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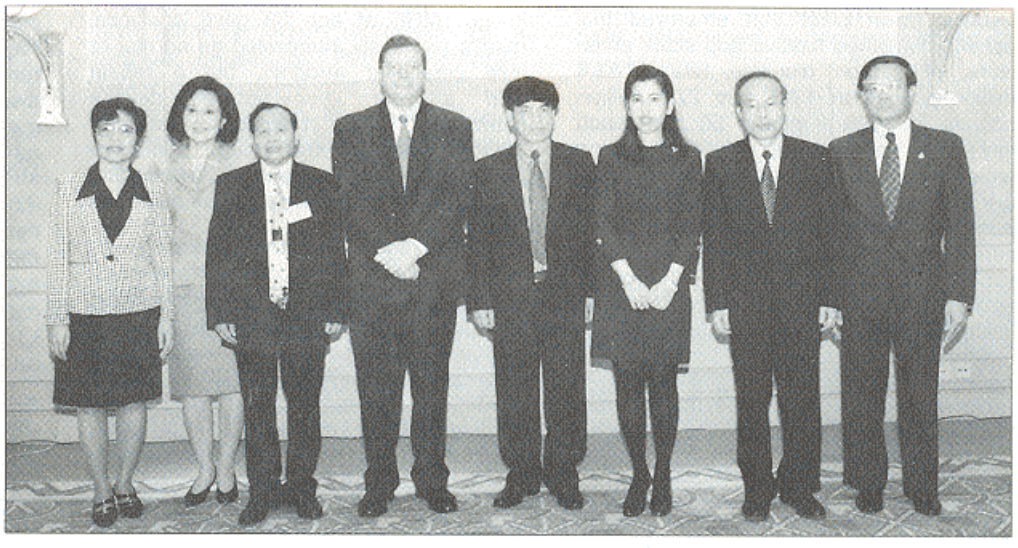
Chulabhorn Research Institute

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".

Princess Chulabhorn Opens Regional Training Courses in Vietnam



Her Royal Highness Princess Chulabhorn, President of the Chulabhorn Research Institute, opened training courses in Vietnam that are the first in the Institute's ongoing regional program of capacity building in environmental toxicology, technology and management for sustainable development to be organized outside Thailand.

An executive seminar and training course on Environmental Toxicology. Pollution Control and Management was organized in Hanoi from 9-20 November and in Ho Chi Minh City from 17-28 November 1998.

In her opening address at the Hanoi training course, Her Royal Highness stated that in the present era of globalization, individual countries need the economic leverage of regional cooperation and support in order to compete more effectively in the global market.

Vietnam and Thailand shared a similar experience in their rapid industrial development in recent years that had changed the traditional way of life and transformed the economic base of both countries.

The rapid industrial expansion that had taken place had led government agencies and industry to examine more critically the effect of this expansion on the environment.

Her Royal Highness emphasized that one area of particular and shared concern is the management of toxic waste and waste reutilization. It is in this area that human resource development is a critical factor since the current lack of trained personnel is a major problem that hampers sustainable industrial development.

Carbon Disulfide Exposure in the Workplace

A wide range of toxic effects from carbon disulfide, including cardiovascular, ocular and reproductive effects have been recognized for over a century. However, the nervous system is the principal target organ of carbon disulfide.

Pathological findings in humans following carbon disulfide exposure have only rarely been reported. They include neuronal degeneration diffusely over the cerebral cortex, globus pallidus, and putamen, and a decrease in Purkinje cells in the cerebellar cortex.

Carbon disulfide exposure is primarily a workplace concern, and ambient environmental exposures are ordinarily low. However, ambient environmental exposures may occur. In 1996, 137 facilities in the United States reported carbon disulfide emissions to the EPA Toxics Release Inventory. At the viscose rayon plant that employed this patient, combined fugitive and stack emissions of carbon disulfide totaled 33.4 million pounds in 1995 and 27.7 million pounds in 1996 – nearly 50 tons each day. In addition to these ongoing emissions, acute releases of carbon disulfide during transport remain a possibility. There is at least one report of cerebral damage following a single exposure to carbon disulfide. Therefore, environmental exposure to carbon disulfide, although rare, remains a concern.

A recent case presentation has been published of a patient who had been employed from age 25 to age 59 in a plant that produced viscose rayon. During most of this period the operant had worked in the spinning room. Although measured air levels of carbon disulfide from this plant were not available, the spinning room has been reported to pose some of the highest carbon disulfide levels in rayon manufacture, ranging from 10 to 20 ppm and sometimes reaching 30 ppm or higher.

The patient first presented at approximately 60 years of age with slowly progressive balance problems, impotence, irritability, and emotional lability. His balance and coordination worsened until, by age 62, he had difficulty with walking, manual dexterity, and speech. He also noted severe nightmares. There were no tremors, no changes in facial expression, no cogwheel rigidity, no bradykinesia, and no impairment of hearing or vision. A magnetic resonance image (MRI) at age 63 gave equivocal results (variously interpreted as normal or mild cerebellar atrophy), but a repeat MRI a year later showed definite cerebellar and brainstem atrophy. Thyroid function, urinary lead and mercury levels, serum vitamin B_{12} levels, and electroencephalography were normal.

At age 64, the patient was evaluated by a neurologist. Blood pressure was 160/80 without orthostatic changes; speech was slightly slurred; cognition and affect were generally intact; and cranial nerve function was normal. Motor examination revealed normal strength without involuntary movements, but with rippling movements of large muscles in the chest and lower extremities. There were impairments of finger-to-nose, heel-knee-shin, and rapid alternating movements. The patient was unable to tandem walk and was unstable when standing with his feet close together, even with his eyes open. Deep tendon reflexes were normal, and no pathological reflexes were present. A computed tomography (CT) scan showed atrophy of the cerebella and pontine regions. He was diagnosed with olivopontocerebellar atrophy of the sporadic type.

In the next few years, the patient experienced progressive deterioration in function. Dysphagia, dysarthria, and ataxia increased. By age 67 he had become unable to walk and had little functional independence. He also suffered multiple medical complications including rectal bleeding, neurogenic bladder with chronic urinary infections requiring intermittent catheterization, a fungal infection of the mouth, peptic ulcer disease, bronchitis with dysphagia, gynecomastia (probably secondary to ranitidine use), and hiccups. A repeat MRI of the brain at age 68 showed advanced cerebellar atrophy and prominent atrophy in the posterior tracts and nuclei of the pons. The patient died at the age of 69. No autopsy was performed.

Source: Environmental Health Perspective, Vol. 106, No. 9, September 1998.

Neurotoxicity of Carbon Disulfide

A team of researchers from the National Institute of Environmental Health Sciences (NIEHS) in collaboration with scientists from the US Environmental Protection Agency (EPA), Duke University Medical Center and the University of North Carolina at Chapel Hill have completed studies on the neurotoxicity of carbon disulfide (CS_2) that are unique in their comprehensive examination of the biochemical, functional and structural changes to the nervous system resulting from exposure to CS_2.

The compound has long been used as a solvent in a number of industrial processes including the cold vulcanization of rubber and the production of rayon and cellophane from wood fiber.

While rayon plant workers are at direct risk of exposure to CS_2, other populations may be exposed through indirect means. Dithiocarbamates and their disulfides, chemicals that are widely used in pesticides and as therapeutic agents for conditions including cancer and drug addiction, can liberate CS_2 upon decomposition within the body. Thus, people who apply pesticides or harvest produce sprayed with pesticides, as well as persons consuming therapeutics such as disulfiram (Antabuse), may also be exposed to CS_2.

The major route of human exposure to CS_2 is inhalation. Absorbed CS_2 is taken up by the blood and distributed throughout the body. Acute exposure to high concentration of CS_2 may result in euphoria, hallucinations, irritability, manic delirium, and convulsions. Prolonged exposure to low concentrations of CS_2 in air can damage both the structural and functional integrity of nerves, particularly affecting long, large-diameter, myelinated axons in both the central and peripheral nervous system.

The NIEHS studies were designed to assess multiple biological end points at various time periods of subchronic exposure.

Researchers used Fischer 344 rats, a strain used in previous CS_2 inhalation studies. Rats were exposed to either 0, 50, 500 or 800 parts per million (ppm) CS_2 for 6 hours per day, 5 days per week for 2, 4, 8 or 13 weeks.

One of the prerequisites for characterizing the toxicity of any compound is to understand how the compound is taken up by the body and either retained or eliminated. The concentration and duration of exposure and the number of previous days of exposure to the compound all can affect the amount that is actually retained. To evaluate the relationship between measures of the inhalation exposure to CS_2 and the toxicologic response and biomarkers of exposure, the research team performed three separate studies characterizing CS_2 kinetics in the test animals.

(Continued on page 8)

Parkinsonism Associated with Occupational Exposure to Lead-Sulfate Batteries

Epidemiologic studies support the hypothesis that environmental toxins may cause Parkinson's disease (PD).

A recent study examined case reports of nine postal workers exposed to lead-sulfate batteries (LSB) over a period of up to 30 years.

On a daily basis, the postal workers cleaned lead-sulfate batteries used for the operation of battery-powered wagons. Seven of the nine workers in the study developed parkinsonian symptoms. One of the remaining two workers showed left-hand bradykinesia, and one was not available for examination.

A typical case history of the patients who developed parkinsonian symptoms is as follows:

"This 63-year-old man was exposed to LSB for 12 years. The diagnosis of PD was made 17 years after his last contact with LSB. He reported deterioration in his ability to walk, freezing phenomenon, short-term memory impairment, and depression, as well as diffuse vertigo. Symptoms such as hypomimia, hypophonia, reduced arm swing, bradydiadochokinesia, lateroflexion of the body, rigidity of all extremities, and resting tremor were found. He presented this parkinsonian symptomatology bilaterally, more evident on the right side (Hoehn and Yahr stage III). He responded to parkinsonian pharmacotherapy consisting of the combination of levodopa/benserazide, bromocriptine, selegiline, and bornaprine. Signs of polyneuropathy were hyporeflexia and pallanesthesia of the lower extremities".

The high prevalence and cause of parkinsonism in the nine patients studied remains unexplained. Lead intoxication may play a role in the occurrence of parkinsonian symptoms, but the involvement of sulfate and other sulfur compounds must also be considered. In the case of lead or lead compounds, major routes of absorption are via the gastrointestinal tract and respiratory system. Chronic lead intoxication of the nervous system induces neuropathy, tremor, meningitis, gliosis, and behavioral changes, notably depression.

Laboratory data of the patients investigated in the present study neither proved nor excluded lead poisoning as the cause of parkinsonism because of the time lapse between onset of exposure and the data collection.

In the case of sulfur compounds, sulfuric acid and hydrogen sulfide have already been identified as a putative cause of PD. Hydrogen sulfide may emerge and be inhaled as a gas from rubber components used in LSB. Hydrogen sulfide inhibits mitochondrial electron transport and cerebral cytochrome oxidase activity, which may result in polyneuritis and encephalopathy. Reduced metabolization of sulfur via oxidation or thiol methyltransferase activity, or both, has been described in relation to PD. Gene polymorphisms, as in the case of thiol methyltransferase, may play a role and may be responsible for reduced activity of detoxification enzymes.

Based on the present findings, it is possible that chronic low-dose exposure to environmental toxins, in this case lead or sulfur compounds, or both, may increase the risk of PD, especially in subjects with a genetically determined hypersusceptibility to xenobiotics.

Source: Neurology, Vol. 50, No. 6, June 1998.

ANTIPLATELET ACTIVITY OF GINKGO BILOBA

Ginkgo biloba is a herbal medication which is marketed as a supplement to improve mental alertness. Although there is some evidence to support the efficacy of the extract in the medical treatment of cognitive impairment, this has not been extensively substantiated. However, the extract is a potent inhibitor of platelet-activating factor, and long-term use has been associated with increased bleeding time, spontaneous hemorrhage, and subdural hematomas.

There have been a number of published reports of a possible hemorrhagic complication of the herbal medication. Reported case studies of patients with spontaneous bilateral subdural hematomas occurring coincidentally with long-term *Ginkgo biloba* ingestion suggest a possible clinically relevant antiplatelet effect of the extract.

However, it should be noted that in a recent placebo-controlled randomized trial of *Ginkgo biloba* extract for the treatment of dementia that involved 309 patients, the one incident of subdural hematomas that occurred was in the placebo group.

Further medical investigations are needed before a potential pathogenic connection can be established

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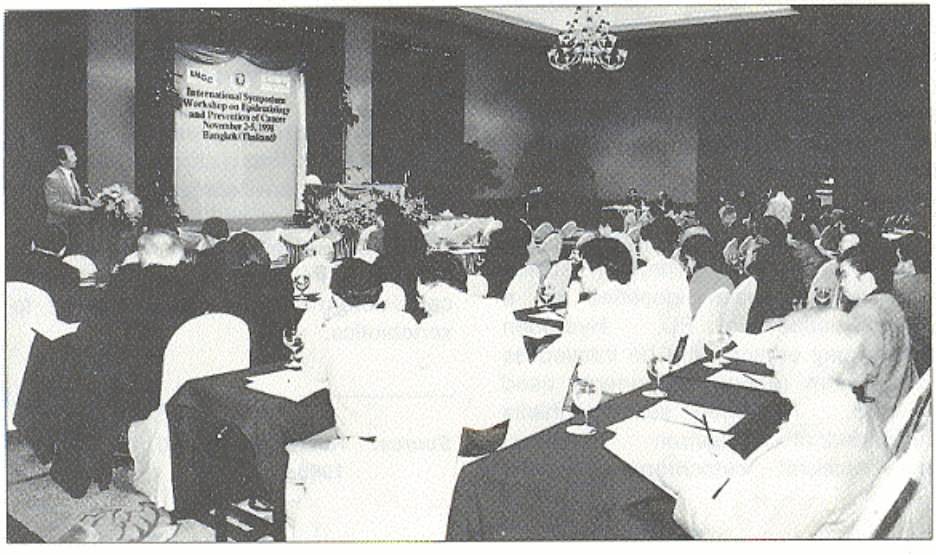
Source: The Lancet, Vol. 352, July 1998.

CRI Hosts International Symposium and Workshop on Epidemiology and Prevention of Cancer

From 2 to 5 November 1998, the Chulabhorn Research Institute (CRI) co-sponsored a symposium and workshop with the Fritz-Bender Foundation and the International Union Against Cancer (UICC).



In her opening address to the symposium, Her Royal Highness Princess Chulabhorn recalled the highly successful sixteenth UICC training course in Cancer Research that the Chulabhorn Research Institute organized jointly with the International Union Against Cancer in January 1995.

Such events provided opportunities for scientists from Thailand and other countries in the region to benefit from the most recent and advanced developments in cancer research.

With regard to the four day seminar and workshop on Epidemiology and Prevention of Cancer, Her Royal Highness stated that the field of preventative oncology, the subject of the symposium, was one in which, at both national and regional levels, there was a serious shortage of qualified scientists and physicians. An important goal of the symposium was therefore the promotion of exchange of knowledge and dissemination of information to stimulate research and training in countries in Asia and the Pacific. Her Royal Highness stated that the workshop to follow the symposium provided an important opportunity for young scientists and medical practitioners from the region to increase their knowledge of concepts and strategies in cancer prevention and to gain experience of the new techniques used in the most scientifically advanced countries.

The scientific program of the three day symposium focused on the areas of Molecular Epidemiology, Population Studies, Pre-ventive Agents, Chemoprevention and Clinical Intervention Studies and the one day workshop comprised presentations on the following topics:

- Etiology and prevention of liver cancer. Studies in China
- Chemoprevention targeting high risk population
- Primary prevention and secondary prevention of cancer
- Chemoprevention: Laboratory studies
- Prevention of pulmonary metastasis
- Population-based cancer registry
- Cervical cancer: Field applications
- Population studies: Requirement and limitations
- Clinical chemoprevention studies: Protocol designs and requirement

The symposium attracted a total of 227 participants.

Hair Mercury Levels of Randomly Selected Populations in Coastal and Inland Areas in China, Indonesia and Japan

Concerns over the high toxicity and ubiquitous nature of environmental mercury contamination have been voiced for the last two decades. A number of studies have focused mainly on the presence of elevated mercury levels in seafood, especially fish, a major human dietary source of mercury. (Three related studies were reported in the October 1998 issue of this Newsletter)

People accumulate mercury in their bodies both via absorption of mercury from their diets and from air in their local environments.

Mercury and its compounds occur naturally in the environment, but their use in industry and their release into the atmosphere via the burning of fossil fuels and the processing of ores can increase levels in the ambient environment. Whereas dietary intake of mercury results mainly from the consumption of fish, occupational exposure is, for the most part, the result of exposure to elemental mercury vapor. Some examples of vulnerable occupations are workers in the chemical industries, pesticide preparers, dentists, dental amalgam filling makers, workers in the chloralkali industry, metal-refining and fluorescent-tube factories, and thermometer manufacturers.

In order to assess the effect of different routes of mercury intake in human populations, a recent study conducted by researchers from the School of Medicine at Tokushima University in Japan used gold-amalgamation cold-vapor atomic spectrometry and ECD-gas chromatography to analyze total mercury and methylmercury levels in hair samples obtained from a population of 362 residents in Harbin, China; Medan, Indonesia; and Tokushima, Japan. In this study, the researchers initially questioned whether mercury levels in hair differed among different study areas, and if there were differences, they questioned the contributing factors. In the three countries surveyed, total mercury and methylmercury levels in hair were lowest in residents of China and were highest in residents of Japan. In the district of Tokushima, Japan, total mercury and methylmercury levels were highest in the coastal district, followed by the middle district; the lowest levels occurred in the mountainous district. In Japan, an individual's total mercury level correlated very closely with that person's methylmercury level; in China and Indonesia, the correlation between these two parameters was low. No subjects in China or Indonesia had high levels of methylmercury in hair; this was true even if their total mercury levels were high. This finding suggests that the high total mercury levels observed in some residents of China and Indonesia reflected exposure to inorganic mercury.

Medan, the fourth largest city in Indonesia, is an important industrial center that includes an oil field. The major industries in Medan are chemical factories, which produce urea-based fertilizers and petrochemicals. Harbin, which is located in northeast China, is also an important industrial city. High total mercury levels (note: methylmercury levels were not high) from the hair of some subjects in Harbin and Medan have resulted from increased exposure to inorganic mercury that results from occupational or environmental sources; however the occupations of these subjects were not identified in the study.

In Japan, mercury (especially methylmercury) levels in hair samples were quite high. Fish and shellfish, caught in seas uncontaminated by human activity, appeared to be major sources of the high levels of hair mercury in Japanese subjects.

The results highlight the necessity of considering regional characteristics (including regional differences in diet) when hair samples are used in the biological monitoring of mercury.

Source: Archives of Environmental Health, Vol. 53, No. 1, January/February 1998.

Experimental Strategies in Gene Repair

An experimental gene repair technique has been developed by researchers at Thomas Jefferson University, Philadelphia, which corrects a single alteration in a gene responsible for skin color in mice.

In albino mice a defective gene fails to produce an enzyme involved in making melanin, the agent which changes the color of skin.

Researchers have developed strategies to correct point mutations using chimeric oligonucleotides composed of RNA and DNA. Melanocytes from albino mice contain a homozygous point mutation in the typosinase gene. Tyrosinase is a key enzyme for melanin synthesis and pigmentation. Correction of this point mutation results in the restoration of tyrosinase activity and melanin synthesis, thus changing the pigmentation of the cells.

Once the mutation is corrected, it takes five or six days for the entire biochemical process to begin producing melanin. The researchers established that the gene correction was permanent and inheritable. The actual mechanism of a specific change in DNA sequence remains to be determined. However, it is plausible that it involves the recombination and DNA repair process. The work thus holds promise for some sufferers of hereditary diseases caused by genetic mutation.

Source: Nature Biotechnology, Vol. 16, December 1998.

Effects of Endocrine Disruptors on the Development of the Reproductive System

Endocrine disruptors are environmental chemicals that alter gene activity during sensitive developmental periods when cell differentiation is occurring, and irreversibly disrupt the functioning of exposed cells.

Alteration of the developmental program can occur as a result of even slight changes in the concentrations of endocrine signaling molecules that are available to bind receptors in target cells. This disruption of the normal developmental program can lead to irreversible changes in the functioning of organ systems throughout the remainder of life.

There are critical life stages during which exposure to endocrine disruptors is most likely to alter the course of development, thus leading to lifetime changes in the functioning of organs. During critical developmental periods in organogenesis, regardless of whether an endocrine disruptor acts an agonist or antagonist after binding to receptors for endogenous signaling molecules, there will be a unique biological response that will not be observed when these receptors are not occupied by the endocrine disruptor. There may also be unique responses observed due to exposure to combinations of chemicals that are not observed when the chemicals are present individually.

The best characterized endocrine-disrupting chemicals are those able to bind to estrogen receptors and act as either estrogen agonists or antagonists. One such chemical, bisphenol A [4, 4'-(1-methylethylidene) bisphenol] is one of the top 50 chemicals produced in the USA, where yearly production is over 1.6 billion pounds. Bisphenol A is the monomer used in the manufacture of the resin used to line food and drink cans and is the monomer from which polycarbonate plastic is made. Bisphenol A is also a component of plastic used in dental fillings, which are often used to protect teeth in children. Bisphenol A has been reported to be released from the resins used to coat the interior of food cans when the cans are autoclaved; in commercial practice cans are autoclaved after the addition of the food. In another study, when MCF-7 breast cancer cells were grown in media prepared with water autoclaved in polycarbonate flasks, the cells began proliferating and progesterone receptors were induced. This finding demonstrated a significant estrogenic response to amounts of bisphenol A released during autoclaving of plastic made with bisphenol A. Another environmental estrogen is octylphenol [(1, 1, 3, 3-tetramethylbutyl) phenol], which is an industrial additive used in a wide variety of detergents and plastics. Octylphenol has been reported to have estrogenic activity in both *in vitro* and *in vivo* studies.

A recently published experimental research study has taken a physiologically based approach to the study of bisphenola A and other estrogenic chemicals on the size of reproductive organs, daily sperm production, and behaviour.

The experiment examined the effects on development of reproductive organs in male mice as a result of fetal exposure to environmentally relevant doses of bisphenol A and octylphenol.

From gestation day 11-17 female mice were fed an average concentration (dissolved in oil) of bisphenol A or octylphenol of 2 ng/g body weight (2 ppb) and 20 ng/g (20 ppb). The 2 ppb dose of bisphenol A is lower than the amount reported to be swallowed during the first hour after application of a plastic dental sealant (up to 931ug; 13.3 ppb in a 70 kg adult). It was found that the 2 ng/g dose of bisphenol A permanently increased the size of the preputial glands, but reduced the size of the epididymides; these organs develop from different embryonic tissues. At 20 ng/g, bisphenol A significantly decreased efficiency of sperm production (daily sperm production per g testis) by 20% relative to control males. The only significant effect of octylphenol was a reduction in daily sperm production and efficiency of sperm production at the 2 ng/g dose.

The findings of the study suggest that an alteration in the course of development of reproductive organs could also occur in human fetuses carried by pregnant women who consume amounts of bisphenol A found in canned food products or foods heated in polycarbonate containers.

Since as much as 931 µg of bisphenol A migrates out of plastic dental sealant during the first hour after application, this suggests that women may be placing their fetuses at risk by having dental sealant applied during pregnancy.

Whether other chemicals in dental sealants, such as bis-GMA, have estrogenic activity after being swallowed, similar to bisphenol A dimethacrylate, is unknown. Also, whether these other chemicals can be metabolized to bisphenol A or other estrogenic metabolites after ingestion requires further investigation

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Source: Toxicology and Industrial Health, Vol. 14, Nos. 1/2, 1998.

Third-Generation Victims of Toxic Pesticides

Medical researchers in Vietnam are collecting evidence of a suspected link between the use of toxic pesticides, in particular Agent Orange, sprayed over areas of the country by the US Air Force between 1968 and 1972 during the Vietnam War and congenital deformities in the children and grand children of the exposed population.

Agent Orange is a mixture of the herbicides 2,4-D and 2,4,5-T. Both chemicals mimic plant hormones and upset the metabolism of growing plants. Concern about the formulation centred largely on the presence of dioxin, or 2,3,7,8-TCDD, an unwanted by-product in the manufacture of 2,4,5-T and one of the most poisonous substances known to science.

Dioxin is strongly suspected of being a human carcinogen, linked with both soft-tissue sarcomas and non-Hodgkin's lymphomas. It is also known to disrupt the body's hormonal, reproductive and immune systems in a variety of ways. Animal studies have shown that it can feminise males and cause birth defects in their offspring. But the biggest concern is that the damage appears to extend to the human reproductive system, causing fathers to produce damaged sperm.

There is currently no evidence that dioxin damages DNA and so causes mutations. So if it is causing second and third-generation birth deformities, the likelihood is that they are congenital, caused by either the continuing presence of dioxin in the environment and human tissue, or lingering effects on the father's or mother's hormonal system.

Appalling second-generation birth defects among the children of veterans exposed during the war to Agent Orange and other pesticides have been well documented. Common symptoms are limbs twisted in a characteristic way or missing altogether, and eyes without pupils.

A study of the families of some 1900 veterans, graded according to whether and for how long they had served in areas subjected to spraying revealed that of the 8000 children born to this population, the proportion with defects rose from 1.1 per cent born to veterans with no known exposure, to 1.9 per cent for light exposure, 2.2 per cent for moderate exposure and 5.1 per cent for high exposure.

Further research is needed to scientifically establish the suspected link between grand parents' exposure to Agent Orange and congenital deformity in their grand children. For this, more sophisticated tests are needed.

Source: New Scientist, No. 2154, October 1998.

Enzyme-catalysed Degradation of Nerve Agents

The decontamination of large areas exposed to chemical weapons such as nerve agents is generally carried out with bleach treatment or incineration resulting in severe environmental consequences. However, now researchers in the United States have developed enzyme-containing foams that are a more environmentally friendly alternative to current decontamination solutions, many of which are non specific in their action and contain significant amounts of hazardous organic solvents.

The newly developed foams incorporate organophosphorus hydrolase (OPH), an enzyme that hydrolyses nerve agents, into aqueous fire-fighting foams to catalyse surface decontamination over wide expanses of affected land area.

Although agent specificity limitations remain, enzyme-catalysed degradation of nerve agents has been demonstrated, with the most widely studied enzyme being the broad-spectrum OPH. Contaminated surfaces can be treated with aqueous OPH solutions, but the free enzyme in aqueous solution is not sufficiently stable or easy to deliver for wide-area decontamination. Surface decontamination methods may be complicated by the agent becoming more volatile, and by the difficulty of extracting agents from surfaces. When OPH is integrated into fire-fighting foam, however, volatilization is minimized and agents can be extracted from surfaces into the surfactant-containing foam.

The primary limitation of the enzymatic bioremediation of chemical weapons lies in the strict specificity of a given enzyme for a particular substrate. This issue is being addressed by the production of foams with several enzymes of varying specificity. Such multicomponent enzyme foams will provide a safe, environmentally acceptable means of performing wide-area decontamination of nerve agents.

Source: Nature, Vol 395, September 1998.

Neurotoxicity of Carbon Disulfide

(Continued from page 2)

A single exposure inhalation study was conducted to investigate the uptake and elimination kinetics of CS_2. A single-exposure characterized the plateau of CS_2 blood levels and 2-thiothiazolidine-4-carboxylic acid (TTCA) excretion.

The studies found that, at the concentrations tested (50, 500 and 800 ppm), there is not a linear dose-response relationship between the amount of CS_2 inhaled and either blood CS_2 concentration or urinary TTCA excretion. Both blood CS_2 and urinary TTCA became saturated at these higher levels. Thus, these measures appear to be useful only as indictors of exposure to relatively low levels of CS_2 exposure and short exposure time frames.

One of the most widely reported findings in people and animals exposed to CS_2 is neurotoxicity in the central and peripheral nervous system. Yet few studies have fully examined the morphologic progression, biology, and mechanism of CS_2 induced neurotoxicity. Therefore, the researchers conducted a study to examine the progression and dose response of CS_2 distal axonopathy by light and electron microscopy and in teased nerve fiber preparations. They then correlated these observations with other biologic and mechanistic findings using inhalation studies.

The study revealed that both behavioral changes and biochemical effects, such as cross-linking of hemoglobin and neurofilament proteins, and increases in NGF-R mRNA expression occur prior to axonal swelling. The study illustrates that the detection of neurotoxic effects prior to morphologic changes can be used to discern potential neurotoxicity and mechanisms of toxicity.

The EPA anticipates using the data from the CS_2 studies in the development and refinement of mechanistically based quantitative human health risk assessments for chemicals listed in the Clean Air Act.

Source: Environmental Health Perspectives, Vol. 106, No. 9, September 1998.

ANNOUNCEMENT

CRI Project: Capacity Building in Environmental Toxicology and Management to Promote Sustainable Development in Asia and the Pacific

Work Plan - 1999

Date	Course	City/Country	Registration Fee
May 10-15	Practical Training Course on Detection of Environmental Pollutants and Monitoring of Health Effects	Hanoi/ Vietnam	N/A
August 16	Executive Seminar on Environmental Toxicology	Bangkok/ Thailand	US$ 150
August 16-28	Training course on Environmental Toxicology, Pollution Control and Management	Bangkok/ Thailand	US$ 1350
November 28-December 2	The Fourth Princess Chulabhorn Science Congress: Chemicals in the 21st Century	Bangkok/ Thailand	US$ 350
December 6-10	Training Workshop on Risk Assessment & Management in Biotechnology	Bangkok/ Thailand	US$ 400

Note: Accommodation and living expenses not included. (These should be calculated at a minimum of US$ 80/day)

Post-Chernobyl Cancer Incidence

Although many experts claim that the only significant health effect linked to fallout from the accident at the Chernobyl nuclear plant in 1986 has been the increase by a factor of 200 in the number of people contracting thyroid cancer, local researchers claim that during this period radiation induced conditions and tumors other than thyroid cancer have increased significantly in the former Soviet republic of Belarus.

An international conference on Chernobyl held in Vienna in 1996 concluded that there was no consistent increase either in the rate of leukemia or in the incidence of any other malignancies other than thyroid cancer attributable to the nuclear accident.

However, researchers from the Institute of Genetics and Cytology of the Academy of Science in Minsk, Belarus, have now reanalysed data on the incidence of congenital conditions collected in 1996 and have found that since 1985, the number of reported cases of congenital malformations in children has increased by 83 per cent in areas contaminated by fallout from Chernobyl, by 30 per cent in mildly contaminated areas and by 24 per cent in what have been classed as clean areas.

It is claimed that the congenital conditions recorded that include cleft palate, Down's syndrome and deformation of lumps and organs are a consequence of radiation damage, since pollution from toxic chemicals, another possible cause, has fallen significantly in the area of study over the past 10 years.

However, scientists responsible for the declaration of the Vienna conference remain skeptical, claiming that the data mainly reflects improvement in the registration of abnormalities in recent years, which could lead to the observed increases.

Source: New Scientist No. 2155, October 1998.

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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