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Chulabhorn Research Institute

INTERNATIONAL CENTER FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

MOU Signing Ceremony between CRI and Tulane School of Public Health and Tropical Medicine

On 6 April 2005 Her Royal Highness Princess Chulabhorn, President of the Chulabhorn Research Institute (CRI), signed a Memorandum of Understanding for educational and scientific cooperation between the Chulabhorn Research Institute and Tulane School of Public Health and Tropical Medicine.

Cooperative activities to be pursued include:

Cooperation will center on joint research activities as well as joint activities in training scientists and public health professionals in basic and applied research.

Under the terms of the memorandum of understanding, provision is made for exchange of information to include library materials and research publications; the exchange of faculty members for research, lectures and discussions; and the exchange of research scientists and graduate students to pursue advanced study and research.

A further and important purpose of the agreement is to facilitate the intiation of new research and the conduct of scientific meetings on topics of mutual interest to the two institutions.

On this important occasion, Her Royal Highness and her party were the guests of Dean Pierre Buekens who opened the ceremony with the presentation of a proclamation by the City of New Orleans in honour of Her Royal Highness' visit.

At the signing ceremony, Her Royal Highness Princess Chulabhorn gave an address to an invited audience of academics and civic dignitaries, describing the work of the CRI in improving the quality of life of the Thai people through the application of science and technology. Her Royal Highness took this opportunity to inform her audience of the future plans of the Institute in establishing the Chulabhorn Cancer Center at CRI. This center for research and treatment of cancer will be opened by the year 2006 and will facilitate the transfer of knowledge and advanced technology from leading centers in the developed world. It will provide facilities for 100 beds with residence facilities for physicians and nurses. The focus will be on chemotherapy and radiation oncology.

The cooperation with Tulane University, a noted center for research into

(Continued on page 2)

MOU Signing Ceremony between CRI and Tulane School of Public Health and Tropical Medicine

(Continued from page 1)

cancer, will make a significant contribution to the establishment of the Chulabhorn Cancer Center at CRI. The agreement for educational and scientific cooperation was signed for Tulane University by Dr. Pierre Buekens, Dean of the School of Public Health and Tropical Medicine and by Dr. Alan M. Miller, Associate Senior Vice-President for Health Sciences, Tulane University Health Sciences Center.

THE SYNERGISTIC EFFECT OF OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE WITH ALCOHOL INTAKE: A CASE-REFERENT STUDY

Although a large body of evidence from experimental and epidemiologic studies has demonstrated the relationship between exposure to vinyl chloride monomer (VCM) and angiosarcoma, there is little evidence of a causal association between VCM and hepatocellular carcinoma (HCC) and liver cirrhosis (LC).

In a study on the U.S. cohort of VCM-exposed workers, researchers found an increased risk of liver cancer, mainly liver angiosarcomas. In the study, however, they distinguished HCC from angiosarcoma on the basis of information on the cause of death reported in death certificates. In the European cohort of VCM workers, researchers scrutinized the best evidence of liver cancer by reviewing all available documentation and found a marked exposure-response relationship for all liver cancers (71 cases), angiosarcoma (37 cases), and HCC (10 cases). This evidence is also inconclusive because the number of HCC cases was small, there was a disproportionate excess of liver cancers with "other and unknown histology", and the risk estimates were not adjusted for the influence of well-known risk factors for HCC: alcohol consumption and viral infection.

A European study carried out in 2003 reported on a cohort of 1,658 workers employed in a VCM manufacturing plant, in which the standardized mortality ratio (SMR) for primary liver cancer of 2.78 was significantly increased. Because cohort studies are unavoidably affected by selection (healthy worker effect), information (misclassification of exposure and diagnosis of diseases based on death certificate), and confounding biases (alcohol intake, HBV/hepatitis C virus carried status), researchers have now carried out a case-referent study nested in the same cohort. In northeast Italy (Porto Marghera, Venice), where the plant is located, alcohol consumption is heavy and viral hepatitis common. These particular exposure conditions appeared suitable for the appraisal of the individual role of VCM exposure, alcohol intake, viral hepatitis infections, and their interactions in the etiology of HCC and LC.

The present case-referent study was carried out on the occasion of a lawsuit by hundreds of workers, local municipalities, and the Italian national government against the VCM plant management. At the beginning of the lawsuit, the company indemnified any health problem that claimant workers themselves attributed to their past exposure in the plant. Among the "claimants" were 13 cases of HCC, and 40 cases of LC (24 with histologic confirmation and 16 with clinical evidence of portal hypertension, ascites, and/or esophageal varices). Out of the 13 HCC cases, 11 also had LC and are included in the series of LC cases.

Information on diagnosis was obtained from hospital records, which were actively searched for deceased subjects (vital status and cause of death were ascertained for all the cohort members through 1999); incident cancer cases (ascertained through the regional cancer registry for all the cohort members from 1987 to 1999); and all other claimant workers.

Six hundred and forty-three former VCM workers belonging to the above cohort were examined from 1999 through 2002 by occupational physicians at the Occupational Health Services (OHS) of two local health authorities in the course of a medical surveillance program launched by the Regione Veneto and the Italian Ministry of Health. Among these subjects, 139 subjects without clinical (including liver sonography) or biochemical (normal serum levels of aspartate aminotransferase, alanine aminotransferase, and γ–glutamyl transpeptidase) evidence of chronic liver disease or cancer in any site were identified. HCC cases and LC cases were separately compared to the above 139 referents in the present cohort-based case-referent study.

For cases, information on the job performed and the corresponding entry/exit dates was obtained from company files; for referents, these data were obtained through the occupational history collected by OHS occupational physicians during the medical surveillance program. Using a job-exposure matrix, researchers estimated cumulative VCM exposure by summing across the calendar years of exposure the product of the average level of VCM exposure in a job (parts per million) and years worked in that job. The variable was split into four classes using the quartiles (160, 500, and 2,500 ppm X years); it was also dichotomized (cut point, 2,500 ppm X years) when examining interactions of VCM exposure with alcohol consumption or viral hepatitis infection.

Alcohol consumption was ascertained in cases and referents through hospital clinical record and/or health surveillance records. The measure was computed in grams of ethanol per day. The variable was split into three classes using 30 and 60 g/day as cut points; it was also dichotomized [cut point, 60 g/day, a threshold considered necessary for alcohol-mediated injury] in examining interactions between VCM exposure and alcohol consumption.

(Continued on page 3)

Childhood Cancers and Atmospheric Carcinogens

An analysis of data on childhood cancers in the United Kingdom suggests that prenatal exposure to industrial and environmental pollutants likely to have been inhaled by the mother during pregnancy were probably to blame for the majority of cases.

Childhood cancer and leukaemia births are closely associated with high atmospheric emissions from combustion processes, mainly oil based, and from organic evaporation. Demonstrated associations with 1,3-butadiene, dioxins and benz(a)pyrene, but possibly others as well, are probably causal.

However, it is difficult to say with certainty whether any particular result based on analyses of emission levels points to a specific carcinogenic effect, or whether it is acting as proxy for other geographically associated substances. Carbon monoxide is a powerful indicator of transport activity, for example, but is itself a generator of many other substances. Thus, it cannot be concluded that it must be an active substance, although it may be.

Benzene is also difficult to assess because the original leukaemogenic suspicion might itself spring from indirect associations. Nitrogen oxides, with their complex trains of secondary atmospheric reactions raise similar issues.

However the author of the recent research analysis claims that the present associations with 1,3-butadiene, dioxins and benz(a)pyrene are sufficiently specific to conclude that they are probably among the truly active agents.

From this analysis, the main policy implications are a need to regulate carcinogenic atmospheric emissions, especially 1,3-butadiene; and for a redirection of research efforts relating to childhood cancer. This research should now try to determine the exact timings of chemically determined air mediated cancer initiations—whether in early infancy or prenatally, or even preconceptually; and to seek engineering and social solutions.

Source: J Epidemiol Community Health 2005, Vol. 59.

PREDICTED IMPACTS OF THE GROWING ACIDITY OF THE OCEANS

Scientists in a conference on climate change in Exeter, UK, warned that extra carbon dioxide in the air, caused by the burning of fossil fuels, is not only spurring climate change, but is making the oceans more acidic, thus endangering the marine life that helps to remove carbon dioxide from the atmosphere. So urgent is the problem that some claim that within the next 35 years, all the coral reefs in the world could be dead. Although the growing acidity is caused by excess carbon dioxide in the atmosphere, it is not a problem of "global warming", but the result of a simple chemical reaction between the air and the sea.

It is estimated that about half the 800 billion tonnes of carbon dioxide put into the atmosphere by mankind since the start of the industrial revolution has been soaked up by the sea. Much of the carbon is fixed in the shells of minute plankton called coccolithphores that live on the ocean surface in trillions. When they die, their shells sink to the ocean bed taking the carbon with them.

Scientists now claim that these creatures could not survive greater levels of acidity and their removal of carbon from the atmosphere would stop.

Experiments show that even a small increase in acidity reduces the ability of shellfish and plankton to grow and causes a fall in their population.

In addition to the loss of corals that would seriously affect small islands and coasts, the major problem is the effect on the food chain.

The Exeter conference concluded that the growing acidity of the oceans was a potentially disturbing phenomenon that would reduce the oceans' capacity to remove CO from the atmosphere and affect that entire marine food chain.

Source: www.guardian.co.uk, February 2005.

THE SYNERGISTIC EFFECT OF OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE WITH ALCOHOL INTAKE: A CASE-REFERENT STUDY

(Continued from page 2)

The main finding of the present study is that VCM exposure is an independent risk factor for the development of HCC and LC. The association between VCM exposure and HCC was suggested in early studies showing the coexistence of nodules of angiosarcoma and hepatocarcinoma in histologic liver specimens.

A multiplicative effect between VCM exposure and alcohol in hepatocarcinogenesis was found in an earlier experimental study. However, the present study claims to be the first to report a synergistic effect between VCM exposure in humans and alcohol consumption in the development of HCC and its associated preneoplastic condition, LC. An attributable proportion of nearly 80% indicated that VCM exposure and alcohol intake have little effect separately but, in association, produce most of the disease. This may explain why the relationship between HCC (or LC) and VCM has been overlooked in epidemiologic settings where HCC cases would be in excess only if alcohol intake were high in VCM-exposed workers, and clinical settings where nonoccupational causes of disease are often present.

Source: Environmental Health Perspectives, No. 11, August 2004.

HEALTH RISKS FROM ENVIRONMENTAL TOBACCO SMOKE

Environmental tobacco smoke, or involuntary smoking, comprises sidestream smoke from the smouldering tobacco between puffs and exhaled mainstream smoke from the smoker. In a recent study researchers analysed data from the large European prospective investigation into cancer and nutrition (EPIC) to assess the relation between environmental tobacco smoke and lung cancer, upper respiratory cancers, and death from chronic obstructive pulmonary disease (COPD) or emphysema, limiting the analysis to never smokers and people who had not smoked for more than 10 years. The advantage of the cohort design is the lack of recall bias as information about exposure was collected before onset of disease.

The nested case-control study (GenAir) studied the relation between air pollution or environmental tobacco smoke and newly diagnosed cancers of the bladder, lung, oral cavity, pharynx, or larynx, or leukaemia. The study also identified and included deaths from respiratory diseases (chronic obstructive pulmonary disease and emphysema). Only people who had never smoked or who had stopped smoking for at least 10 years were included.

Three controls per case were matched for assessment of exposure and the analysis of questionnaire data and two controls per case for laboratory analyses. Controls were matched for sex, age (plus or minus 5 years), smoking status (never/former smoke), country of recruitment, and time elapsed since recruitment (months).

Information on exposure to environmental tobacco smoke was collected from 123 479/303 020 (40.8%) participants who had never smoked or former smokers in the EPIC cohort. Of these 97 people developed lung cancer, 20 developed upper respiratory cancers (pharynx, larynx), and 14 died from chronic obstructive pulmonary disease or emphysema during the seven years of follow up.

Plasma cotinine was measured in 1574 GenAir subjects and we excluded 47 participants with values > 10 ng/ml because they were likely to be active smokers (n = 41) or sniffers/chewers (n = 6). Of the 1527 remaining subjects, 461 (30%) had detectable concentrations of plasma cotinine with an overall mean value of 0.92 ng/ml (SD 0.96 ng/ml).

Increased odds ratios and hazard ratios were associated with environmental tobacco smoke exposure at recruitment for all respiratory diseases and for lung cancer alone in the whole cohort and in the nested study.

Former smokers had a higher relative risk for respiratory disease (attaining significance) than those who had never smoked in both the whole cohort and the case-control analyses. The raised risks, in both analyses, were limited to exposures related to work, with significant relative risk ratios around 1.5. to 2.0. Cotinine was not associated with lung cancer or other diseases. The odds ratio for detectable versus undetectable cotinine concentrations and respiratory disease/cancer was 0.9 (0.5 to 1.8).

The role of environmental tobacco smoke in lung cancer was analysed according to the score of "at risk" alleles for polymorphisms in metabolic genes. The odds ratio associated among carriers of at least three of the at risk polymorphisms was 2.86 (0.79 to 10.35), while for those with one or two alleles it was 1.33 (0.82 to 2.18).

The biological plausibility of a causal association between environmental tobacco smoke exposure and lung cancer is reinforced by the suggestion that having more than three polymorphic genes increases the odds ratio to 2.86. This, if confirmed, would be an example of "mendelian randomisation". Previous studies have found that the association between environmental tobacco smoke and lung cancer was stronger in subjects with polymorphisms in GSTM, but one study had negative results, although statistical power was limited.

Cotinine concentrations were not associated with the risk of lung cancer. This could be expected, as previous studies have stressed the limitations of cotinine as a biomarker of exposure. Cotinine is an expression of the past 24 hours of exposure and is valuable mainly to exclude current smoking rather than estimating long term exposure to environmental tobacco smoke.

The study contributes to the existing literature reinforcing the conclusions of the IARC Monograph Working Group that there is sufficient evidence on the carcinogenicity of environmental tobacco smoke in humans.

Source: BMJ, Vol. 330, February 2005.

Effect of Environmental Tobacco Smoke on Levels of Urinary Hormone Markers

In many regions of the world, tobacco use is much more common among men than among women. In China, for example, 63% of men and only 3.8% of women are estimated to be smokers. Nevertheless, research has consistently shown that many women are exposed to environmental tobacco smoke (ETS), based both on self-reports and on biologic indicators of exposure. Thus, the effects of ETS on reproductive health are of major public health importance.

Many studies have shown that active smoking has adverse effects on a broad spectrum of reproductive outcomes, including fertility, time to pregnancy, spontaneous abortion, and birth weight. Active smoking has also been associated with menstrual disturbances. Some studies have suggested that smoking may reduce levels of estrogen and possibly progesterone, although results have been mixed.

The evidence regarding adverse effects of ETS on reproductive outcomes is less robust. Studies have shown that ETS in the absence of maternal smoking significantly reduced infant birth weight and increased risk of preterm birth. Studies of the effects of ETS on spontaneous abortion have been inconsistent.

Now a new study has been carried out to investigate the effect of ETS exposure on the levels of urinary pregnanediol-3-glucuronide (PdG; the

(Continued on page 5)

Effect of Environmental Tobacco Smoke on Levels of Urinary Hormone Markers

(Continued from page 4)

major metabolite of progesterone) and estrone conjugates (E_1C; the major metabolite of estrogen) in a cohort of women who participated in a reproductive health study in Anhui, China. These women were followed prospectively from the beginning of stopping contraception and attempting to conceive, through the end of pregnancy (or for up to 1 year without conception). The women provided daily diary records of vaginal bleeding and active and passive smoking and also submitted daily urinary specimens, which permitted researchers to accurately determine the onset of each menstrual cycle, the day of ovulation, and hormone levels specific to cycle day relative to ovulation. This was a homogenious cohort of young women, all of whom were newly married, nulliparous, and employed full time in the textile industry. Few of the women studied smoked cigarettes, but exposure to ETS was very high because of the high prevalence of smoking among their husbands. Few women used pills or hormone shots as contraceptive methods before entering the cohort. These characteristics provided a unique opportunity to study the adverse effects of ETS exposure on reproductive hormones while minimizing potential confounding factors.

The result of this prospective study indicated that ETS exposure in demographically homogeneous nonsmoking women was significantly decreased urinary E_1C levels throughout the nonconception menstrual cycles, suggesting that the adverse reproductive effect of ETS may act in part through its antiestrogen effects.

Source: Environmental Health Perspectives, Vol. 113, No. 4, April 2005.

SPECIAL ANNOUNCEMENT
GRADUATE DIPLOMA IN ENVIRONMENTAL TOXICOLOGY

This 12 month diploma course will be held by CRI from January 15, 2006 to January 10, 2007. It is sponsored by the Royal Thai Government under the Thai International Cooperation Programme (TICP) in collaboration with the Colombo Plan Secretariat.

Participants should fulfill the following criteria:

- Must hold a bachelor degree or equivalent in chemistry, biological sciences, medical sciences, environmental sciences or environmental engineering.
- Pass the English proficiency examination; TOFEL 500, IELTS 5.5 or equivalent.
- Age – under 50 years.
- At least two years of working experience in the related field.

The terms and conditions of fellowship awards are as follows:

1. A return air ticket on economy class from the closest international airport to Bangkok, THAILAND
2. Local training costs
3. Accommodation
4. An allowance of Baht 6,000 per month (Approximately US$160)
5. Book allowance

Applications are invited from Colombo Plan developing member countries.

Please note that nominations of up to 5 candidates should be made through Colombo Plan focal points by completing the Thailand-Colombo Plan Joint Training Application Form and medical certificate.

One set of nomination forms should be forwarded NOT LATER THAN SEPTEMBER 30, 2005 to the Colombo Plan Secretariat at the following address:

Secretary-General
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13th Floor, BoC Merchant Tower
28, St. Michael's Road
Colombo 3
SRI LANKA
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OCCUPATIONAL FENVALERATE EXPOSURE AND SPERMATOZOA DNA DAMAGE OF PESTICIDE FACTORY WORKERS

Pesticides have been used in developing nations to eradicate insect borne endemic diseases for food production and protection of forested plantations. Pesticide application has increased in recent years, resulting in more pesticide production. Nevertheless, several currently used pesticides especially those having endocrine disruptive properties, are known to adversely impair reproductive competence of males working in laboratories, fields, clinics, or factories. Pesticide factory workers have a higher exposure risk and are more prone to the damage made by pesticides. There have been few investigations of potential genotoxic effects in pesticide industry workers. In China, pesticide production is a year-round activity, and pesticide industry workers log in 40 hours a week. These workers have constant exposure to a variety of pesticides such as pyrethroids (fenvalerate). Organophosphorus compounds (phoxim), and carbamates (carbaryl). However, there have been few reports of genetic damage in occupational populations exposed to pesticides in China.

Fenvalerate (FE, 4-chloro-α-(1-methylethyl) benzeneacetic acid cyano (3-phenoxyphenyl) methyl ester) is a synthetic pyrethroid insecticide which is widely used for fruit and vegetable protection due to its strong neurotoxic activity for insects but low toxicities for mammals, birds, and plants. Evidence from general population exposure studies and *in vitro* studies suggest that FE is hormonally active. Reports from animal studies have shown that FE and testicular toxicity are associated. It is known that FE induces a significant reduction in testes weight, epididymal sperm count, sperm motility, and marker testicular enzymes for testosterone biosynthesis. This conclusion generated both public health and scientific concerns about potential reproductive effects of FE.

A lack of consensus on which semen quality tests are the best predictors of human male fecundity has led to the development of several new methods to evaluate semen quality. The traditional semen analysis focused on measurements for sperm concentration, motility, and morphology. Although these analyses may describe some aspects of the function of the testis and sperm, they do not address the integrity of the male genome contained in the sperm head. Alkaline single cell gel electrophoresis (SCGE) assay or Comet assay and terminal deoxynucleotidyl transferase mediated dUTP-biotin end labelling (TUNEL) assay have also been used to evaluate sperm DNA damage.

Comet assay is a visual fluorescent technique for measurement of DNA strand breaks in individual cells. The Comet assay was chosen as it gave detailed information on the quantitation of individual sperm DNA integrity. This method depends on unwinding of nuclear DNA under alkaline conditions, following electrophoresis that draws out the broken strands of DNA. These strands form a tail in one side of the sperm head nucleus that has been characterised as a “Comet”.

Now a new study carried out with volunteer subjects working in a pesticides factory in Changzhou city in southeast China conducts a risk assessment using both Comet and TUNEL assays to determine nuclear DNA integrity and the DNA fragmentation level of spermatozoa in FE exposed workers.

FE production workers were the exposed subjects in the study. Men from the office area of the same factory were used as internal controls. Volunteers recruited from different departments at the local board of health, which is located in the urban district of Changzhou city, were used as an external reference for comparison.

Based on the production process and environmental monitoring data, these workers were exposed to low levels of FE. A CD-1 air sampler (Beijing Detection Instrument Factory, Beijing, China) was used to detect the air concentration of FE at different areas of three groups for three days continuously. At the end of each work shift, an exposure assessment was conducted on three randomly selected subjects per day for three days. This assessment consisted of two components: individual sampling using active personal samplers (Xinyu Analysis Instrument Factory, Jiangsu, China); and measurement of dermal contamination by attaching fibrous filter membranes to 10 body areas. Monitoring indicated that the mean concentration of FE was 21.55 x 10^{-4} mg/m^3 at operation sites. The mean concentration of FE was 1.19 x 10^{-4} mg/m^3 at the internal control area and was not detected at the external control area. The concentration of FE in the workplace was significantly higher than concentrations in control areas ($p < 0.001$). Simultaneously, the concentrations of FE with individual sampling (mean concentration 0.11 mg/m^3) and dermal contamination (mean concentration 1.59 mg/m^2) detected in the FE exposure area were significantly higher than those in control areas ($p < 0.01$).

All semen samples from subjects were obtained by masturbation into sterile containers after abstinence from sexual activity for 3-5 days. After liquefaction at 37°C for 30 minutes, a routine semen analysis and sperm motility test were carried out by light microscopy and computer assisted sperm analysis (CASA) to provide details of sperm concentration and motility within 30 minutes. Sperm number was determined using a micro-cell slide. Sperm motility parameters were determined for sperm tracts: curvilinear velocity (VCL, μm/s; a measure of the total distance travelled by a given spermatozoon divided by the time elapsed); average path velocity (VAP, μm/s; the average velocity of sperm movement; spermatozoa were counted as exhibiting rapid progressive motility if VAP >25 μm/s); straight line velocity (VSL, μm/s; the straight line distance from beginning to end of a sperm track divided by the time taken); beat cross frequency (BCF, Hz; the frequency of the sperm head crossing the sperm average path); amplitude of lateral head displacement (ALH); straightness (STR, %); and linearity (LIN, %).

The results of the study indicated that occupational exposure to FE induced a significant increase in sperm DNA damage. Specifically, there was a significant positive association between FE exposure and percentage DNA in the tail, the olive tail moment (OTM), and positive sperm damage.

Biomonitoring studies of populations exposed to pesticides are rather specific because different populations have different lifestyles, nutritional habits, and climatic and environmental conditions, and are exposed to different pesticides. It is why some studies have found an increase in genetic damage in populations exposed to pesticides while other studies showed negative results. Since sperm DNA damage is an important step from spermatogenesis to malfunction such as infertility, the present study represents an important evaluation for the potential health risks associated with agrochemical exposure.

Source: Occupational and Environmental Medicine, Vol. 61, No. 12, December 2004.

INGESTED ARSENIC, CIGARETTE SMOKING, AND LUNG CANCER – A STUDY FROM TAIWAN

Residents of the southwestern and northeastern coasts of Taiwan had been drinking well water contaminated with a high concentration of arsenic before the establishment of the public tap water system. They were found to have an increased risk of cancers, including lung cancer. An earlier study followed up residents of the southwestern coast for 7 years and found a significant dose-response relationship between cumulative arsenic exposure and risk of lung cancer (relative risk [RR], 4.01; 95% confidence interval [CI], 1.00-16.12; for the highest level of arsenic exposure [≥20 mg/L per year) compared with unexposed residents. However, there were only 27 lung cancer cases identified; hence, the arsenic-exposed residents could only be divided into 3 groups.

Cigarette smoking has been found to be a major cause of lung cancer during the past 50 years, and it was estimated that quitting cigarette smoking may prevent more than 90% of lung cancers. A meta-analysis of studies on occupational arsenic exposure via inhalation found a synergistic effect of cigarette smoking and arsenic on lung cancer, and 30% to 54% of lung cancer cases were attributable to both exposures. A population-based case-control study reported an odds ratio (OR) of 32.0 (95% CI, 7.2-198.0) for cigarette smokers who had an ingested arsenic exposure level of 200 µg/L or higher compared with nonsmokers exposed to an arsenic level of less than 41µg/L. The OR was much higher than that for cigarette smoking alone (OR, 6.1; 95% CI, 1.3-39.2; for cigarette smokers compared with non-smokers) and elevated arsenic exposure alone (OR, 8.0; 95% CI, 1.7-52.3; for arsenic exposure of ≥200 µg/L compared with <49 µg/L).

Now, a new study has combined 2 study cohorts recruited from southwestern and northeastern Taiwan with 10591 residents who had been followed up for an average of 8 years in an effort to elucidate the dose-response relationship between ingested arsenic exposure and lung cancer risk. The larger number of study participants, longer period of follow-up with more incident lung cancer cases, and wider range of arsenic exposure levels provided researchers with a unique opportunity to further investigate the modifying effect of cigarette smoking on the association between ingested arsenic and lung cancer.

A total of 2503 residents in southwestern and 8088 in northeastern arseniasis-endemic areas of Taiwan were followed up for an average period of 8 years. Information on arsenic exposure, cigarette smoking, and other risk factors was collected at enrollment through standardized questionnaire interview, whereas the incident lung cancer cases were identified through linkage with a national cancer registry in Taiwan. The joint effect of arsenic and cigarette smoking was estimated by both etiologic fraction and synergy index.

The analysis of research findings confirms the earlier finding of an increased risk of lung cancer associated with increasing levels of arsenic exposure via drinking water. In addition, a significant dose-response trend in the finer categories was found. Although this study is an extension of the previous findings, the results are relevant and of general medical interest. Furthermore, this effect was found to be stronger among those who smoked cigarettes, and the risk could be as high as more than 10-fold.

The study provides evidence of a synergistic relationship between cigarette smoking and ingested arsenic on the risk of lung cancer. The reductions in cigarette smoking would likely reduce the lung cancer risk accompanied by exposure to arsenic, and similarly, reductions in arsenic exposure would reduce the lung cancer risk among cigarette smokers. Appropriate public health interventions, such as cigarette smoking cessation programs and reduction in arsenic concentration of drinking water, are warranted. Furthermore, it is essential to take cigarette smoking into consideration in the risk assessment and the determination of the maximal contamination level of arsenic in drinking water.

Source: JAMA, Vol. 292, No. 24, December 2004.

OXIDATIVE STRESS AND THE PROTECTIVE ACTION OF VITAMINS: A STUDY IN LEAD-TREATED SWISS MICE

Lead-induced oxidative stress is thought to play an important role in the pathogenesis of numerous degenerative diseases. Experimental evidence successfully relates this to lead-induced reactive oxygen species (ROS), which damage the cell causing pathological problems. ROS, in general, are capable of chemically altering all major classes of biomolecules like proteins, lipids, and nucleic acids. On the other hand, aerobic organisms including human beings have evolved a variety of mechanisms to protect themselves from the potential damaging effects of ROS which include enzymes such as catalase, peroxidase, superoxide dismutase, tripeptides like glutathione and a variety of water and lipid-soluble antioxidants like ascorbate (vitamin C) and α-tocopherol (vitamin E). It is generally believed that oxidative stress and damage affects the organism when the generation of ROS products exceeds the capacity of the cells to protect or repair themselves.

Starting from this hypothesis, a new study has been undertaken to assess the protective action of vitamins C and E against lead acetate-induced reduced sperm count and sperm abnormalities in Swiss mice.

(Continued on page 8)

Environmental Impacts of Stain Removers

Perfluorinated chemicals, widely used in stain removers in domestic cleaning agents, are increasingly causing concern because of the byproducts' ubiquitous presence and possible toxicity. Scientists are puzzled as to how a class of chemicals that isn't manufactured in large quantities and that cannot travel far has become so pervasive.

Fluorinated stain protectors consist of fluorinated surfactants chemically bound to polymers. The fluorinated surfactants work because their strong and rigid carbon-fluoride backbones act like tiny bristles to keep dirt, water, and grease off fabrics, carpets, and paper. Most surfactants don't travel in the environment. But their volatile precursors, fluorotelomer alcohols, travel and degrade into a class of chemicals, perfluorocarboxylates, that is extremely persistent. After a half-century of increasing use, the perfluorocarboxylates are showing up at growing levels in seals and polar bears roaming the Arctic as well as dolphins patrolling the mid-Atlantic.

Researchers from the University of Toronto, Canada, have developed a theory to explain both the diffusion and transport of volatile fluorotelomer alcohols, the chemicals used to make fluorosurfactants that sometimes serve as stain protectors themselves. The alcohols can be released into the air during surfactant manufacturing or the application of stain protectors. Domestic releases also occur. When telomer alcohols are the fluorosurfactant, they can be released if the bond between the surfactant and the polymer breaks through use or abrasion. They disperse and then break down to the indestructible perfluorocarboxylic acids found in arctic animals.

A growing number of scientists and industrial chemists now accept this explanation. However, given the widespread use and the domestic advantages of stain protectors, rather than imposing a blanket ban on the materials, many would like to see companies that make the products find ways to reduce their products' impact on the environment. Unless companies act quickly, there is a danger that government regulators could demand substitutes to perfluorocarboxylates whose impact on the environment is unknown and possibly worse than the fluorinated stain protectors currently produced.

Source: Science, Vol. 306, No. 5703, December 2004.

OXIDATIVE STRESS AND THE PROTECTIVE ACTION OF VITAMINS: A STUDY IN LEAD-TREATED SWISS MICE

(Continued from page 7)

Intraperitoneal injection of lead acetate (10 mg/kg body weight) in the present study stimulates lipid peroxidation in the testicular tissue, indicated by a significant increase in malondialdehyde content in the experimental mice group. This is associated with an increased generation of noxious ROS. Significantly reduced sperm count associated with increased percentage of sperm abnormality in the lead-injected mice group compared to controls substantially proves the ongoing damaging effects of lead-induced ROS on developing germ cells. However, intraperitoneal administration of vitamin C (Vit C) at a concentration equivalent to the human therapeutic dose (10 mg/kg body weight) was able to minimize significantly the testicular malondialdehyde content with a concomitant increase in sperm count and significant decrease in the percentage of abnormal sperm population. Vitamin E (Vit E) (100 mg/kg body weight) treatment of a batch of lead-injected mice had a similar effect as Vit C but with a comparatively lower efficacy. On the other hand, co-administration of both vitamins (Vit C + Vit E) at the above mentioned doses to lead-treated mice led to the most significant decline in malondialdehyde content along with elevated sperm count and reduction in the percentage of abnormal sperm population.

This result explicitly emphasizes that both vitamins appear to function most effectively when they are in concert. In fact, Vit C is widely known to restore and recycle the antioxidative properties of Vit E, when attacked by pro-oxidants. Such synergistic action of Vit C and E has been found under different experimental conditions and *in vivo*.

The study thus indicates the possibility of preventing lead-induced cytotoxicity in testes leading to male infertility by supplementation with vitamins C and E.

Source: Journal of Trace Elements in Medicine and Biology 18, March 2004.

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

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