



**CRI/ICEIT
NEWSLETTER**

VOL. 14 NO. 1 – January 2004
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".

GLOBAL WARMING: NEW FINDINGS ON SOOT

NASA scientists have published new findings on how soot reduces the ability of snow and ice to reflect sunlight, thus contributing to global warming.

Published in the proceedings of the National Academy of Sciences, these findings on how soot affects reflective ability, known as *albedo*, raise new questions about human-caused climate change.

The soot effect on snow, *albedo*, may be responsible for a quarter of observed global warming. Restoration of snow *albedo* to something approaching pristine preanthropogenic values would have the double benefit of reducing global warming and raising the global temperature threshold at which dangerous anthropogenic interference with climate occurs.

Future trends of the soot effect on climate could be positive or negative. The SHEBA (Surface Heat Budget of the Arctic Ocean) finding, that there was less black carbon (BC) in the Arctic in 1998 than existed in the 1980s, is qualitatively consistent with a reduction of Russian BC emissions. However, it is doubtful whether one can generalize from the SHEBA, because the measurement was local for a brief period, and future BC emissions in the Arctic could increase. There is a need for more complete measurements of BC in

Arctic snow and better quantification of the links to snow *albedo*, melting ice, and climate change.

On the optimistic side, technology is within reach that could greatly reduce soot, restoring snow *albedo* to near pristine values, while having multiple other benefits for climate, human health, agricultural productivity, and environmental esthetics. Already, soot emissions from coal are decreasing in many regions with transition from small users to power plants with scrubbers. The largest source of soot in developed countries is now diesel fuel, and in developing countries biofuels are also important. Much cleaner diesel engines and biofuel technologies are possible. There are opportunities for scientific and technologic cooperation among developing and developed countries with mutual benefits.

The substantial role inferred for soot in global climate does not alter the fact that greenhouse gases are the primary cause of global warming in the past century and are expected to be the largest climate forcing the rest of this century.

ADVANTAGES AND DISADVANTAGES OF A TRANSFER FROM FOSSIL FUELS TO H₂ FUEL CELLS ON TRANSPORT-RELATED EMISSIONS

H₂ is a naturally occurring trace gas with an abundance of ~0.5 ppm (parts per million molecules of air). The atmosphere thus contains a total of ~175 Tg of H₂. About half of this total is produced in the atmosphere by photochemical oxidation of methane and other hydrocarbons. The other half originates from biogenic processes and combustion, including biomass burning, at Earth's surface. Of the estimated total emissions of 70 to 90 Tg/year, one-quarter is associated with human activities. H₂ is destroyed photochemically in the atmosphere through reaction with the hydroxyl radical (OH) and biologically at the surface through consumption by soil microorganisms.

The photochemical loss of H₂ is well constrained, but the soil loss is quite uncertain. A recent analysis confirms the current view that today, the soil sink is three to four times the size of the photochemical sink. The

dominance of the soil sink is the reason why H₂—unusually for a trace gas influenced by human activities—is less abundant in the Northern Hemisphere than in the Southern Hemisphere.

Research studies derive a total atmospheric lifetime of H₂ of ~ 2 years. Given this lifetime, H₂ leakage of 18 Tg/year would increase its atmospheric abundance by 36 Tg (0.1 ppm or 20%). Thus, the H₂ increase from 0.5 to 2.3 ppm that has been postulated would require leakage rates of 320 Tg/year. This amount exceeds their highest leakage estimates.

H₂ is often portrayed as an environmentally friendly gas whose atmospheric degradation yields only water vapor. However, chemically reactive gases such as H₂ have been recognized as indirect greenhouse gases in international climate assessments since 1990. Atmospheric H₂ affects global atmospheric chemistry in the same way as CO: its photochemical

loss reaction with the OH radical takes up one OH and releases one HO₂ radical. The net effect of adding H₂ to the atmosphere is to reduce OH (the primary methane sink) and thereby increase methane abundance. Thus, H₂, like CO, is an indirect greenhouse gas.

Evaluation of the climate impacts of a shift in the transport sector from fossil fuel combustion to H₂ fuel cells has just begun. Technologically based bounds on the leakage rates are needed, the total atmospheric impact from the ground to the top of the atmosphere needs to be evaluated, and the concurrent changes in other transport-related emissions must be considered. Only with this information will we be able to say with confidence what the advantages and disadvantages of an H₂ economy will be.

Source: Science, Vol. 302, October 2003.

ADVERSE HEALTH EFFECTS RESULTING FROM FREQUENT EXPOSURE TO ELECTROMAGNETIC FIELDS

The possible risks from radio-frequency electromagnetic fields for the human body is a matter of growing concern given the increasingly widespread use of mobile phones. This is the subject of research currently being carried out by a team of scientists in Sweden who focus on the possibility that exposure to radio-frequency electromagnetic fields (RF EMFs) could cause damage to the brain.

Prior experiments by the group with a rat model had shown that RF EMF exposure significantly breached the animals' blood-brain barrier. This allowed the plasma protein albumin to pass out of the bloodstream and into the brain, accumulating in the neurons and glial cells surrounding the capillaries. In their new study, the investigators address the question of whether this leakage of albumin could damage brain tissue.

The investigators exposed 32 rats to controlled doses of RF EMF generated by a Global System for Mobile Communications mobile phone (a type commonly used in Europe). The rats were divided into 4 groups and exposed for 2 hours each to power outputs of 0 (control), 10,100, or 1,000 milliwatts, exposure levels that are roughly comparable to what a human mobile phone user might receive over the same time period. The animals' brains were examined 50 days after the single exposure.

As expected, a large proportion of the exposed rats showed evidence of albumin leakage. In this experiment, however, the Swedish team also found that the albumin appeared to cause significant and serious neuronal damage. "Dark" neurons, which appeared shrunken and homogenized, with loss of discernible internal cell

structures, were seen in all locations of the exposed rats' brains, particularly in the cortex, hippocampus, and basal ganglia. The number of dark neurons discovered was significantly and positively associated with the RF EMF dose received by the animals.

The researchers acknowledge that their study sample was small but claim nevertheless that the combined results are highly significant and show a clear dose-response relationship. Although the neuronal damage revealed in the study may not have immediately demonstrable consequences, it raises concern about the long-term effects of frequent RF EMF exposure such as in the intense use of mobile phones.

Source: Environmental Health Perspectives Vol. 111, No. 7, June 2003.

Effects of Air Pollution on Levels of Maternal Methemoglobin During Pregnancy

In recent years, the focus of much research has been on explaining the role of oxygen, free radicals, and oxidative stress during embryogenesis and placental stages, and development of pathologic pregnancy, especially preeclampsia and fetal intrauterine growth restriction (IUGR). Due to lack of any evidence that methemoglobin levels had been tested during human pregnancy in an air-polluted environment, a prospective research study was carried out in Croatia with the objective of determining if a correlation could be established between the ground-level concentrations of sulfur dioxide and methemoglobin concentrations in pregnant women when a coal-powered thermoelectric power plant was in operation ("dirty" period) and when it was closed ("clean" period).

The location of the power plants, Plomin 1, in Labin, Croatia, was taken into consideration. Blood and urine samples of each pregnant woman in the study were tested three times in the clean period (n=138) and three times in the dirty period (n=122), with 1 month between each test. A correlation between the increase in

mean values of methemoglobin and the ground-level concentration of SO₂ was observed on corresponding dates during the dirty period ($r=0.72, p\leq 0.01$). In the clean period, the negative mean value of methemoglobin was significant ($r=0.60, p\leq 0.05$), whereas in the dirty period, the positive mean value of methemoglobin was significant ($r=0.73, p\leq 0.01$). The increase of maternal methemoglobin could be a useful biomarker to determine when the health of pregnant women is threatened by toxic substances in the environment.

The role of NO_x as an oxidant is well known, but the role of SO₂ and its metabolites on human antioxidants is not clear and requires further epidemiologic and laboratory research. Methemoglobin, which is a result of exposure to toxic substances in the environment and which may lead to hypoxia and hypoxemia in pregnant women, has an important influence on maternal health and placental and fetal development.

Source: Environmental Health Perspectives, Vol. 111, No. 16, December 2003.

children and 1,000 mg/kg for adults. The remaining components of mosquito coil are organic fillers, binders, dyes, and other additives capable of smoldering well. The combustion of the remaining materials generates large amounts of submicrometer particles and gaseous pollutants. These submicrometer particles can reach the lower respiratory tract and may be coated with a wide range of organic compounds, some of which are carcinogens or suspected carcinogens, such as polycyclic aromatic hydrocarbons (PAHs) generated through incomplete combustion of biomass (mosquito coil base materials). Researchers have found that the gas phase of mosquito coil smoke contains some carbonyl compounds with properties that can produce strong irritating effects on the upper respiratory tract – for example, formaldehyde and acetaldehyde. Because coil consumers usually use mosquito coils for at least several months every year, cumulative effects from long-term exposure to the coil smoke may also be a concern.

In order to determine the level of risk, a recent study has analysed the emissions from four common brands of mosquito coils from China, and two common brands from Malaysia. In the study, mass balance equations were used to determine emission rates of fine particles, polycyclic aromatic hydrocarbons (PAHs), aldehydes, and ketones. When applying these measured emission rates to predict indoor concentrations under typical room conditions, it was found that pollutant concentrations resulting from burning mosquito coils could substantially exceed health-based air quality standards.

The study also identified a large range of volatile organic compounds in the coil smoke, including carcinogens and suspected carcinogens.

The findings from the study suggest that exposure to the smoke of mosquito coils can pose significant acute and chronic health risks. However, despite the fact that mosquito coil smoke may have many potential adverse health effects, large populations, particularly in developing countries, still use mosquito coils in their daily lives

Source: Environmental Health Perspectives, Vol. 111, No. 12, September 2003.

HEALTH RISKS FROM EXPOSURE TO THE SMOKE OF MOSQUITO COILS

Mosquito coil is widely known as an efficient mosquito repellent. The major active ingredients of the mosquito coil are pyrethrins, accounting for about 0.3-0.4% of coil mass. When a mosquito coil is burned, the insecticides evaporate with the smoke, which prevents the mosquito from entering the room. Pyrethrins are of low chronic toxicity to humans and low

reproductive toxicity in animals, although headache, nausea, and dizziness were observed in male sprayers exposed to 0.01-1.98 µg/m³ pyrethrins for 0.5-5 hr. No carcinogenic and mutagenic effects have been found for these insecticides. The lowest lethal oral dose of pyrethrum as stipulated by Occupational Health Services (OHS) in 1987 is 750 mg/kg for

Health effects of long-term exposure to arsenic

Long term arsenic exposure is associated with an increased risk of vascular diseases including ischemic heart disease, cerebrovascular disease, and carotid atherosclerosis.

Natural arsenic is disseminated within our living environment by groundwater from wells drilled into arsenic-rich geologic strata or by ambient air during the process of mineral extraction. Man-made sources of arsenic also include uses in agriculture, husbandry, and medicine. However, the main route of exposure for the general population in arseniasis-endemic areas of the world is through the ingestion of arsenic-contaminated well water, including those in Taiwan, the India-Bangladesh border, and Latin America. The latest estimates indicate that more than 100 million people worldwide are exposed to groundwater contaminated by arsenic compounds.

Ingested arsenic has been associated with the development of blackfoot disease (BFD) subsequent to longterm exposure. BFD is a unique peripheral vascular disease endemic in the southwestern coast of Taiwan. Pathological studies have demonstrated that 70% of BFD patients have histologic lesions compatible with the changes of arteriosclerosis obliterans and 30% with the changes of thromboangiitis obliterans. The funda-

mental vascular change of BFD in both types is a severe generalized arteriosclerosis.

However, the pathogenic mechanisms of arsenic atherogenicity are not completely clear. A fundamental role for inflammation in atherosclerosis and its complications has become appreciated recently. To investigate molecular targets of inflammatory pathway possibly involved in arsenic-associated atherosclerosis, an exploratory study has been conducted by researchers in Taiwan using cDNA microarray and enzyme-linked immunosorbent assay to identify genes with differential expression in arsenic-exposed yet apparently healthy individuals. As an initial experiment, array hybridization was performed with mRNA isolated from activated lymphocytes of 24 study subjects with low (0-4.32 µg/L), intermediate (4.64-9.00 µg/L), and high (9.60-46.5 µg/L) levels of blood arsenic, with each group comprising eight age-, sex-, and smoking frequency-matched individuals. A total of 708 transcripts of known human genes were analyzed, and 62 transcripts (8.8%) showed significant differences in the intermediate or high-arsenic groups compared with the low-level arsenic group. Among the significantly altered genes, several cytokines and growth factors involving inflammation, including interleukin-1

beta, interleukin-6, chemokine C-C motif ligand 2/monocyte chemoattractant protein-1 (CCL2/MCP1), chemokine C-X-C motif ligand 1/growth-related oncogene alpha, chemokine C-X-C motif ligand 2/growth-related oncogene beta, CD14 antigen, and matrix metalloproteinase 1 (interstitial collagenase) were upregulated in persons with increased arsenic exposure. Multivariate analyses on 64 study subjects of varying arsenic exposure levels showed that the association of CCL2/MCP1 plasma protein level with blood arsenic remained significant after adjustment for other risk factors of cardiovascular diseases. The results of this gene expression study indicate that the expression of inflammatory molecules may be increased in human subjects after prolonged exposure to arsenic, which might be a contributory factor to the high risk of atherosclerosis in arseniasis-endemic areas in Taiwan. Further multidisciplinary studies, including molecular epidemiologic investigations, are needed to elucidate the role of arsenic-associated inflammation in the development of atherosclerosis and subsequent cardiovascular disease.

Source: Environmental Health Perspectives Vol. 111 No. 11 August 2003.

Use of transgenic plants in pest management

Although transgenic plants offer many unique opportunities for the management of pest populations, they also present new challenges, one of the main ones being the potential evolution of resistance. There are at least four possible ways in which plants with constitutive expression of Bt toxins can be used to delay resistance: (i) engineer plants to express toxin genes at a level at which not all susceptible individuals are killed; (ii) provide refuges for susceptible insects while engineering plants to express the genes at levels as high as possible within acceptable limits to avoid deleterious effects on yield, health or the environ-

ment; (iii) deploy different toxins individually in different varieties; and (iv) deploy plants expressing a mixture of different toxins. Among these options, the refuge-high dose (ii) and pyramiding (iv) strategies seem most promising. A major difficulty for the refuge-high dose strategy is managing the insect population within the refuge to ensure that sufficient susceptible alleles will exist, while at the same time ensuring that damage to the refuge plants is minimized. Until late in 2002, refuge-high dose was the only commercially available strategy for corn and cotton. However, regulatory applications for pyramided cotton

plants (Bollgard II) with two genes derived from *Bt* (*cry1Ac* and *cry2Ab2*) were approved for commercial use in Australia and the United States in 2002. Few, if any, *Cry1Ac*-resistant pink bollworms, *Pectinophora gossypiella*, survived on Bollgard II, a result supporting the use of two *Bt* genes.

Plant breeders have considered and frequently endorsed the concept of using pyramided genes to delay the development of resistance in pest species, especially pathogens. Theo-

(Continued on page 8)

MERCURY EXPOSURE AMONG CHILDREN IN GOLD MINING COMMUNITIES

Mercury intoxication is a growing health problem in children of gold miners in some indigenous communities where the hazards of mercury (Hg) exposure are ignored or not understood, and medical assistance is unavailable. A recent field study investigated the prevalence and neurophysiological effects of Hg exposure in children of gold mine workers living in an area of extensive Hg use in gold-mining operations in the Ecuadorian gold mining settlement of Nambija. School-aged children were observed to participate in gold panning and Hg-Au amalgam burning throughout the Nambija study area. Brainstem auditory-evoked responses (BAER) were measured as biomarkers of subtle mercury-induced neurological impairment. Measures of the total mean blood mercury (HgB) level of children in the BAER study group revealed a wide range of exposure levels, with most presenting HgB levels in excess of the normal limits for the United States (10 µg/L) and Canada (20 µg/L). The HgB levels of the children of Nambija gold miners were significantly higher than those of a reference (control) group of 21 children of comparable age, nutritional status, and altitude adaptations. However, it is possible that some of the children in the reference group who had lower HgB levels than children in the study group may have been exposed to other toxic substances in their environment such as cadmium and lead, as well as arsenic and cyanide, all of which may affect neurophysiological responses.

The noninvasive BAER electrophysiological measures used in this study are useful and effective in field investigations of central

nervous system (CNS) impairment, where other well-established neurological tests of CNS lesions, such as magnetic resonance imaging or positron emission tomography are impractical or unavailable. In the present investigation, statistical analysis of the relation between Hg exposure and BAER in the children of the study group suggested that Hg intoxication is associated with delays or prolongation in neural conduction time in the auditory brainstem. The I-V and III-V interpeak intervals of the BAER have been used as a bioassay of neurological impairment in persons with elevated HgB levels. The BAER recordings in this field study revealed statistically significant positive relations between HgB and the prolongations in the I-V and III-V neural conduction times in the tracts and nuclei of the brainstem auditory system, suggesting neural tissue damage. The I-V interpeak interval of the BAER is the most widely used measure of neural transmission time from the eighth nerve through the ascending auditory tracts and nuclei of the pons and lower midbrain. The correlations between HgB level and the wave V latency, and the I-V interval observed in this study may reflect Hg-induced damage of neural tissue in the area of the inferior colliculus, which is the putative source of wave V.

Increases in auditory stimulus rate above the conventional clinical rate of 10 pps causes measurable changes in several parameters of the BAER that may have clinical import. An increase in the stimulus rate to 50 pps induced temporal, amplitude, and morphological deviations in the BAER of Hg-exposed children that differed significantly from the latencies at stimulus rate of 10 pps. Children in the study group with higher HgB levels revealed abnormal BAER

morphology of the absolute wave-forms, increases in wave latencies and intervals, and decreases in the amplitudes of waves I, II, III, V, and VI when the stimulus rate was increased to 50 pps. Theoretically, increasing the auditory stimulus rate causes corresponding increases in the discharge rate (frequency) of neurons in the eighth nerve and contiguous ascending auditory tracts and nuclei, thus taxing neuronal metabolic capacity and possibly fatiguing the summing neural units that contribute to the BAER. It is possible that driving the auditory neurons of Hg-intoxicated subjects at higher stimulus rates may reveal electrophysiological response patterns that more readily reflect neural tissue damage. Additional BAER studies on a larger Hg-exposed group using varying rates of auditory stimulation must be conducted for further confirmation of this conclusion.

The results of the present study indicate that a high percentage of the children of gold miners in the Nambija gold-mining settlement have abnormal blood levels of Hg and anomalous BAER activity. The findings suggest that the children of the gold miners are at risk for neurocognitive impairment and the neurodevelopmental disabilities associated with Hg exposure. The findings of this investigation also indicate that field BAER electrophysiologic tests, particularly at higher stimulus rates, may serve as a sensitive index or biomarker for subtle CNS effects of Hg exposure in children.

Source: Journal of Occupational and Environmental Medicine, Vol. 45, No.1, January 2003.

CHILDREN'S EXPOSURE TO FOOD CONTAMINATED FROM CONTACT WITH PESTICIDE-LADEN SURFACES

Exposure of children to environmental contaminants is expected to vary from adults and in many cases can be higher. Increased dietary exposures occur because children eat foods that have come into contact with the floor and other contaminated residential surfaces. Young children (1-6 years old) consume foods with their fingers as well as foods that have been picked up from the floor and other contaminated surfaces. Their lack of basic hygiene patterns can contribute to higher dietary exposure. In the United States the most commonly eaten finger-foods are apples, grain products (e.g., bread and crackers), cold cuts, cheese, and bananas. Other differences in the behavior of children, especially in their interaction with the environment, that is, where they eat, the time their food remains on a surface prior to ingestion, and the amount of foods they eat from the surface, need to be assessed because these factors may have a profound effect on the magnitude of their dietary exposure.

Several studies have used videotaping to quantify children's behavior for specific activities. The frequency and duration of hand-to-surface and hand-to-food contacts, and time foods remain on surfaces prior to ingestion, are highly variable. Currently, such data on children's eating behaviors and their impact on excess dietary exposure caused by them are limited and total dietary exposures to pesticides cannot be fully assessed.

A new study was designed to measure the transfer of pesticides from common household flooring surfaces to foods as a first step in estimating the surface transfer coefficients needed to model a child's dietary intake of pesticides. An emphasis was placed on simulating conditions that occur with children in residential or day-care settings to better understand the measurements needed to improve assessments of children's dietary exposure in the context of aggregate exposure assessment. The foods chosen were common finger-foods that young children might ingest after contact with contaminated surfaces. The surfaces chosen were flooring

materials often found in homes and day-care settings where pesticides are typically applied by spraying and would be potential sources of high contamination if foods were dropped before being eaten. The pesticides were chosen based on a combination of the following factors: (1) most frequently found in food samples from previous residential exposure studies, (2) high systemic toxicity of carcinogenic potential, (3) most often applied in 1998 in residential areas by pest control professionals, (4) applicability to a single analytical method, and (5) ones found in environmental samples from residential studies.

The primary objective of this study was to evaluate transfer efficiency (TE) of pesticide contaminants available for transfer from various flooring surfaces to foods to determine the factors that have the most potential to impact dietary exposures of young children when foods are dropped on floors or similar surfaces before they are eaten. Pesticide transfer was determined after simulation of surface-food contact scenarios, including variable contact durations between foods and surfaces, and added forces on the foods contacting the surfaces, such as those occurring when children press on foods with their hands. Transfer efficiency was determined as the amount of pesticide transfer to a food after contact compared to the amount available on the surface, as measured by a surface wipe typical of those used to measure surface contamination in residential exposure studies. It was found that, under certain defined laboratory conditions, pesticides transfer readily to foods that come into contact with contaminated hard flooring surfaces, similar to those found in homes or day-care facilities. Most significant were organophosphate pesticides, which were shown to transfer more readily than *cis-* and *trans-*permethrin or heptachlor. For aqueous applied pesticides, hard floors, as compared to soft carpet, were the more important surfaces for contaminating foods. Overall mean TE values for all pesticides and foods were 35% and 22% for the hard surfaces tested (ceramic tile and hardwood flooring, respectively). Carpet is probably not

an important source of contamination to foods from aqueous applied pesticides because most concentrations measured were near the quantitation limits for the pesticides wiped from carpet or recovered from foods after contact with carpet. Both contact duration and applied contact force notably increased TE for the hard surfaces, thus demonstrating the need to include these variables when defining TE. Understanding and determining TE is the first step in assessing children's dietary exposure from handling and eating foods that have contacted surfaces. The TE measurements provided by this study will be used as input parameters for modeling children's total dietary intake.

The TE defined for this study was based on surface wiping because surface wipes are the current generally acceptable measure of surface contamination in residential exposure studies. It should be noted that pesticides applied to surfaces were not generally recovered at applied levels by wiping the surfaces. Therefore, an improved method for measuring pesticide residues on surfaces, a better understanding of pesticide dynamics after application to surfaces, or both, is needed for more accurate evaluations of pesticides available on surfaces. Once a standard surface measurement is defined, a standardized definition of TE should be defined.

Further investigations examining current-use pesticides that have been directly applied to surfaces for their potential to transfer to foods are underway, and are focused on both flooring and other hard surface materials, such as those used for counters and table-tops, as well as soft surfaces, such as table cloths and upholstered furniture. Activity patterns of eating behaviors for children, in particular the time foods remain on a surface prior to consumption, and the contact force applied to foods by the child's hand, need to be understood when evaluating exposures of children to pesticides.

Source: Journal of Exposure Analysis and Environmental Epidemiology, 2003.

Bioremediation – *Dehalococcoides* strain BAV1, a novel bacterium that destroys harmful chlorinated compounds

Scientists and engineers have worked for many years on the problem of cleaning up sites contaminated by the common solvents tetrachloroethene (PCE) and trichloroethene (TCE). Now researchers in the U.S. have succeeded in isolating a novel bacterium that destroys harmful chlorinated compounds, promising more efficient bioremediation procedures. The isolate, designated BAV1, is a small non-

motile organism of no more than 0.8 μm in diameter, which belongs to the recently discovered *Dehalococcoides* group.

The researchers have used the bacterium in a pilot demonstration at a former dry cleaning operation in Michigan. At this site, PCE had contaminated drinking-water wells and migrated into nearby Lake Huron.

Using a technique called bioaugmentation, the researchers achieved complete dechlorination of PCE to ethene within six weeks after injecting a mixed culture containing high numbers of BAV1 and nutrients. The researchers believe bioaugmentation is a viable remediation option, especially at sites contaminated with chlorinated solvents.

Source: Nature, Vol. 424, July 2003.

ARSENIC EXPOSURE AND METHYLATION PATTERNS IN HUMAN POPULATIONS: A STUDY OF ARSENIC METABOLITES DURING PREGNANCY

In addition to causing cancers of the skin bladder, kidney and lung, and other life threatening conditions, chronic exposure to inorganic arsenic (In-As) may also be associated with various reproductive and developmental effects.

The metabolism of In-As is mainly through methylation to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). Until recently, methylation was regarded as the main metabolic detoxification pathway by which the highly toxic In-As species were converted to the less toxic and more easily excreted methylated species. Because most In-As, MMA, and DMA is eliminated in the urine, the sum of urinary arsenic species has been considered a good measure of In-As exposure, and the

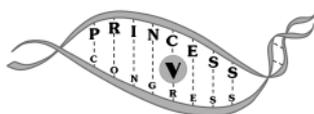
relative proportion of urinary species, particularly the methylated forms, has been considered an appropriate indicator of methylation efficiency and detoxification capacity.

Now, a recent study carried out in Chile has investigated the profile of urinary In-As, MMA, and DMA of pregnant women.

Periodic urine samples were collected from early to late pregnancy among 29 pregnant women living in Antofagasta, Chile, who drank tap water containing 40 $\mu\text{g/L}$ In-As. The total urinary arsenic across four sampling periods increased with increasing weeks of gestation, from an initial mean value of 36.1 to a final value of 54.3 $\mu\text{g/L}$. This increase was mainly due to an increase in DMA, resulting

in lower percentages of In-As and MMA and a higher percentage of DMA. The findings indicate that among women exposed to moderate arsenic from drinking water during pregnancy, changes occur in the pattern of urinary arsenic excretion and metabolite distribution. The toxicologic significance of this is not clear, given recent evidence suggesting that intermediate methylated species may be highly toxic. Nevertheless, this study suggests that arsenic metabolism changes throughout the course of pregnancy, which in turn may have toxicologic effects on the developing fetus.

Source: Environmental Health Perspectives, Vol. 111, No. 16, December 2003.



The 5th Princess Chulabhorn International Science Congress
“Evolving Genetics and Its Global Impact”
August 16-20, 2004, Bangkok, THAILAND

Call for Abstracts – NEW DEADLINE on July 1, 2004

The Secretariat – PC-V
Chulabhorn Research Institute (CRI)
Office of Academic Affairs
Vipavadee-Rangsit Highway, Bangkok 10210, THAILAND
Tel: (66-2) 574-0615, 574-0622-33 ext. 3900, 3939
Fax: (66-2) 574-0616, 574-0617
E-mail : pc5@tubtim.cri.or.th

For more information please visit <http://www.cri.or.th/~pc5>

Use of transgenic plants in pest management

(Continued from page 4)

retical models suggest that varieties pyramiding two dissimilar insect toxin genes in the same plant have the potential to delay the development of resistance much more effectively than single-toxin plants used sequentially or in mosaics or seed mixtures, even with relatively small and more economically acceptable refuge sizes. To test predictions of the models and to assess the effects of gene pyramiding on resistance management, a recent study has used a model system composed of broccoli plants transformed to express different Cry toxins (Cry1Ac, Cry1C) combined with four populations of diamondback moth, which carries resistance either to both, one or neither of the toxins. The objective of this study was to compare how quickly an insect population that contains a relatively high frequency of alleles for resistance to Cry1Ac and Cry1C evolves resistance to each or both toxins when exposed to plants that express both toxins simultaneously, sequentially or in mosaics.

Results of the study showed the mosaic was clearly inferior to the pyramiding strategy. Both population densities and the resistance frequencies were significantly higher on both Cry1Ac and Cry1C plants in the mosaic than in the pyramid treatments after 18 generations of selection. This is consistent with models and experiments with other insecticides showing that mosaics select for resistance more quickly than either pyramid treatment (or mixtures, in the case of insecticides) or sequential deployment. The responses to selection for resistance on the Cry1Ac plants in both the sequential and mosaic treatments were entirely consistent with results from models developed in 1998. The models were run with an initial resistance allele frequency of 0.1 and it was assumed that all of the resistant homozygotes survived, but that heterozygotes and susceptible homozygotes died when on Cry1Ac plants. Under these conditions, the frequency of resistant homozygous larvae in a sequential treatment would reach 80-90% by generation 7. Population increases would begin by generation 4, with density increases of more than 100-fold by generation 12, limited only by larval food supply. In a

mosaic treatment, resistance would be slightly slower to evolve, but the frequency of resistant homozygotes would still reach 80% by generation 12 and 95% before generation 18 (when resistance was first measured), again with rapid increases in larval numbers even from generation 4.

Farmers may plant crops in mosaic pattern when different products are available. The experiments showed that allowing the concurrent release of cultivars with the two *Bt* genes, is not the best way to delay resistance. Even sequential release would result in control failure of at least one cultivar sooner than if pyramided varieties were used. The absence of a significant difference between the survival of insects on the two-gene plants in the pyramided and sequential strategy was due to the lack of resistance to Cry1C in both treatments, and not to the marked differences in resistance to Cry1Ac in the two treatments. Thus, the researchers believe the pyramided plants provided better resistance management than the sequential deployment for at least Cry1Ac. Although it is tempting to speculate that the absence of evolution of Cry1C resistance after 12 generations of selection in the sequence treatment may have something to do with the order of selection, the reverse sequence was not tested, so no conclusions can be drawn for this case.

Since single-gene *Bt* plants were first grown commercially in 1996, they have had an overall positive impact on agriculture, human health and the environment by reducing the use of broader-spectrum foliar insecticides to control lepidopterous pests. Although insect resistance resulting in control failures of any of the present *Bt* crops has not occurred, reducing the risk of resistance remains a top priority. The current resistance management strategy requires relatively large refuges in which susceptible alleles can be maintained. The maximum benefits to crop production, farm profitability and reduction of pesticide use would come from larger proportions of transgenic insecticidal crops, but long-term enjoyment of these benefits may only be feasible by limiting the percentage

of the crops that are transgenic. The conflict between the economic costs of refuges and the need for resistance management may not be easily resolved with single-toxin strategies. Modeling work and the data generated from these experiments with the diamondback moth-*Bt* broccoli system suggest that stacking or pyramiding toxin genes that express toxins with different modes of action or binding characteristics at a "high" dose offers a potential route for achieving longer delays in the development of resistance. The researchers believe that industry should be encouraged to develop such plants for their increased durability for insect management and suggest that the smaller refuge size required by pyramided toxin plants may be an additional incentive for them to do so.

Source: Nature Biotechnology, Vol. 21, No. 12, December 2003.

EDITORIAL BOARD

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

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

Correspondence should be addressed to:

ICEIT NEWSLETTER
Chulabhorn Research Institute
Office of Academic Affairs
Vibhavadee-Rangsit Highway
Bangkok 10210, Thailand
Tel: (66-2) 574-0622 to 33 ext. 1610
Fax: (66-2) 574-0616 or (66-2) 247-1222
CRI Homepage: <<http://www.cri.or.th>>

For back issues of our newsletter, please visit

http://morakoth.cri.or.th:250/et_newsletter.htm