CRI/ICEIT
NEWSLETTER

VOL. 8 NO. 3 – July 1998
ISSN 0858-2793
BANGKOK, THAILAND

Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

CRI Organizes Workshop on "Environmental Biotechnology: Research and Applications for Sustainable Development"

Chulabhorn Research Institute (CRI) initiated the UNDP supported Regional Program in Capacity Building in Environmental Toxicology, Technology and Management to Promote Sustainable Development in Asia and the Pacific with a regional workshop that was opened by Her Royal Highness Princess Chulabhorn, President of CRI, on 24 June 1998.

The six day workshop was attended by 53 participants from 10 countries.

In opening the workshop, Her Royal Highness Princess Chulabhorn stated that the essentially practical emphasis of this training course exemplified the importance that the Chulabhorn Research Institute places on human resource development as a necessary basis for progress in all areas of scientific and technological activity. With the benefit of such resource development, countries in the Southeast Asia region will be able to meet the challenges of changing economic conditions and establish a sound framework for sustainable development. In her opening speech, Her Royal Highness Princess Chulabhorn thanked the Japanese government and the German government for the generous support provided to CRI in the form of scientific equipment essential for the organization of a hands-on training course for a large number of participants.

The workshop program comprised 17 lectures and 19 experiments providing opportunity for hands-on experience to ensure the maximum practical benefit to all participants.

HEALTH IMPLICATIONS OF SILICA IN THE BUILT ENVIRONMENT

In 1997 the International Agency for Research on Cancer (IARC) in Lyon issued an opinion that "there is sufficient evidence in humans for the carcinogenicity of inhaled crystalline silica in the form of quartz or cristobalite from occupational sources". The implications of this are potentially far reaching since, quite apart from those who are occupationally exposed to silica, we all live on a silicaceous planet and live and work in buildings which are, in many cases, high in silica, and we are generally surrounded by the material.

A Special Report by

Dr. G B Leslie and
Dr. J A Hoskins

International Society of the Built Environment (ISBE)

For a great many years there has been debate over whether respirable silica can cause lung cancer. Some have argued that lung cancer only occurs in the presence of silicosis while others say that pre-existing disease is not necessary for the formation of a tumour. Certainly it is well established that the risk of lung cancer in those with silicosis is more than double that of those without the disease. Recently (June 15th 1998) the International Society of the Built Environment organised an international seminar[4] at the Royal Institution in London which brought together leading experts on this subject. This seminar set out to explore the breadth of the problem by considering an economic evaluation of silica and its products, the presentation of its role in so much of our built environment, epidemiological studies including the very difficult problem of confounders and a vision of the way problems such as this might be studied in the future by computer modelling.

There is no doubt that sufficient respirable silica particles in the lung will cause disease. There are many historical references and the opening speaker at the seminar, Professor Bob Brown, talked about some well documented examples. He explained how mechanistic studies in the laboratory show that if silica is a direct causative agent for cancer it does not act like 'normal' carcinogens. There are many anomalies such as the fact that devitrified mineral wool which contains some 28% of cristobalite, said to be a more dangerous polymorph than quartz, does not cause cancer in experimental animals. If, through good occupational hygiene, we prevent future cases of silicosis, will we see any more cases of lung cancer caused by exposure to silica?

Silica is a vital part of our world. Its economic importance is incalculable. Several speakers from industry gave talks on what silica is, where it comes from, what it is used for and how over-reaction and wrong reaction to the IARC evaluation could financially damage us all. The first such speaker was Dr Martin Moore who presented the background on crystalline silica, discussed its polymorphs and pointed out that it was ubiquitous. He also introduced one of the key points of the proceedings which was that pure silica is rare and most silica is modified both by cations and by water. This seems to have a significant effect on its biological interactions and was a point several speakers returned to throughout the day.

Not only do we live with silica, it is part of the air we breathe. Away from civilisation in the so-called remote continental air, there are some 300,000,000 particles.m-3 in the size range from 0.1 to 0.01 mm diameter. This can be translated into a mass of 0.4 mg.m-3 of which some 10% is crystalline silica.

The scale of silica usage is huge. In the UK about 150 million tonnes of aggregate and crushed rock are used annually. The excavation of the raw materials and production of the final products of commerce have their own problems. The purest form of silica is sand. The most important product produced from this in the UK is glass which accounts for about 2 – 2.5 million tonnes. Foundries use 1 – 1.5 million tonnes and many other industries, particularly the ceramic industry, use large quantities as well. Occupational exposure does not come just from industry involved directly with silica. For example, to obtain many other minerals (eg. bauxite), silica containing over-burden has to be removed to expose the ore.

Professor David Goldsmith explained how IARC classifies materials and how their evaluations have produced regulatory concerns and affected the thought processes of regulators. As a Californian, he had to discuss an important piece of legislation from that State. Proposal 65 says that if a product causes a biological response such as cancer it has to be labelled and those who use it must be made aware of its carcinogenic property. It has to be remembered that risk assessment by legislators involves both cancer and non-cancer health effects.

Professor Ken Donaldson discussed the toxicity of quartz and how it is affected by any admixture such as may occur in coal dust. He considered the fundamental problem of how particles damage the lung. This organ is well adapted to dealing with particles through the employment of the muco-ciliary escalator in the ciliated regions and the action of alveolar macrophages in the deep lung. However, there is still the fundamental problem of how quartz causes injury in spite of these protective devices and why it behaves differently from other types of particles. In time such mechanistic studies may well define a plausible theory for particle induced carcinogenesis.

Professor J Corbett McDonald, who was a member of the IARC evaluation panel, talked about the decision process which led to the evaluation and noted that it was not a unanimous decision. During their deliberations the panel were not allowed to discuss any conclusion from registered silicotics. These people have a substantially increased risk of lung cancer. They concentrated on the studies with the least confounding from various occupational groups. The SMRs for these groups were generally

(Continued on page 8)

Impairment of the Central Nervous System Resulting from Occupational Exposure to Lead

Researchers from the Finnish Institute of Occupational Health have carried out a study to evaluate the neuropsychological effects of current low level and previous higher levels of exposure to lead in the workplace in order to assess the relation between effects of lead and bone lead.

In a previous study, the content of lead in tibial bone was studied among 87 workers from two small lead acid battery factories. For the present study, 30 of these workers with a low tibial lead content and 30 with a high concentration were invited to participate, and all accepted the invitation. Both plants were situated in a suburb of Helsinki and had similar working conditions. Absence of any central nervous system illness or handicap, excessive alcohol consumption, and previous neurotoxic exposures were verified by both a questionnaire and a neurological interview.

The group consisted of both men and women. The mean age of the group was 43 years for the men and 48 years for the women.

Exposure assessment was based on statutory, regular blood lead (BPb) levels covering the total exposure period.

Among the people studied, BPb values over 2.4 µmol (which has been the statutory limit in Finland since June 1985) had been common in the past, but non-existant in recent years. For the subjects in the low blood lead level group, the BPb had never exceeded 2.4 µmol and for subjects in the high blood lead level group, higher values had been documented in the past.

During the bone lead measurements the subjects filled out two questionnaires on subjective effects – that is, a symptom questionnaire with 31 items and three response alternatives and the Finnish version of the profile of mood states (POMS). The symptom questionnaire asked about symptoms experienced during the past year. The following six symptom scales were included: sleep disturbances, fatigue, memory problems, emotional lability, somatic complaints, and sensory and motor symptoms. The POMS inquired about feelings and moods during the past seven days. The scales yielded by this POMS version were tension, anger, depression, fatigue, vigour, memory problems, and helplessness.

In the neuropsychological tests carried out in the study, reaction speed was measured by visual and auditory simple reaction time (RT) tasks.

In both tasks the stimuli were presented at random intervals (3-10 s) for six minutes. For the speed of visuomotor function the Santa Ana dexterity test with the preferred and non-preferred hand (Santa Ana 1 and Santa Ana 2, respectively), and the digit symbol test from the Wechsler adult intelligence scale (WAIS) were used. Santa Ana is pure test for visuomotor function or dexterity, whereas the digit symbol test has a notable cognitive component and is often used as a test for attention.

The tests used for visual and visuospatial function were block design from WAIS, Valciukas' embedded figures test, the memory for design test, and the retention task of digit symbol. These tests tap different aspects of visuospatial function. Block design and memory for design are visuoconstructive tasks and require the analysis and reconstruction of abstract visual patterns, but memory for design also taps visual memory. Embedded figures measures visuoperceptual function and requires recognition of familiar objects that are superimposed on the visual field. Digit symbol retention requires the subject to reproduce correct symbols in the right places immediately after the digit symbol task. It is a test for incidental visual learning.

Analysis was with SAS statistical software. The association between the exposure and outcome variables was studied by partial correlations and by two covariate analyses. Correlations between the exposure and outcome variables were calculated for both the total group and the low and high BPb groups separately.

The study found that for the people whose BPb had never exceeded 2.4 µmol/1 there was a significant deterioration of neuropsychological performance related to lead, similar to that found in previous studies.

Low limit values for occupational exposure to lead are based on two arguments: *(a)* that even the mild effects found at low BPb can essentially lower the ability to cope with the demands of everyday life, at least for subjects with restricted adaptive resources, and *(b)* that early mild effects can be taken as warning signals that indicate incipient changes in the function of the nervous system, likely to accelerate along with cumulative dose of lead. This argument has recently been questioned because of insufficient documentation of any association between long term exposure and neuropsychological functioning. This subject matter has, indeed, been neglected in existing research on adult exposure to lead.

Whether the effects due to long term exposure at more moderate levels of exposure are more reversible remains to be investigated in future studies.

Source: Occupational Environmental Medicine, Vol. 55, 1998.

Re-evaluation of Post Chernobyl Thyroid Cancer Risk in Children

The Chernobyl reactor accident in 1986 was followed by a sharp increase in the incidence of thyroid cancer among children and adolescents in Belarus and Ukraine in the former Soviet Union. Exposure to iodine-131 was responsible for most of the doses that affected the thyroids of these children. However, among evacuees from the contaminated regions, up to 40 percent of each dose could derive from other incorporated radionuclides and external exposures. Now researchers have estimated the increased risk of developing thyroid cancer after exposure to radioactive iodine from the data set compiled after the Chernobyl incident. The figure thus obtained for most of the affected regions fell within the 95 percent confidence interval of a previously conducted follow-up of thyroid cancer after external exposures.

In Ukraine, more than 150,000 measurements of radioactive iodine activity in the thyroid were performed during the period mid-May to mid-June 1986. In their re-evaluation of these measurements researchers have now reconstructed average thyroid doses due to radioactive iodine exposure for three regions close to Chernobyl comprising over 4,400 towns or villages, and for evacuees. For children less than three years old living in contaminated areas, the dose received exceeded that of adults by a factor of five, while among evacuees the child dose was about 20 times greater than that received by adults. Individual doses show large variability, but this contributed only slightly to the uncertainty of average thyroid dose estimates because of the size of the study. During the observation period of the present study, the excess thyroid cancer incidence was rising. Thus the excess absolute risk per unit dose is expected to increase for longer observation periods.

The excess relative risk per unit dose ranges between 22 Gy^{-1} and 90 Gy^{-1} in the study area. These results are higher than those obtained from longer observation periods after external exposure, possibly because the population of the study is still young and therefore has very low baseline rates.

Source: Nature Vol. 392, March 1998.

Pollution Control Measures: The Critical Load Concept for Emission Abatement Strategies

Over the last two decades the debate on air pollution control has assumed both national and international dimensions. With the establishment and transport of air pollutants in the mid-1970s, air pollution and acid rain have been seen as an international problem leading to increased research into the impact of air pollutants on the environment. Critical loads studies have been used as the basis for assessing European strategies for reduction of sulphur emissions within the UN Economic Commission for Europe Convention on Long-Range Transboundary Air Pollution (LRTAP).

A review of critical load studies has recently been published by Professor Vladimir Bashkin of the Russian Academy of Sciences, Puschino. The critical load concept involves a quantitative estimate of an exposure to one or more pollutants below which no harmful effects may occur. Thus, a critical load (CL) is an indicator for sustainability of an ecosystem in that it provides a value for the maximum permissible load of pollutant at which risk of damage to an ecosystem is reduced. By measuring or estimating certain physical and chemical properties of an ecosystem, sensitivity to acid deposition and/or eutrophication deposition can be calculated, and a 'critical load of acidity', or the level of acidic deposition which affects the sustainability of an ecosystem can be identified, as well as 'critical nutrient load' which affects the biodiversity of species within ecosystems.

Within defined areas, CLs are calculated for all major combinations of tree species and soil types (receptors) in the case of terrestrial ecosystems, or water biota (including fish species) and water types in the case of freshwater ecosystems. These combinations include the great variety of different ecosystems, the sensitivity of which to both acidification and eutrophication inputs by atmospheric pollutants differs greatly, determining the necessary reduction needs when CLs are exceeded by modern deposition levels.

This information on ecosystem sensitivity can be compared with a pollutant deposition map, to determine which areas currently receive deposition levels which exceed the area's CL. These areas of 'exceedance' indicate where present levels of pollutant deposition increase the risk of damage to ecosystems. The critical load concept uses information on CLs and exceedances provided by National Focal Centre groups under the LRTAP Convention to help in developing strategies for reducing emissions of sulphur and nitrogen.

Source: Environmental Conservation 24 (1), 1997.

Effects of Aluminium on the Neurologic Development of Prematurely Born Infants

Aluminium toxicity occurs in adults and children with renal insufficiency who are treated by dialysis with aluminium-contaminated solutions or oral phosphate-binding agents that contain aluminium. The substance accumulates in the body when protective gastrointestinal mechanisms are bypassed, renal function is impaired, and exposure is high.

Since aluminium is a known contaminant of commercial intravenous feeding solution, it has been hypothesized that increased aluminium exposure in intravenously fed preterm infants would probably have detrimental effects on neurological development.

To test this hypothesis, a prospective study of preterm infants has been carried out by researchers in the United Kingdom to investigate the effect of intravenous feeding solutions on the infants' subsequent neurological development.

The results of the study suggest that aluminium intake in preterm infants is associated with reduced development attainment at the corrected post-term age of 18 months. In the study, the infants who received the standard intravenous feeding solutions (providing 25 µg of aluminium per deciliter) had a lower mean Bayley Mental Development Index than those who received aluminium-depleted solutions (providing 2.2 µg of aluminium per deciliter), although this difference was not statistically significant. However, a substantial number of infants received little or no intravenous feeding after randomization, and explanatory analysis showed that the effect of aluminium exposure was dose related.

Aluminium exposure from the standard intravenous solutions was calculated to be associated with a mean loss of one point on the Bayley Mental Development Index per day of full intravenous feeding, after adjustment for potentially confusing factors. In infants fed intravenously for 10 or more days, those receiving the standard solutions had a major (10 point) deficit in their Mental Development Index and were twice as likely to have a Mental Development Index below 85.

These results provide support for the hypothesis that intravenous aluminium may have neurotoxic effects, with longer-term consequences for neurological development.

Source: The New England Journal of Medicine, Vol. 336, No. 22, May 1997.

Lead Exposure and Behavioural Problems in Children

A substantial amount of evidence is available concerning the relationship between lead exposure and behavioral problems in school-aged children. Well documented problems include both hyperactive and impulsive behavior with low thresholds of frustration as well as withdrawal behavior accompanied by fear and disinterest.

Now a group of American researchers has focused research on the period of early childhood, to explore evidence of the effects of lead exposure on early child development. One recent study has examined whether small elevations in blood lead level were associated with measurable behavioral changes in a group of children aged between 1 and 3 years from a poor socio-economic background.

In this study researchers were able to document a statistically significant association between postnatal lead levels in the range of 0.48 to 1.20 µmol/L (10-24.9 µg/dL) and increased hyperactivity, distractibility and low frustration tolerance, and a trend toward a similar association with increased fearfulness, social withdrawal and disinterest in surroundings.

The study revealed that these associations persisted after controlling for potential confounding factors including child's age and gender, and mother's age, verbal IQ, depression score, and provision of cognitive stimulation.

The researchers claim that it is particularly important to consider the association between lead exposure and behavior in children from poor socio-economic backgrounds, whose behavior may be adversely affected on the basis of environmental factors.

Source: Pediatrics, Vol. 101, No. 3, March 1998.

Mechanisms for Detoxifying Aluminium

A number of mechanisms for detoxifying metals have been reported. These include metallothioneins and phytochelatins in the detoxification of cadmium and copper; and free histidine has been reported to be coordinated with nickel in the nickel hyperaccumulation phenotype. Recently, Japanese researchers have reported that oxalic acid takes part in detoxifying aluminium in both external and internal processes. They found that the aluminium-resistant Juanxi cultivar of buckwheat secretes oxalic acid from its roots specifically and rapidly in response to aluminium stress. It was further found that aluminium accumulates in the leaf cells in a non-toxic Al-oxalate complex with a 1:3 ratio of aluminium to oxalic acid.

When buckwheat roots were exposed to aluminium chloride solution, oxalic acid was secreted within 30 minutes. The amount secreted increased linearly with treatment time and with the external aluminium concentration. Neither phosphorus deficiency nor toxic metals such as lanthanum could induce the secretion of oxalic acid, indicating that this response is specific to aluminium stress.

Source: Nature, Vol. 390, December 1997.

Benefits of Fish Consumption versus Risks of Mercury Exposure

In order to attempt to reduce industrial emissions of mercury, the U.S. Environmental Protection Agency (EPA) developed a new reference dose for MeHg in 1996. The EPA reference dose of 0.1 µg per kilogram per day is only one-fifth of the intake guidelines of 0.47 µg per kilogram per day set by the World Health Organisation, and if followed, would severely restrict fish and seafood consumption. Average total mercury concentrations in such fish as halibut, mackerel, pike, snapper and tuna range from 0.2 to 0.3 ppm. Thus for an adult weighing 60 kg, routine consumption of 4 ounces per week of fish containing average mercury tissue concentrations of 0.25 ppm would reach the reference dose for methylmercury exposure.

Although the process of developing a reference dose is valuable in efforts to regulate industrial emissions or to establish target levels in site-specific clean-up efforts, food consumption advice should occur within a broader multidisciplinary public health context that incorporates and weighs information on both risks and benefits. Fish and shellfish are food sources that are high in protein and low in saturated fat, are direct dietary sources of beneficial omega-3 polyunsaturated fatty acids (PUFAs) and contain antioxidants such as selenium and vitamin E.

Fish consumption has also been related to a reduced risk of coronary heart disease. Although not all studies show a protective effect of fish consumption on coronary heart disease, fish and fish oils lower very-low-density lipoprotein cholesterol and triglyceride levels, inhibit platelet aggregation, and may reduce blood pressure.

Severely limiting the consumption of fish and seafood may do more harm than good by reducing the consumption of foods with health benefits and by increasing the consumption of alternative foods that have potential health risks. For populations that rely heavily on subsistence fishing, restrictive fish consumption advisories could damage the social, economic, and personal well-being of entire villages.

Although MeHg exposure in the U.S. population occurs mainly through the consumption of fish and seafood, the EPA reference dose was determined by an acute poisoning episode that occurred in Iraq between 1971 and 1972, when consumption of bread baked from grain treated with a fungicide containing mercury led to the hospitalization of over 6000 people and caused 400 deaths.

However, data from the Iraqi episode may not be appropriate for calculating risks from low level MeHg exposures through fish consumption.

The Iraqi exposures were high-dose and acute, and exposures may have included Hg compounds other than MeHg. In addition, the delay of several years before data was collected could have limited the accuracy of recall of relevant developmental milestones by the mothers of affected children. A wide range in risk estimates was obtained by using different assumptions and modeling approaches.

Hg is ubiquitous in the environment, and some level of MeHg has always been present in the freshwater and marine food chain. Dietary factors present in fish and seafood, such as naturally occurring selenium and vitamin E, may protect against the potential effects of low-level MeHg exposure.

The neurodevelopmental damage associated with industrial mercury pollution in Minimata and Nigata, Japan, and the effects of contaminated bread in Iraq are clear. However, published studies of populations consuming fish indicate no deleterious effects associated with MeHg exposures at levels comparable to or twice as high as WHO intake guidelines.

There is, therefore, some reason to question the scientific merits of restrictive fish consumption advisories. In United States, as state public health workers use the new EPA reference dose to develop fish consumption advisories, there are additional factors that should be considered. These include the potential health benefits of fish consumption, the competing risks associated with other available food sources, the potential medical impact of dietary and lifestyle changes on a population, and the social and economic implications of restrictive fish and seafood consumption advisories.

However, it is important to note that risk balance is not static. While methylmercury toxicity is expected to follow a dose-response relationship, it is not clear whether an increased benefit can be derived during pregnancy from eating more than a certain minimal level of seafood. Mercury toxicity may therefore outweigh the benefits, especially when consumption of contaminated seafood is high.

Source: Science, Vol. 278, December 1997 and Vol. 279, January 1998.

Consequences of the Use of Antibiotics in Agriculture

A matter of great concern in medicine is that, over the last decade, bacteria that cause disease in humans have developed resistance to many of the antibiotics used in treatment. Resistance to antimicrobial drugs may result either from new mutations in the bacterial genome or through the acquisition of genes coding for resistance. Such genetic changes alter the defensive functions of the bacteria by changing the target of the drugs, by detoxifying or ejecting the antibiotic, or by routing metabolic pathways around the point of disruption.

The development of antibiotic resistance is facilitated by current practices in animal husbandry in which antibacterials are used for growth promotion. Animals receiving antibiotics in their feed gain 4 to 5 percent more body weight than animals that do not receive such supplements.

Antibiotic resistance that results from this practice affects zoonotic pathogens such as *Salmonella* serovars and *Campylobacter* spp. and human and animal commensals such as *Escherichia coli* and enterococci.

E. coli, in particular, easily disseminates drug resistance genes, as demonstrated by the spread of antibiotic resistance associated with antibiotics in animal feed.

In the former East Germany, nourseothricin was used as a growth promoter from 1983 to 1990, replacing the similar use of oxytetracycline. Resistance to nourseothricin in *Enterobacteriaceae* from humans and animals was negligible in 1983. Two years later, resistance (by means of the transposon-encoded streptothricin acetyltransferase gene) was found in *E. coli* from the gut of pigs and in meat products. By 1990, resistance to nourseothricin had spread to *E. coli* from the gut flora of pig farmers, their families, citizens from municipal communities, and patients suffering from urinary tract infections. The spread among humans occurred without apparent selective pressure. In 1987, the same resistance determinant was detected in other enteric pathogens, including *Shigella*, an organism found only in humans.

Antibiotic use in animals also has resulted in resistance among nontyphoid *Salmonella* serovars. The resistant bacteria are transmitted to humans in food or through contact with animals. Resistance in *Salmonella* limits the therapeutic options available to veterinarians and physicians in the treatment of certain human cases of salmonellosis. *Salmonella typhimurium* strain DT 104, which is resistant to ampicillin, tetracycline, streptomycin, chloramphenicol, and sulfonamides, has been identified in many places, including the United Kingdom, Europe, and the United States. The recent development of fluoroquinolone resistance is of special concern.

Over the last thirty years, there has been continuing debate about the extent to which bacterial antibiotic use in food animals promotes resistance in bacteria that infect humans.

Worldwide differences in the use and licensing of antibiotics are large. In the countries of the developing world, which are responsible for some 25 percent of world meat production, policies regulating veterinary use of antibiotics are poorly developed. In China, raw mycelia are used as animal growth promoters; in Russia, chloramphenicol is still used in animal husbandry; and in Southeast Asia, use of antimicrobials in shrimp farming is unregulated.

The problems caused by inappropriate use of antibiotics are transboundary, since meat products are traded worldwide. Management of antimicrobial resistance, therefore, requires worldwide coordination of both national and international licensing agencies, with increased surveillance and more research into the linkage of antimicrobial consumption to the development of resistance.

Source: Science, Vol. 279, No. 5353, February 1998.

The Role of Estrogen in Cancer

Currently there is considerable controversy concerning the view that hormones initiate as well as promote cancer. Since the 1970s researchers have recognised that the growth-stimulating effects of estrogen could make it a cancer promoter. Both epidemiological and cell biology studies have indicated that estrogen contributes to the development of cancers of women: those of the breast, ovaries and uterus. The generally accepted view has been that cell growth promotes cancer development by increasing the chances that a cell bearing a potential cell-causing mutation will multiply.

Previously, researchers have tended to attribute the initial genetic damage either to spontaneous mistakes in DNA replication as cells divide, or to damage triggered by an external source such as environmental chemical or radiation exposure.

However, recent studies suggest that initiation of a cancer could be caused by hormones themselves: the metabolic by-products formed by estrogen in the body.

Cell culture studies have shown that estrogen metabolites can bind to DNA and trigger damage. If the data from these studies hold up, researchers would have to reconsider the role of hormones in the body.

Although many estrogen researchers do not support any metabolite hypothesis as the cause for a cancer, evidence is building up and most estrogen metabolite researchers believe that the hypothesis will be confirmed as more research evidence becomes available. If this is so, it will open up new possibilities for intervention to reduce the risk of the three most common types of cancer in women.

Source: Science, Vol. 279, March 1998.

CONTROVERSY OVER RESEARCH CLAIMS LINKING HCFC TO LIVER DISEASE

A report by researchers at the Industrial Toxicology and Occupational Medicine Unit, Catholic University of Louvain, Belgium, details the case of nine workers at a smelting plant who were accidentally exposed over a period of several weeks to a mixture of HCFC 123 and HCFC 124, used as replacements for CFC. The workers were all drivers of an overhead gantry with a cooling system to provide protection against the heat from smelting metals. In 1996 the CFC 114 used in the system had been replaced by a mixture of HCFCs 123 and 124 for environmental reasons. It was later found that the HCFC mixture had perforated the plastic pipes of the cooling system and was leaking out into the enclosed drivers' cabin on the gantry.

According to a report published by the researchers in 1997, all nine gantry drivers developed liver disease as a result of exposure to the leaked gases. On cessation of exposure to the HCFCs, the workers all made full recoveries.

In their report, the researchers concluded that repeated exposure of humans to HCFCs 123 and 124 can result in serious liver injury in a large proportion of the population. Although the exact mechanism of the hepatoxicity of these agents is not known, the research results suggest that trifluoroacetyl-altered liver proteins are involved. The researchers assert that the marked hepatoxicity of HCFCs in humans and their possible carcinogenicity should give rise to concern over their widespread use as a replacement for CFCs.

However, the US Environmental Protection Agency (EPA) has expressed strong disagreement with the report's conclusions claiming that the suggestion that a chemical is not safe because incorrect handling practices resulted in a health hazard is unsustainable. The EPA firmly supports the position that all of the available alternatives to CFCs can be used safely when industrial standards and correct practices are followed.

Sources: [1] The Lancet, August 1997.
[2] Chemistry in Britain, Vol. 33, No. 10, 1998.

(Continued from page 2)

below 1.5 which was taken as a threshold for increased risk. The final conclusion was that there was little excess of lung cancer in mining and quarrying but there may be excess in the manufacturing industries notably those which entail high temperature processes.

Dr Jim Chisholm looked at the problems of collecting good exposure data. The starting point is to decide what are the circumstances under which exposure occurs. Also, the problems encountered in actually making measurements. It takes a lot of work to get sufficient data for any meaningful statistical analysis.

Professor Bernard Gee considered the confounding caused by cigarette smoking. Many of the lung cancer cases of today worked at a time when smoking was common. Smoking as a confounder was a major problem for epidemiologists and one which had not always been properly considered in past studies. Professor Pat Hessel looked at some past studies particularly the study of mortality in the diatomaceous earth industry by Checkoway and others. His analysis of the way in which this study was conducted proved contentious.

Chris Holwell, a lawyer, was at pains to persuade participants that the last thing the construction industry needed was another asbestos. It was essential that there should be good communication between industry and scientists which should avoid scaring industrials. Finance was important to keep industry moving but scares in the past had meant that there was a list of difficult materials whose use was proscribed. Investors in construction were paranoid about asbestos and even though a scientific evaluation put it more into perspective, a doubt would always remain. It was a fact of life that higher standards in the industry cost more throughout the lifetime of a building up to and including its demolition. Because of this, it was important to avoid any condemnation of materials because they contained silica, since they would be added to the 'prohibited materials list' used by industry.

* The proceedings of the seminar will be published in "Indoor and Built Environment" later this year. Details from ISBE, PO Box 73, Buckden, Cambs. PE18 9SS, UK, Fax No: +44 1480 810 768 or see website: http:\\www.isbe.demon.co.uk.

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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