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Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

HRH PRINCESS CHULABHORN RECEIVES SPECIAL RECOGNITION AWARD FROM THE INTERGOVERNMENTAL FORUM ON CHEMICAL SAFETY (IFCS)

At a special session to mark the opening of Forum V held in Budapest, Hungary, 25 September 2006, Professor Dr. Her Royal Highness Princess Chulabhorn was presented with the IFCS Special Recognition Award in recognition of her exceptional efforts to increase scientific and technical capacities and capabilities for chemical safety through the work of the Chulabhorn Research Institute.

The Award acknowledges the special contributions to the goals of global chemical safety that have been made by the education and scientific exchange programs at the Chulabhorn Research Institute.

In her speech of acceptance, Her Royal Highness paid tribute to the important work of IFCS and also to all those who, for many years, had contributed to the work of the Chulabhorn Research Institute in raising awareness of the vital importance of chemical safety.

In his opening speech at Forum V, Dr. Suwit Wibulpolprasert, IFCS President, said that, since its establishment, the IFCS had emphasized the importance of scientific and technical assistance to enable countries in the sound management of chemicals. The last decade had seen remarkable achievements in many countries in a number of areas of chemical safety and this advancement can be attributed to efforts such as those of the Chulabhorn Research Institute.

Traffic Exposure and the Diagnosis of Asthma in Children

Studies have indicated that children who live near traffic have greater symptoms and increased hospitalizations for asthma. The severity of asthma symptoms is also associated with ambient benzene concentrations.

Now a recent study has investigated the association between a traffic-density related measure of exposure and the prevalence of diagnosed asthma among school children 5 to 7 years of age in Anchorage, Alaska, USA in an area with high ambient benzene concentrations.

Traffic is known to produce a mixture of both particulate and gaseous air pollution. In Anchorage, gasoline has an unusually high (35-50%) aromatic content (benzene content 5%), causing volatile organic compounds (VOCs) to be a large component of air pollution. The predominant source of VOC pollution is gasoline emissions both from traffic and from cold starts. The average annual ambient benzene concentration in Anchorage is eight parts per billion, higher than any other US city. The predominant particulate matter (PM) is coarse fraction (2.5 μm<PM>10 μm) generated from road surfaces. Other air pollutants that have been associated with asthma severity, such as $PM_{2.5}$ and ozone, are very low to nonexistent in this area. The fine fraction of PM_{10} averages less than 15% of the measured particulate mass.

A survey of parents of children in kindergarten and first-grade in 13 schools was completed and Geographical Information System (GIS) mapping was used to obtain an exposure measure based on traffic density within 100 m of the cross streets closest to the child's residence.

Using the range of observed exposure values, a score of low, medium or high traffic exposure was assigned to each child. After controlling for individual level confounders, relative to the low referent group, relative risks (95% confidence intervals) of 1.40 (0.77, 2.55) and 2.83 (1.23, 6.51) were obtained in the medium and high exposure groups, respectively. For the null hypothesis of no difference in risk, a significance level of 0.056 was obtained, which suggests that further investigation would be worthwhile. Children without a family history of asthma were more likely to have an asthma diagnosis if they resided in a high traffic area than children who had one or more parents with asthma. The relative risk for children without a family history of asthma is 2.43 (1.12, 5.28) for medium exposure and 5.43 (2.08, 13.74) for high exposure. For children with a family history of asthma, the relative risk is 0.66 (0.25, 1.74) for medium exposure and 0.67 (0.12, 3.69) for high exposure. The *p*-value for the overall "exposure-effect" (i.e. both main effects and interaction terms) is 0.0097.

Thus the study provides evidence of a weak association between asthma prevalence in 5-7 years old children exposed to traffic in an area where the primary air pollutants are VOCs and coarse fraction PM. Children without genetic predisposition to asthma appear to be most at risk.

Source: Journal of Exposure Science and Environmental Epidemiology, Vol. 16, Issue 1, January 2006.

THE EFFECT OF LEAD EXPOSURE AND ERGONOMIC STRESSORS ON PERIPHERAL NERVE FUNCTION

Long-term lead exposure among industrial workers can result in neuropathy (a disorder of the peripheral nervous system), while lower exposure levels cause muscle weakness.

In the past, the usual biomarker used to study lead neuropathy was a blood lead measure of recent exposure. More recently, studies have shown an association between several biomarkers of chronic lead exposure---working lifetime-weighted average blood lead (TWA), working lifetime-integrated blood lead (IBL), and bone lead---and impairment of peripheral nerve function at a time when concurrent blood lead was not elevated. Which of these is the best metric for modeling chronic lead effects on the peripheral nerve remains to be demonstrated.

In the older literature, lead poisoning presented as muscle paralysis, typically occurring in the muscles most used. In fact, patterns of weakness differed by occupation but did not necessarily follow the distribution of a specific nerve. Although it is established that lead impairs peripheral nerve function, not studied to date is the effect of the interaction between lead exposure and chronic repetitive muscle use on that function.

Researchers from the Center for Occupational and Environmental Neurology in Baltimore now report that the impact of chronic lead exposure is augmented by concomitant ergonomic stress.

The study included 80 lead smelter workers who were routinely exposed on the job to inorganic lead dust and (to a lesser extent) lead fumes. Historical blood lead records for all the workers were available from the smelter, which checked all employees' blood lead at least quarterly. These records showed that workers had high chronic exposure in the distant past, much lower exposure in the more proximate past, and still lower exposure at the time of the study. The researchers also measured current blood and bone lead levels and used the historical records to calculate two metrics of cumulative lead exposure—TWA and IBL.

(Continued on next page)

THE EFFECT OF LEAD EXPOSURE AND ERGONOMIC STRESSORS ON PERIPHERAL NERVE FUNCTION

(Continued)

The team used the current perception threshold test to examine nerve fiber populations in the workers' shoulders, arms, wrists, and hands. This test measures the amount of electrical current needed to induce a sensation. The team also created a three-tiered ergonomic stress rating based on all the different jobs the workers had ever performed, cumulated over their employment history. This was used to arrive at a time-weighted average ergonomic stressor. Sensory nerve conduction threshold was measured in large myelinated, small myelinated, and unmyelinated nerve fibers.

The results showed that decrements in nerve function---a precursor to neuropathy---were limited to large and small myelinated sensory nerve fibers, with a threshold effect at a TWA of 28 mg/dL. At higher levels of lead exposure and presence of ergonomic stress, nerve fibers were more susceptible to increased damage, something that has never before been shown in human studies. The investigators suggest that nerves affected by lead are more susceptible to traction or mechanical compression, as would occur in the carpal tunnel of workers who perform activities such as heavy lifting and shoveling.

The investigators point out that although TWA and IBL are associated with peripheral nerve damage, bone lead is a weak predictor of lead effects in the nervous system because it shows only the lead stored in the bone compartment and not the cumulative blood lead to which the peripheral nerves were exposure.

Source: Environmental Health Perspectives, Vol. 113, No. 12, December 2005.

Reduced Antibody Responses to Vaccinations in Children Exposed to Polychlorinated Biphenyls

The response of normal children to routine prophylactic vaccinations varies substantially. While reduced vaccination responses are well described with regard to specific immunodeficiency syndromes, the reasons for the wide variation in healthy children's production of specific antibodies are poorly understood. Immunotoxic effects may be elicited by certain persistent organochlorine pollutants, such as polychlorinated biphenyls (PCBs), as indicated by decreased concentrations of immunoglobulins and increased frequencies of childhood infections in children who had been exposed to PCBs and related compounds by their mothers' contaminated diets. Most experimental evidence, but not all, points to PCB-associated immunotoxicity being due to effects caused by dioxin-like PCB congeners.

A relevant and feasible strategy for a quantitative evaluation of the immune system of infants and small children is to measure antibody responses to immunization with thymus-dependent neoantigens. Antibody formation to such antigens is dependent on antigen presentation, T lymphocyte function, and B lymphocyte function and therefore reflects overall efficacy of the immune system in relation to infection. Because standardized methods for antibody assessment and extensive experience on vaccine efficacy are available, antibody responses to diphtheria toxoid and tetanus toxoid are highly suitable for this purpose.

The Faroe Islands represents a unique setting for studies of PCB immunotoxicity. While dioxin exposure is not increased, average PCB exposures are up to 10-fold higher than average levels in Northern Europe, due to the traditional habit of eating pilot whale blubber.

A recent study has therefore examined vaccination responses in two Faroese birth cohorts in relation to developmental immunotoxicant exposure.

Prenatal exposure was determined from maternal concentrations of PCBs in pregnancy serum and milk. Following routine childhood vaccinations against tetanus and diphtheria, 119 children were examined at 18 months and 129 children at 7 years of age, and their serum samples were analyzed for tetanus and diphtheria toxoid antibodies and for PCBs. The antibody response to diphtheria toxoid decreased at age 18 months by 24.4% (95% confidence interval [CI], 1.63-41.9; p=0.04) for each doubling of the cumulative PCB exposure at the time of examination. The diphtheria response was lower at age 7 years and was not associated with the exposure. However, the tetanus toxoid antibody response was affected mainly at age 7 years, decreasing by 16.5% (95% CI, 1.51-29.3; p=0.03) for each doubling of the prenatal exposure. Structural equation analysis showed that the early postnatal exposure was the most important predictor of a decreased vaccination response.

Increased perinatal exposure to PCBs may adversely impact on immune responses to childhood vaccinations. The clinical implications of insufficient antibody production emphasize the need for prevention of immunotoxicant exposures.

Source: Public Library of Science (PLoS) Medicine, Vol. 3, Issue 8, August 2006.

Neurotoxicity of Prenatal Benzene Exposure in Rats

Teratogenicity of benzene has been studied in mice, rabbit and rats. Fetal death and delayed ossification, increased frequencies of jaw and palatal defects have been observed in mice exposed to benzene during pregnancy. Benzene is present in cord blood at concentrations at least as high as those in maternal blood. Data on humans derive from studies performed in subjects with occupational exposure to benzene during pregnancy and are insufficient to confirm the absence of risk. A significantly increased frequency of spontaneous abortion was observed in the pregnancy of 485 women who were occupationally exposed to benzene during the first trimester. Children whose mothers were chronically exposed to benzene in pregnancy showed an increased frequency of acquired lymphocyte cytogenetic abnormalities.

Chronic benzene exposure in animals and humans during pregnancy may cause neurological effects, like euphoria, headache, vertigo, ataxia, narcosis, confusion, neuropathies and electroencephalogram abnormalities. However, epidemiological studies on congenital anomalies are difficult to interpret. Furthermore, no evidence has been provided yet that acute exposure to benzene may induce neurological and psychic effects in the progeny.

Now a new study has been undertaken in order to assess motor and behavioral changes in rats after a prenatal acute exposure to benzene. For this purpose, in order to ensure a standard exposure to animals, benzene was not administered by air but injected acutely by the subcutaneous route. A single dose was selected, 0.1 mg/kg, between doses from 5 ng/kg to 500 mg/kg body weight, that have been considered as equivalent to polluting quantities of benzene for human. The behavioral and motor effects of benzene exposure were then assessed with a battery of tests applied in new-born pups and adult animals 2 months after birth.

At birth no difference was found in body weight and total number of neonates between animals prenatally exposed to benzene and controls. No malformations were observed in either group and no difference was found in eye opening time.

The percent appearance of all neonatal reflexes appeared to be as anticipated (i.e., more pups exhibited reflexes each day) in the group of pups exposed prenatally to benzene compared to that of controls. Also, the completion (maximum appearance, i.e. 100% of the brood was found to exhibit each reflex) of neonatal reflexes in benzene-exposed animals preceded that of controls. Statistical analysis revealed several time points in which the incidence of forelimb placing, cliff aversion, startle and righting reflexes was significantly higher for benzene-exposed pups than for controls. Exception was found only for forelimb grasping and bar holding reflexes, which appeared and completed on the same day for benzene-exposed and control animals showing a similar time points incidence.

In the open-field test, adult male rats exposed prenatally to benzene showed reduced ambulation than control animals. The number of areas explored by the former with at least the forelegs in three minutes was smaller than that of controls, although the number of rearing and grooming episodes were similar in the two groups.

The analysis of the data obtained with a single session shuttle-box active avoidance test revealed that male rats exposed prenatally to benzene exhibited a reduction in number of conditioned avoidance responses and a more pronounced reduction in percent of learners as compared to control animals.

Latency in seconds to re-enter the dark box as a measure of passive avoidance reaction in the step-through type of passive avoidance test appeared to be much inferior in benzene-exposed male rats than in control animals, either in the first (24 h after the learning trial) or in the second (48 h after the learning trial) retention test.

This study provides for the first time evidence that acute exposure to benzene in pregnant rats may induce in the progeny long-lasting behavioral changes, i.e. reduced motor activity and cognitive capacity. This result is particularly important if one would consider that animals were exposed to a very low dose of the toxic agent, far from the maximum dose considered equivalent to polluting quantities of benzene for human, i.e. 500 mg/kg body weight.

Results of the present study cannot be extended to humans. However, it is known that agents found to be neurotoxic in animals often exert the same effects in humans. Besides, analysis of behavioral functions may represent a more sensitive tool to study neurotoxic agents at low doses, particularly when such studies are performed with drugs in order to uncover possible deficient neurochemical mechanism. This is also possible for those neurotoxic agents that do not behave as teratogenics, such as benzene. For this reason, a major concern is that although limits of benzene in air have been established in the USA and the European Union (5 $\mu g/m^3$), individual exposure levels, and therefore risk estimates, cannot merely be extrapolated from environmental concentrations.

Source: Toxicology, Vol. 223, Issue 3, June 2006.

HEARING LOSS IN WORKERS EXPOSED TO TOLUENE AND NOISE

A recent study conducted in Taiwan investigated the risk of hearing loss among workers exposed to both toluene and noise. A cohort of 58 workers was recruited at an adhesive materials manufacturing plant who were exposed to both toluene and noise, 58 workers exposed to noise only, and 58 administrative clerks in the same company in Taiwan.

The participants were interviewed to obtain sociodemographic and employment information, and physical examinations were carried out including pure-tone audiometry test between 0.5 and 6 kHz.

A contracted laboratory certified by the Council of Labor in Taiwan conducted on-site toluene and noise exposure measurements. The prevalence of hearing loss of > 25 dB in the toluene plus noise group (86.2%) was much greater than that in the noise-only group (44.8%) and the administrative clerks (5.0%) (p<0.001). The prevalence rates were 67.2, 32.8, and 8.3% (p<0.001), respectively, when 0.5 kHz was excluded from the estimation.

The study is the first to identify such a strong effect of hearing impairment from simultaneous exposure to toluene and noise in humans. The average noise exposure levels were similar between the toluene plus noise group and the noise-only group. However, the risk for hearing loss at > 25 dB was much greater in the toluene plus noise group than in the noise-only group. The overall odds ratios adjusted for covariates were 140 versus 12.8 with 0.5 kHz included in the measurement and 29.1 versus 5.0 with this pure-tone excluded. This indicates that the risk for hearing loss boosted by toluene exposure may be more than six times greater than the risk induced by noise only.

The other unique finding in this study is that the magnitudes of ototoxic effect were different for various tested pure-tone frequencies among workers exposed to toluene plus noise, noise only, and administrative clerks. This finding has not been reported previously for toluene. It is worthwhile to note that the patterns of hearing impairment, measured by the pure-tone frequencies, associated with toluene plus noise exposure are similar to those associated with the simultaneous exposure to carbon disulfide and noise. Both toluene and carbon disulfide have greater impact on the speech frequencies than does noise alone, with the gap the largest at the frequency of 500 Hz. Therefore, the toluene plus noise group had poorer thresholds than did the noise only group at 1 kHz frequencies, but not necessarily at high frequencies. However, the poorest mean hearing threshold in the toluene plus noise group was at 6 kHz. This was similar to the mean hearing threshold pattern found for the ototoxicity of styrene. Other types of ototoxic solvents may have other types of effects on hearing measured by pure-tone frequency.

The average air concentrations of toluene at work sites for the three divisions of the toluene plus noise group were 33.0 ppm, 107.6 ppm, and 164.6 ppm, but with similar noise exposure levels. It was surprising to find that the risk for hearing loss in workers with the lowest toluene exposure was only slightly lower than that for those with higher levels of toluene exposure. The dose-response analysis based on measures of toluene cumulative exposure index (CEI) showed a peak effect at the cumulative exposure level of 200-530 year-ppm and failed to estimate the threshold dose of toluene on the hearing loss effect due to the solvent.

This observation might reflect variations in exposure history and healthy worker effect. Most of the study participants in the toluene plus noise group (all three areas) may have been exposed to higher levels of toluene during their long employment. Those who had a CEI > 200-530 year-ppm may have quit their jobs because of hearing problems or other reasons, which would lower the estimated ORs. This is one of the limitations of this study. Another limitation of this study was the sample size. No data were available for estimating the impact of hearing loss for workers due to toluene only exposure.

Results from this study showed that there was an elevated hearing impairment for workers who were exposed to toluene plus noise compared with those exposed to noise alone. Although the overall hearing loss was rarely > 55 dB, the impact was greater for the speech frequencies than for the higher frequencies. These data suggest that the current work site threshold limit value of 100 ppm established for toluene does not protect workers from hearing loss in the simultaneous presence of noise at the work site. Effective intervention is needed to improve industrial safety of individuals experiencing ototoxic effects of solvents. Findings from this study and studies of other solvents can help policy makers as they establish threshold limit values for solvents and implement such interventions.

Source: Environmental Health Perspectives, Vol. 114, No. 8, August 2006.

LOW LEVEL CADMIUM EXPOSURE AND OSTEOPOROSIS

A group of Swedish researchers has shown for the first time that even low level exposure to cadmium can have negative effects on bone in humans.

To investigate associations between cadmium retention and bone effects, the researchers assessed a cohort of women ranging in age from 53 to 64 years. The 820 subjects were recruited from a large population-based survey in Lund, Sweden, [Women's Health in the Lund Area (WHILA) study].

The lack of known history of excessive cadmium contamination in this area implied that exposures were reasonably constant over time.

The researchers measured cadmium in blood and urine; lead in blood; several biochemical markers of bone metabolism; and forearm bone mineral density (BMD), a test used to assess osteoporosis status.

Statistical analysis of the results incorporated a number of potential confounders and effect modifiers, including weight, menopausal status, use of hormone replacement therapy, age at menarche, alcohol consumption, smoking history, and level of physical activity.

This is the first study on cadmium-associated effects on bone in a population residing in an area with no known historical cadmium contamination, assuming a rather constant exposure over time. Nevertheless, the results are in accordance with findings of cadmium-associated effects on BMD and fractures in Swedes (of both sexes) with a similarly low present environmental exposure, Belgians with a somewhat higher exposure, Japanese women, and Chinese men and women with considerably higher exposure levels. In the present study, detailed information was obtained on several possible risk modifiers and confounders for osteoporosis, such as physical activity, menarche, menopausal status, and hormone replacement therapy. This enabled researchers to ascertain associations between low cadmium exposure and bone effects and the findings support a causal explanation. The effect of cadmium on bone resorption in the study was even more pronounced after menopause (interaction), in accordance with results from animal and human studies, and in line with the fact that those affected by the Itai-itai disease were mainly women after menopause.

Although the mechanism by which cadmium exerts effects on bone is far from clear, studies on humans have indicated an effect mediated through kidney damage. The mechanism was explored by measuring markers of both bone metabolism and kidney effects. In contrast to previous reports, the study suggested a direct effect of cadmium on bone resorption (osteoclasts), resulting in increased urinary deoxypyridinoline. Such stimulation of bone resorption has been demonstrated in both animal and *in vitro* studies. Because parathyroid hormone (PTH) is the main regulator of calcium metabolism, an increased bone resorption would lead to a compensatory decrease in PTH, which is in line with these results. The fact that no association was found between cadmium and bone formation (osteocalcin and bone alkaline phosphatase) may reflect a cadmium-induced uncoupling between bone resorption and formation. In contrast, studies on patients with Itai-itai showed increased levels of markers of bone formation compared with controls, and studies of other subjects with cadmium-induced tubular damage showed increased PTH. This may indicate other mechanisms are involved in subjects with severe kidney damage.

An indirect effect on bone due to cadmium-induced kidney damage, via impaired activation of vitamin D, and increased excretion of calcium and decreased bone formation has been proposed. However, no association was found between cadmium and urinary calcium or markers of bone formation (osteocalcin and bone alkaline phosphatase). The present study indicates that the kidney was not involved, although the associations between the effect on bone and some of the renal effect markers may indicate some kidney-mediated effect.

Even though radius BMD is likely to reflect the risk of forearm fractures, it may not be a good index of osteoporosis in other parts of the skeleton, although there was correlation, albeit weak, between BMD of the radius and the hip in 81 women of the WHILA cohort. Evaluation of cadmium exposure in relation to BMD of other sites associated with increased fracture risk, such as hip and lumbar spine, is required.

Clearly, the overall role of cadmium in the etiology of osteoporosis is limited. The observed difference in BMD between high- and low-exposed individuals corresponded to that of a 6-year increase in age or an 11-kg lower body weight. However, in view of the high prevalence of this disease, even a minor contribution is important at the population level. Furthermore, because the main cadmium exposure is via foods considered healthful and because everyone has lifelong exposure, these findings in combination with the observed effects on kidney emphasize the importance of activities to reduce cadmium pollution of the environment.

Source: Environmental Health Perspectives, Vol. 114, No. 6, June 2006.

Effect of Ambient Fine Particles on Heart Rate Variability

Air pollution is a major public health problem, which has been associated with an increase in cardiopulmonary morbidity and mortality in many cities around the world after short-term exposure. Acute as well as chronic exposure to suspended particulate matter (PM) has been linked to a rise in hospital admissions and emergency room visits due to respiratory and cardiovascular causes, especially in children under 5 years of age with asthma and elderly people with known cardiac or pulmonary disease. Moreover, cohort epidemiological studies have linked long-term exposure to particulate air pollution to a reduction of life expectancy due to cardiovascular mortality. Although understanding of the underlying biological mechanism of these associations remains limited, several hypotheses have been postulated, from inflammation, accelerated atherosclerosis and altered cardiac autonomic function.

Since the 1980s, heart rate variability (HRV) has been widely used in clinical fields to stratify the risk of arrhythmic death of the patients with ischemic heart disease in whom a low HRV could be a negative predictor. Alterations of the autonomic nervous system accompanying the early stages of essential hypertension have also been studied using HRV, and it was found that sympathetic activity increases while parasympathetic decreases. Patients with congestive heart failure had clinical signs of enhanced sympathetic activity and progressive decrease in RR variance. A low HRV has been associated to an increase mortality rate in people with heart disease.

Recent studies that included elderly individuals with heart diseases in Baltimore, Boston and Mexico City suggest that $PM_{2.5}$ air pollution measured with ambient monitors was associated with a reduced HRV.

Now a new study has been carried out to test whether this association could also be observed in 44 healthy young adults, using personal exposure monitors, at ambient levels currently observed in the Mexico City metropolitan area.

All 44 subjects had Holter electrocardiographic (ECG) and $PM_{2.5}$ personal exposure monitoring; four were eliminated, and the participation rate was of 91%. The losses were attributable to: $PM_{2.5}$ personal monitors malfunction in two subjects, the presence of multiple premature ventricular beats in a young male and a 40-year-old woman who decided to withdraw from the study because she was uncomfortable with Holter ECG electrodes. The mean age of the participants was 27 years, range 21-35 years, and 29 were women. Average body mass index (BMI) was 24 kg/m^2 and an eighth of the participants exercised regularly. The median (25-75 percentiles) $PM_{2.5}$ personal concentration exposure was 74 $\mu g/m^3$ (49-111 $\mu g/m^3$), the median (25-75 percentiles) of the standard deviation of all normal RR intervals (SDNN) was 74 ms (59-92 ms) and the percentage of differences between adjacent normal RR intervals larger than 50 ms (pNN50) was 8.9% (4-19%).

This study is consistent with previous evidence that ambient $PM_{2.5}$ air pollution is associated with decreased HRV, particularly for parasympathetic (vagal) modulation of cardiac autonomic function. This association was stronger at 1.5 and 2 h of accumulative personal exposure when adjusted for gender, age, physical training and BMI.

Studies in susceptible groups have helped to explain the short-term effects of $PM_{2.5}$ air pollution and possible mechanisms of mortality displacement after pollution episodes as the 1952 "4 days fog" event in London with an increase in morbidity and mortality related to respiratory or cardiovascular disease. The possible mechanisms for the acute cardiovascular effects may include endothelial cell, platelet and leukocyte activation as part of inflammatory response, along with increased blood viscosity and physiological changes such as acute arterial constriction responses that may trigger acute cardiovascular events.

The present study found stronger effects of $PM_{2.5}$ in 1.5 and 2 h of accumulative exposure than in the concurrent 30 min. As air pollution concentrations from 30 min. were available, it was possible to evaluate several lagged models with end times matched to each participant's ECG recordings; however, no significant association was observed.

The public health consequences of the effects found in a young healthy population in this study could be different from those informed in previous studies. A decrease of HRV is a common finding in the elderly and in patients with heart disease, which has been demonstrated to be a predictor of an increased mortality in both populations. However, in the long term, cardiac autonomic imbalance may play a role in the development of cardiovascular diseases. A reduction in the pNN50 suggesting a decreased parasympathetic cardiac autonomic control with sympathetic nervous system overactivity has been associated with the development of hypertension among previously normotensive men. A study carried out in 2002 reported preliminary results explaining how sympathetic stimulation through peripheral acute arterial construction was related to PM as well as other pollutants exposure.

However, the significance of a decreased parasympathetic activity in the young healthy adults over a lifetime exposure in urban areas as Mexico City needs to be clarified. Further studies are needed to assess if these cardiac autonomic changes could be related to the association between $PM_{2.5}$ air pollution and the increase in cardiovascular morbidity and mortality.

Source: Journal of Exposure Science and Environmental Epidemiology, Vol. 16, Issue 2, March 2006.

SHORT-TERM INTERNATIONAL TRAINING COURSES 2007

	Activity	Date	Final Date for Application
1.	Biotechnology for Toxics Assessment and Control*	June 18 – July 4	April 30
2.	Environmental Toxicology**	June 29 – July 19	March 31
3.	Environmental and Health Risk Assessment and Management of Toxic Chemicals**	December 3 – 19	To be Announced
4.	Environmental Health*	To be Announced	To be Announced

* Applications are invited from Colombo Plan developing member countries. All applications for fellowship and medical reports are required to be sent through the focal point of the **Colombo Plan Secretariat** in the applicant's own country.
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For more information, please visit:
http://www.mfa.go.th/internet/TICA/AITC2007/AITC2007.htm

The 6th Princess Chulabhorn International Science Congress

Congress Theme:
The Interface of Chemistry and Biology in the "Omics" Era: *Environment & Health and Drug Discovery*
November 25 – 29, 2007, Shangri-La Hotel, Bangkok, THAILAND

The 6th Princess Chulabhorn International Science Congress – "The Interface of Chemistry and Biology in the 'Omics' Era" is organized as a forum that will highlight how linkages between these areas of research contribute to the treatment and prevention of diseases in the global population.

The significance of fast-growing inter-disciplinary research, spanning work from the level of the molecule to the whole body system will be brought into focus on 2 main themes:

- **Environment and Health, and**
- **Drug Discovery**

Developments in both of these areas at catalyzed by "INNOVATIVE TECHNOLOGY", a sub-theme that will cut across the two main themes. It is expected that the interface of chemistry and biology in the "Omics" era will result in an increased knowledge and understanding necessary for extending this exciting new frontier of science.

The Congress will be held from November 25 – 29, 2007 to commemorate the 80th birthday celebration of His Majesty King Bhumibol Adulyadej.

Following the main Congress there will be a satellite workshop organized by Collegium Ramazzini on *"Occupational and Environmental Health in the Asia/Pacific Region"*.

Invited speakers at the Congress will include Nobel Laureates and other world renowned scientists and researchers from U.S.A., Europe and Japan.

For further information, please contact the Conference Secretariat at:
Tel: +66 2 574 0622 ext. 3911
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E-mail: pc@cri.or.th
Website: http://www.cri.or.th/pc6

Call for Abstracts
Deadline:
September 30, 2007

CHULABHORN GRADUATE INSTITUTE (CGI)
International Graduate Program

The recently established multidis-ciplinary post-graduate academic institute, Chulabhorn Graduate Institute (CGI) is presently offering international programs at Diploma, Master's degree and Ph.D. degree levels in Environmental Toxicology, Applied Biological Sciences: Environment & Health, and Chemical Biology.

Participating teaching faculty are from world-renowned international academic and research institutions in Europe, North America, and Asia, in addition to the faculty members from the CGI. The Master's and Doctoral Degree Programs are organized in a 2-semester system:

- 1st Semester, June-September
- 2nd Semester, November-February

Prospective students should have com-pleted a first degree in a relevant area of study.

Master's Degree Program:
- Candidates must hold a Bachelor's degree or its equivalent with a cumulative GPA of at least 2.75.

Doctoral Degree Program:
- Candidates should hold a Master's degree or its equivalent in a relevant field with a GPA of at least 3.5 at the Master's level.
- Candidates holding a Bachelor's degree with First Class Honors are also eligible.

Regular admission and entry: June (starting in 2007)

CHULABHORN GRADUATE INSTITUTE (CGI)
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http://www.cgi.ac.th

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