted odds ratios (ORs) for regular mobile phone users being 1.22 for glioma and 0.70 for meningioma. When the maximal SAR value inside the tumor tissue was accounted for in the exposure indices, the overall OR was again not increased and there was no significant trend towards an increasing OR in relation to SAR-derived exposure indices.

To date, several case-control studies have been reported from the United States and Sweden before the INTERPHONE study. Two US studies showed negative results for the overall risk of brain tumors, whereas in a Finnish population register-based study, the OR for glioma with relation to ever use of analogue mobile phones was 2.1. Risk was estimated for the left/right laterality of the tumor or for the affected lobe in relation to that of mobile phone use, but no increased risk was observed for tumors on the same side as phone use. In a series of Swedish studies, the risk of tumors in the temporal area on the same side as that used for mobile phone calls was increased for analogue phones, OR 2.3. However, no increased risks by histological types were observed.

Four studies from the INTERPHONE study showed no increased overall risk of glioma or meningioma in relation to regular mobile phone use, although glioma risk increased non-significantly among long-term users (10 years or more), but no excess risk was found for temporal lobe tumors, considered to be exposed to the highest radio frequency RF-EMF. In a Swedish study, the OR for glioma on the same side as mobile phone use increased to 1.8 among long-term (≥ 10 years) mobile phone users, but the corresponding OR for glioma on the opposite side was found to decrease to 0.6 among long-term users. In a UK study, the OR for glioma on the same side as mobile phone use was 1.24, but for gliomas on the opposite side, it decreased significantly to 0.75. In both studies, it was suggested that such 'complementary risks' above and below unity could reflect recall bias, in which glioma patients tended to recall that they used mobile phones on the same side as the tumor location simply because they knew where the tumor was. In summary, the findings to date on mobile phone use and glioma and meningioma risks are inconsistent.

Most studies of the non-thermal effects of RF-EMF indicate no direct DNA effects such as mutagenicity or genotoxicity of RF-EMF exposure in the range of 800 – 1900 MHz and an SAR of less than 2 W kg^{-1}. There is also little evidence for indirect DNA effects, including alterations in gene expression, cell proliferation, or apoptosis. Thus, laboratory studies do not support the possibility that mobile phone use increases the risk of brain tumors.

The Japanese study observed no increase in overall risk of glioma or meningioma in relation to regular mobile phone use among the Japanese subjects.

Source: British Journal of Cancer, Vol. 98, No. 3, February 2008.

FACTORS AFFECTING RISK OF ARSENIC INDUCED SKIN LESIONS IN BANGLADESHI MEN AND WOMEN

(Continued from page 3)

The present study confirms previous studies, with the risk for skin lesions being almost three times higher in the highest tertile of %MA (adjusted OR 2.8, 95% CI: 1.9-4.2, $p < 0.001$) compared to the lowest tertile. The present study is the first to show that the well documented higher risk for men to develop arsenic-related skin lesions compared to women is mainly explained by the less efficient methylation of arsenic, as defined by a higher fraction of MA and lower fraction of dimethylarsinate (DMA) in the urine, among men. Previously documented lower risk for skin lesions in individuals exposed since infancy, or before, was found to be independent of the observed arsenic methylation efficiency. Thus, it can be speculated that this is due to a programming effect of arsenic *in utero*.

Source: Toxicology and Applied Pharmacology, Vol. 230, No. 1, July 2008.

THE HEALTH EFFECTS OF NONINDUSTRIAL INDOOR AIR POLLUTION

There is growing public awareness regarding the risk associated with poor indoor air quality (IAQ) in the home and workplace. Because Americans spend approximately 22 hours every day indoors, susceptible individuals are at much greater risk of adverse health effects from chronic low levels of exposure to indoor air pollutants over time. Along with particulate matter, gases such as ozone, nitrogen dioxide, carbon monoxide, and sulfur dioxide; microbial and chemical volatile organic compounds; and passive smoke are the most common types of air pollutants encountered indoors. A major limitation of understanding the adverse health effects of these specific air pollutants is the inability to directly equate measurable ambient air concentrations to personal exposure. To complicate matters, in the nonoccupational indoor setting, environmental exposures are often more subtle and not readily recognized. In the most extreme cases, controversial terms like *sick building syndrome, toxic mold syndrome,* and *multiple chemical sensitivity* have been coined for lack of a better way to characterize unexplained constellation of symptoms that are attributed to some exposure in the home or nonindustrial occupational setting. Furthermore, very little information is available regarding permissible exposure levels for the home or nonindustrial workplace for known indoor air pollutants. Many experts recommend indoor air pollutant levels be maintained at 50% or less than the National Ambient Air Quality Standards for outdoor air pollutants established by the Environmental Protection Agency.

A recent review attempts to provide allergists with necessary information that will assist them in making useful recommendations to patients seeking advice regarding indoor environmental triggers beyond traditional perennial allergens.

The review also gives directions on the creation of a healthier indoor environment, recommending that the allergy specialist should have some familiarity with building a healthy home because patients are frequently presenting with health complaints related to poor IAQ attributed to their home or workplace. The 3 primary considerations in improving IAQ are evaluation of construction failures that allow moisture into the walls of a building, poor ventilation causing excessive humidity and accumulation of gaseous and/or chemical exposure from materials in the living space, and poorly designed or failing air conditioning systems that contribute to poor air circulation. An extensive overview of building sciences and the guidelines for new home construction can be found at http://www.healthhouse.org. Building a healthy home should take into account costs versus energy savings and improved health outcomes. Further studies are needed to confirm the health benefits of healthy home construction.

In contrast with the industrial workplace setting, quantitative standards for chemical, biological, and particulate exposures as well as ventilation requirements have not been well established and are not routinely monitored. Although some government entities provide guidelines related to IAQ concerns, these generally take the form of recommendations for the control or elimination of sources and strategies for exposure reduction, rather than for achieving pollutant levels below some specific air concentration. Legislation such as Clean Indoor Air acts ban or restrict smoking in workplaces and in public places and reduce exposures to environmental tobacco smoke for workers and patrons. The Environmental Protection Agency's IAQ Tools for Schools program addresses IAQ management in schools by providing guidance for those aspects of building maintenance, housekeeping, and daily school operations that can influence IAQ, such as the importance of preventing water intrusion; carefully selecting, using, and storing cleaning and pesticide products; and ensuring proper ventilation. This program also provides resources and strategies for remediation of allergen and irritant-induced IAQ problems and strategies to maintain good IAQ over time. These voluntary programs are gaining widespread acceptance.

Source: Journal of Allergy and Clinical Immunology, Vol. 121, No. 3, March 2008.

SUNSCREEN LINKED TO CORAL DAMAGE

(Continued from page 5)

results provide new insights into the functional and ecological role of aquatic viruses and indicate that induction of the lytic cycle in zooxanthellae with latent infection represents an important factor contributing to coral bleaching.

Recent studies have reported that pesticides, hydrocarbons, and other contaminants can cause coral bleaching. Now, the present studies suggest that these factors, which also have the potential to induce the vital lytic cycle in microorganisms or algae with latent infections could act synergistically with sun-care products, thereby increasing the frequency and extent of coral bleaching.

The results indicate that sunscreens promoting lytic cycle in viruses can cause coral bleaching. Because human use of tropical ecosystems and coral reef areas is progressively increasing, researchers predict that the impact of sunscreens on coral bleaching will grow considerably in the future on a global scale. Actions are therefore needed to stimulate the research and utilization of UV filters that do not threaten the survival of these endangered tropical ecosystems.

Source: Environmental Health Perspectives, Vol. 116, No. 4, April 2008.

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
Vibhavadee-Rangsit Highway
Bangkok 10210, Thailand
Tel: +66 2 574 0615
Fax: +66 2 574 0616
CRI Homepage: <http://www.cri.or.th>

For back issues of our newsletter, please visit:

http://www.cri.or.th/en/envtox/et_newsletter.htm