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Chalabhorn 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".

TEN YEARS ON FROM RIO *The World Summit on Sustainable Development Johannesburg, South Africa 2002*

Representing H.M. King Bhumibol Adulyadej of Thailand, H.R.H. Princess Chulabhorn led a Thai delegation of over 30 officials to the World Summit on Sustainable Development that was held in Johannesburg from 26 August to 4 September.

In her address to the conference Her Royal Highness stated that Thailand's current Ninth Economic and Social

path in all aspects of social interaction at individual, family and community levels.

In her speech, Her Royal Highness commented thus on the global concern for environmentally sound and sustainable development:

"In 1992, I had the honour of leading the Thai delegation at the Earth Summit in Rio de Janeiro and this provides a



Development Plan for the period from 2002-2006 has been guided by the philosophy of "sufficiency economy" first propounded in Thailand by His Majesty King Bhumibol. This philosophy places people at the center of development. The main principle of this approach to development is adherence to a middle

perspective from which to assess and appraise the efforts that have been made to address the issues of environmental protection and sustainable development that remain a matter of urgent global concern.

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TEN YEARS ON FROM RIO

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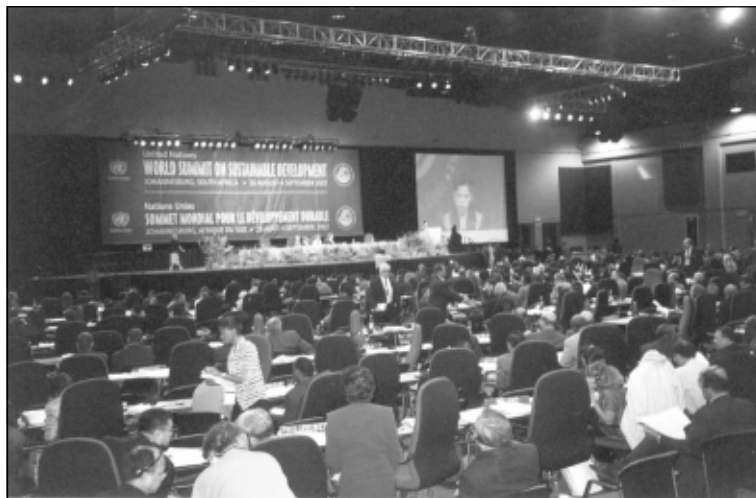
This is why the Johannesburg Summit is of critical importance, since it provides us with the opportunity to renew our commitment to Agenda 21 for the benefit of present and future generations. This commitment is reflected in the plan of implementation for this World Summit on Sustainable Development which represents our collective effort to assess the progress that has been made over the past ten years, and what still needs to be done in the future to ensure full and effective implementation of Agenda 21. I believe that there is now a shared realization that our most urgent goal is to address the needs of the world's poorest populations, which is why this summit has placed great emphasis on the challenges currently being faced by the African peoples, as well as by developing countries in other regions of the world."

Her Royal Highness also informed the conference about the work of the Chulabhorn Research Institute:

"On my part, I have actively participated in these endeavours through the work of the Chulabhorn Research Institute, under whose auspices the International Centre for Environmental and Industrial Toxicology (ICEIT) was established in 1987. The Centre, designated by the UNEP as a Centre of Excellence in Environmental and Industrial Toxicology in 1990, has developed capacity building programmes in research and human resource development in the field of environmental and industrial toxicology, benefiting participants from Thailand and other developing countries, particularly in the Asia/Pacific Region. On behalf of the Chulabhorn Research Institute, of which I am the President, I would like to express my appreciation to UNDP's Regional Bureau for Asia and the Pacific and the ASEAN Foundation for providing funds to the Institute for undertaking this regional capacity building programme."

In conclusion, Her Royal Highness stated:

"I believe that the Johannesburg Summit marks a critical juncture in our path to fully sustainable development as envisaged ten years ago at the Rio Summit. We must now demonstrate our commitment to continued efforts along this path and at the same time to ensuring a more equitable basis for



global partnership, in order to both protect the environment and to enhance economic and social development for people in all parts of the world.

In our endeavours we must ensure that we do not disappoint future generations. Let us strive to make the Johannesburg Summit a beacon for continued development in a more equitable and healthier world."

The key outcomes of the Johannesburg Summit have been summarized thus:

- The Summit reaffirmed sustainable development as a central element of the international agenda and gave new impetus to global action to fight poverty and protect the environment.
- The understanding of sustainable development was broadened and strengthened as a result of the Summit, particularly the important linkages between poverty, the environment and the use of natural resources.
- Governments agreed to, and reaffirmed, a wide range of concrete commitments and targets for action to achieve more effective implementation of sustainable development objectives.
- Energy, water and sanitation issues were critical elements of the negotiations and outcomes to a greater degree than in previous international meetings on sustainable development.

Support for the establishment of a world solidarity fund for the eradication of poverty was a positive step forward.

Africa and New Partnership for Africa's Development (NEPAD) were identified for special attention and support by the international community to better focus efforts to address the development needs of Africa.

The views of civil society were given prominence at the Summit, in recognition of the key role of civil society in implementing the outcomes and in promoting partnership initiatives. Over 8,000 civil society participants attended the Summit, reinforced by parallel events which included major groups, such as NGOs, women, indigenous people, youth, farmers, trade unions, business leaders, the scientific and technological community and local authorities as well as Chief Justices from various countries.

The concept of partnerships between governments, business and civil society was given a large boost by the Summit and the Plan of Implementation. Over 220 partnerships (with \$235 million in resources) were identified in advance of the Summit and around 60 partnerships were announced during the Summit by a variety of countries.

Acrylamide in food: an unknown risk

An expert consultation on the implications of acrylamide in food, hosted in Geneva by the World Health Organization (WHO) and the United Nations Food and Agricultural Organization (FAO) now plans to establish a network for research on acrylamide in order to achieve a better understanding of its possible health effects.

The experts who took part in the recent consultation identified a number of important issues for research. While acrylamide is known to cause cancer in laboratory animals, no studies have so far been undertaken of the relationship between this substance and cancer in humans.

The theoretical models to predict whether cancer would develop in humans from current average intake levels are not reliable enough to develop firm conclusions. When investigated in rats, acrylamide has a potency similar to certain other well-known carcinogens formed through cooking, such as certain aromatic hydrocarbons formed in meat when fried or grilled. However the intake levels for acrylamide are likely to be higher. Therefore, the consultation recognized that the issue of acrylamide in food is a major concern.

The consultation did not consider the data available to be adequate to present specific quantitative estimates of cancer risk posed by levels of acrylamide in people's diets. The scientists urged investigation of the possibilities for reducing the levels of acrylamide in food by changes in formulation, processing and other practices.

Acrylamide is a chemical used in the manufacture of plastics. It was first discovered to be present in certain foods cooked at high temperatures as the result of work announced in Sweden in April 2002. It is a known carcinogen and causes nerve damage.

The Swedish research, and subsequent studies in Norway, Switzerland, the United Kingdom and the United States, have found that acrylamide levels in certain starch-based foods, such as potato chips, french fries, cookies, cereals and bread, were well above the level given

in the World Health Organization's Guideline Values for Drinking Water Quality.

Yet the average intake levels of acrylamide from all sources were determined to be in the range of 70 micrograms per day for an adult, i.e., a range significantly below that which is known to cause nerve damage in laboratory animals.

Foods in which acrylamide develops when cooked at above 120 degrees Celsius include potato chips, french fries, bread and processed cereals. However, the scientists noted, they were not able to determine if other foods also contained acrylamide, as the research has not yet been conducted. The experts emphasized that

data on foods consumed as parts of diets in regions other than Europe and North America is missing and more research is needed here.

Consequently, it is not yet possible to determine what percentage of overall acrylamide presence in the human body comes from starch-based foods. Indeed, because other food, such as fruits, vegetables, meats and seafood, and beverages and other exposures such as cigarettes, can also result in acrylamide entering the human body, it is not known what percentage of the total acrylamide in a human body is from food sources.

Source: Joint WHO/FAO Press Release/ 51 June 2002.

Environmental risk assessment of pesticides using the SoilFug model

An environmental risk assessment was recently conducted of the pesticides used in Xiamen, China. The goal was to assess the impact on water resources, particularly on fisheries and mariculture. The study involved the collection of data on ecotoxicological properties of pesticides used in agriculture to determine their physico-chemical profile. A simulation of the environmental behaviour of the pesticides in relation to the load applied on agricultural areas was carried out using the SoilFug model, a model that predicts potential surface water contamination derived from pesticide use on agricultural fields. It is essentially an unsteady-state but equilibrium event model that takes into account the disappearance of the chemicals according to different phenomena (degradation, volatilisation, and runoff) but then calculates the partition among the different phases of the soil in the rain event period using a fugacity calculation. The model considers the four different

compartments in the soil: soil air, soil water, organic matter, and mineral matter. A capacity for each component can be calculated and therefore the fugacity can be determined, once the volume and the chemical input are known. From the fugacity, chemical amounts and concentrations in each compartment can be calculated.

In the risk assessment performed in Xiamen, approximate concentrations of pesticides were calculated, the highest risk chemicals were identified and risk management measures were indicated.

This study represents a cost-effective method that may be used before engaging expensive monitoring programs. The findings could be useful to sustainable development of agriculture and risk assessment for pesticide use in developing countries, where analytical facilities are lacking.

Source: Toxicology Letters No. 1-3, March 2002.

PRINCIPLES OF ENVIRONMENTAL TOXICOLOGY

THE WATERVILLE MUNICIPAL LANDFILL

The municipal landfill was in operation from 1957 to 1985. During that time, the facility accepted residential and commercial waste. Historical information indicates that waste solvent was disposed at the landfill site. One chemical in particular, tetrachloroethylene (also called perchloroethylene or PCE), was disposed of in large quantities.

The landfill site is situated in the coastal plain overlying an unconfined aquifer that serves as a drinking water source for nearby residents via domestic supply wells. Local residents are concerned that the landfill may be releasing contaminants into the ground water. The Environmental Protection Agency has initiated a study because of the potential for residential exposure to PCE through drinking water. Two drinking water wells are within 1/4 mile and are hydraulically downgradient from the site.

Ground Water Monitoring Data	PCE Conc. (SI/194)	
	GW4	GW5
Loganville Well (LW)	ND	ND
Morningstar Well (MW)	1350	1250
Municipal Well A (MWA)	27	29
Municipal Well B (MWB)	14	17

Direction view of Waterville Landfill site
 LW -- Loganville well MW -- Morningstar well
 MWA -- municipal well A MWB -- municipal well B



This two week training course, sponsored by the ASEAN foundation, was opened on 23 September 2002 by HRH Princess Chulabhorn.

The 40 trainees attending the course were from 12 countries with the majority being from the ASEAN countries including Cambodia, Indonesia, Malaysia, Myanmar and Vietnam.

The international faculty members who taught the course came from Canada, Denmark, Italy, the United Kingdom and the United States of America.

This training course was part of the Chulabhorn Research Institute's ongoing capacity building program, now in its fourteenth year, with courses being organized in Thailand and in other countries in Southeast Asia for key personnel from government, academia, and industry, in the important developmental area of environmental toxicology.

Participants on the training program are selected on the basis of their potential to be future trainers in their respective institutions and countries.

It is recognized that in a multidisciplinary area such as environmental toxicology, training in both theoretical and practical elements is essentially a long term endeavor since it constitutes the very basis for sustainable development at national, regional and global levels.

Among the special features of the present training course were the range of specialist areas taught by the faculty of world renowned international experts, covering both theory and application. This aspect of the training was especially commended by the 40 trainees in their evaluation of the course.

Another feature of the training course that was widely appreciated was the level of opportunity provided, particularly in the practical sessions, for interaction between the trainees and the resource group of experts as well as among trainees themselves.



BALLAST WATER DISPOSAL

A CASE STUDY IN ENVIRONMENTAL TOXICOLOGY

A major oil company plans to build an oil terminal in a sheltered bay. The bay is approximately circular with a narrow opening to the sea, a radius of about 1 km, and a maximum depth of about 80 metres. Oil tankers of 80,000 tonnes capacity will arrive with ballast water in their tanks. This ballast water, about 12% of the total tanker capacity, must be discharged before oil can be loaded. The company management is sensitive to the possible legal consequences and cost of damages if the discharge causes environmental damage. They have information that the ballast water contains polychlorinated biphenyls, 1 ppm, tributyltin oxide, 3 ppm, nitrate, 4 ppm, polystyrene, 5 ppm, nickel, 2 ppm, cadmium, 1.5 ppm, chromium, 3 ppm, copper, 1 ppm, and zinc, 10 ppm, as well as oil residues, 5000 ppm, from the tanker. Near to the bay where the oil terminal is to be located is a commercial syster factory and just beyond this is a small town of 12,000 inhabitants, which is largely a fishing community. You are asked by the oil company to advise them on the safe disposal of the ballast water. What further information would you require before you can give reasonable advice? What disposal methods do the civil engineers tell you are available and how would you choose between them?

GUIDANCE:

What are the potential toxic effects of discharges of ballast water directly, without treatment, into the bay at the oil terminal?

Would discharge through a pipe into the open sea beyond the bay be acceptable? If not, why not?

If you recommend water treatment before discharge, which substances would you try to remove and how?

What conditions, if any, would you wish to impose on the oil company with regard to the operation of the terminal?

NOTE: Use risk assessment, where appropriate, to justify your management decisions.



TOXICOLOGY AND POLLUTION CONTROL

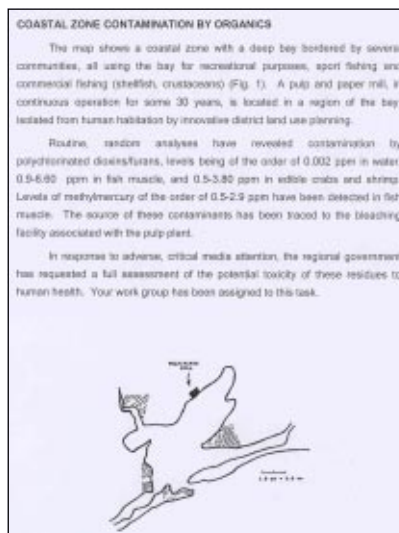
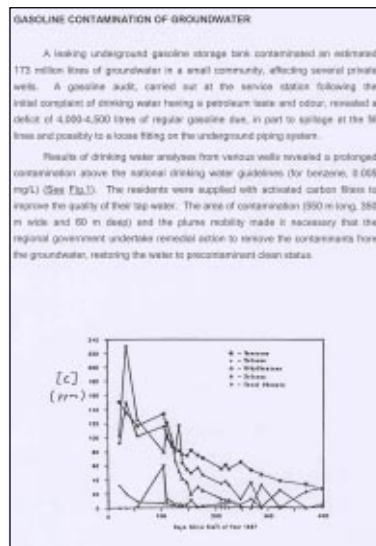
This was achieved through the scheduling and organization of the training in small groups engaged in case studies involving specific aspects of the management of toxic chemicals, toxic waste and remediation, relevant to the developmental needs and conditions of the trainee's own countries and to their institutional duties.

It was by means of the carefully selected and designed case study scenarios that the international faculty were able to relate the training to the most urgent priorities in environmental management in countries in Southeast Asia and in developing countries throughout the world.

This concern of relating the theory of environmental toxicology to solving specific environmental problems affecting countries in Southeast Asia is a central concept in Chulabhorn Research Institute's capacity building program and one which the trainees themselves recognize and appreciate as an important basis for successful training.

Some of the topics presented on the present course and related to the practical case study applications were the following:

- The Impact of Toxic Effects of Chemicals
- Environmental Distribution and Fate of Chemicals in the Environment
- Dose-Response Relationships
- Absorption, Distribution and Excretion
- Principles of Ecotoxicology
- Cellular Responses to Toxic Injury
- Introduction to Environmental Carcinogenesis
- General Aspects of the Use of Pesticides
- The Toxicity of Industrial Chemicals
- The Toxicity of Hazardous Wastes
- Applications of Biotechnology for Hazardous and Chemical Waste Treatment Biomonitoring and Biomarkers



A study of dimethylsulfoxide neurotoxicity in rats

Dimethylsulfoxide (DMSO) was previously used to treat some musculoskeletal diseases but since 1965 its clinical use has been banned in the United States on claims of its neurotoxicity. Previous studies are of *in vitro* or animal experiments using local injections. However no data report the behavioural neurotoxicity of DMSO in animals.

A recent study demonstrated that repeated intraperitoneal administration of DMSO in rats, at commonly used concentrations, produced a dose-dependent reduction in nerve conduction velocity, and at the highest doses some pathological changes were noted.

These included wrinkling of the myelin and swelling of the axons. Other studies have shown, however, that DMSO was able to decrease potassium and sodium channel currents, increase membrane fluidity and modify its structure. Such results suggest that rats chronically exposed to DMSO could display behavioural disorders, and a new study has now been carried out to examine this possibility.

This study focused on the behavioural effects of repeated intraperitoneal injections of various concentrations of DMSO in male Sprague-Dawley rats. The effects were assessed by a battery of sensory and motor tests. The motor tests used were actimeter and grip

strength test, and the sensory tests used noxious and non-noxious mechanical and thermal stimuli.

The clinical status of the animals used in the experiment was good throughout and no motor deficits were observed. However, sensory assessment displayed a mechanical allodynia of short duration. This suggests that it is necessary to take solvent toxicity into account during preclinical studies and the neurotoxic assessment of pharmaceutical drugs.

Source: Toxicology Letters No. 2, June 2002

CAFFEINE TOXICITY

Caffeine is present in several beverages consumed world-wide such as coffee, tea and carbonated drinks. It is also used for therapeutic purposes and is included in a wide variety of prescription as well as over-the-counter drugs. However, it is known to be toxic at high concentrations, and due to the increasing practice of self-medication and the over consumption of tea and coffee, some human health problems may arise from caffeine toxicity.

Some of the observed clinical conditions include cardiovascular disease and reproductive disorders, among others. The possible toxic effects of caffeine on heart mitochondria are still poorly understood. The influence of caffeine on the mitochondrial permeability transition has not been clarified so far. The objective of a recent study was to investigate whether caffeine, at toxic concentrations, had any stimulating effect on the permeability transition of heart mitochondria isolated from Wistar rats, as well as whether it influenced mitochondrial respiratory parameters. The re-

sults show that caffeine reduced mitochondrial ability to accumulate calcium by increasing the susceptibility of heart mitochondria to the opening of the transition pore. Caffeine not only hindered mitochondrial capacity to recover membrane potential after calcium addition but also increased the rate of calcium-dependent mitochondrial swelling and calcium-induced calcium release. The increased swelling was also observed in nonenergized mitochondria. Caffeine also showed a complex array of effects on heart mitochondrial bioenergetics, as evaluated by respiratory parameter measure-

ments. An increase in state 4 respiration and a depression in state 3 respiration was discernable, although no effect was observed on succinate-sustained mitochondrial membrane potential in the absence of calcium. This study may be relevant to cardiovascular problems linked to caffeine toxicity and also to *in vitro* experiences involving caffeine-induced calcium release from the sarcoplasmic reticulum and uptake by mitochondria.

Source: Toxicology and Applied Pharmacology, No. 1, February, 2002.

Cadmium and lead blood and urine levels among a general population in Thailand

There is increasing recognition that the presence of heavy metals in the environment pose a health hazard to the general population since epidemiological studies suggest that chronic low exposure to metals such as cadmium and lead can cause adverse health effects. Numerous population groups exposed to environmental cadmium and lead have been studied to find reliable biological indicators for detecting the toxic effects of the metals.

Many studies have suggested that blood concentration of cadmium was a useful indicator of recent cadmium exposure, whereas urinary cadmium reflected the cadmium body burden and the concentration in the kidney. In addition, the concentration of lead in blood has been used to estimate the degree of exposure and diagnose lead intoxication, while urine lead has become a widely used index of body burden of lead.

A recent study in Italy was carried out to determine heavy metal concentrations in whole blood and urine of unexposed healthy subjects. The results showed the geometric means of blood and urine cadmium levels to be 0.60 and 0.86 $\mu\text{g/l}$ respectively and lead levels of 157.7

$\mu\text{g/L}$ in whole blood and 17 $\mu\text{g/L}$ in urine.

A study of the blood cadmium and lead levels of a general population in Czechoslovakia was undertaken in which the levels were reported as 0.99 and 93.4 $\mu\text{g/L}$ respectively.

Data on blood and urine cadmium and lead concentrations in Thai people are limited. Thus a new study was conducted to determine blood and urine levels of cadmium and lead in a non-occupationally exposed population in Thailand.

In 1999-2000, 356 healthy subjects (187 males, 169 females) took part in the present study. The average age of subjects was 33.5 years (range 17-55). Occupational exposure to any toxic substances, including cadmium and lead, was ruled out in a medical interview. In addition, each subject was interviewed about demographic information, medical history, smoking habit, alcohol intake and other health-related habits.

Blood samples were taken from the cubital vein between 09.00 and 12.00 hours (with fasting) into heparinized tubes. Morning spot urine was collected also on the same day as physical examination. Both blood

and urine samples were taken to avoid possible metal contamination and kept at -20°C until analyzed in the laboratory.

A noteworthy finding in the Thai study is that the results do not reveal differences in blood and urine cadmium concentrations of people living outside Bangkok and those living in the Bangkok urban area. However, the blood lead levels of subjects resident in Bangkok was higher than for those resident outside the capital at levels of 32.6 and 28.3 $\mu\text{g/l}$ respectively. This agrees with previous reports indicating that blood lead values of non-occupationally exposed populations were highest among urban residents, especially those living in the center of cities, but became progressively lower with lower degrees of urbanization.

In the Thai study, blood and urine levels of cadmium and lead are in an acceptable range and can be used as reference values for the non-occupationally exposed Thai population.

Source: The Southeast Asian Journal of Tropical Medicine and Public Health, Vol. 33, No. 1, March 2002

CADMIUM AND LEAD IN BLOOD IN RELATION TO LOW BONE MINERAL DENSITY AND TUBULAR PROTEINURIA

Long-term exposure to cadmium has long been suspected of causing kidney and bone damage in humans. Until now, the most common method of assessing the body burden of cadmium has been to measure the presence of cadmium in urine. However, elevated concentrations of cadmium in urine can also be caused by renal dysfunction, and this potentially confounding factor has left open to question any results that imply a direct causal link between cadmium exposure and adverse kidney and bone effects.

In a recent study carried out in Sweden, researchers have used measurements of cadmium in blood to strengthen the evidence of the link between cadmium exposure and kidney and bone damage.

The investigators studied 1,021 residents of two communities in southeastern Sweden with documented cadmium and lead pollution. The pollution was a result of two local factories' production of nickel-cadmium and lead batteries over the course of many decades. The subjects were required

to have lived in the area for at least five years between 1910, when battery production began, and 1992. One hundred and seventeen of the subjects currently or had previously worked in one of the battery plants and were considered occupationally exposed to the pollutants.

The researchers measured blood lead and cadmium concentrations among the subjects, and also looked at the incidence of two conditions.

(Continued on page 8)

Solar Ultraviolet-B radiation may combat cancer

The most important risk factors for many types of cancer are generally accepted as being environmental, attributable for the most part to diet and lifestyle. However, these risk factors do not explain the variability in mortality rates for a number of cancers in the United States where studies reveal large geographical variations.

There have been reports that inverse correlations exist between exposure to solar radiation and the development of carcinoma of the breast, colon, non-Hodgkin's lymphoma (NHL), ovary and prostate, one explanation for this being that solar ultraviolet (UV)-B radiation exposure reduces the risk of cancer through photoinitiation of vitamin D production.

Based on these reports, an ecologic study has recently been made of cancer mortality rates in the United States with respect to levels of solar UV-B exposure.

Two solar UV-B indices and data sets were used in the current study. The primary data set used for the current analysis was the DNA-weighted UV-B radiation exposure map obtained by using the Total Ozone Mapping Spectrometer (TOMS). TOMS is a space-based instrument that yields UV data for the entire country with a 1-degree x 1.25-degree grid spacing. The July 1992 TOMS

data, posted at the TOMS website, was used. The color images were digitized to yield average values for each State Economic Area (SEA) or population center within the SEAs, including major urban areas. The color contour interval was 0.75 kilojoule (kJ)/m², with a noontime average range in the U.S. of 3.4-10kJ/m². The location of the SEA can be determined to approximately 33-50% of a contour or approximately 0.3-0.4 kJ/m². This represents approximately 10% of the dose at the lower exposures and 4% at the higher exposures. However, the TOMS estimate of UV-B radiation apparently underestimates the reduction due to aerosols, which is a very important consideration in the northeastern United States.

In addition to the TOMS data, UV-B data obtained from ground-based UV-B monitoring stations operated by the U.S. Department of Agriculture (USDA) also were used. This network has 26 stations in rural locations in the U.S., 24 of which were in operation by 1999.

The findings of the current study confirm previous results that solar UV-B radiation is associated with reduced risk of cancer of the breast, colon, ovary, and prostate as well as non-Hodgkin lymphoma. Eight additional malignancies were found to exhibit an

inverse correlation between mortality rates and UV-B radiation: bladder, esophageal, kidney, lung, pancreatic, rectal, stomach, and corpus uteri. The annual number of premature deaths from cancer due to lower UV-B exposures was 21,700 (95% confidence interval [95% CI], 20,400-23,400) for white Americans, 1400 (95% CI, 1100-1600) for black Americans, and 500 (95% CI, 400-600) for Asian Americans and other minorities.

The results demonstrate that much of the geographic variation in cancer mortality rates in United States can be attributed to variations in solar UV-B radiation exposure. Thus, many lives could be extended through increased careful exposure to solar UV-B radiation and more safely, vitamin D3 supplementation, especially in nonsummer months.

Source: Cancer 2002, Vol. 94, No. 6

CADMIUM AND LEAD IN BLOOD IN RELATION TO LOW BONE MINERAL DENSITY...

(Continued from page 2)

The first, low bone mineral density, is a marker for osteoporosis. The second, tubular proteinuria (an increase in the presence of low-molecular-weight proteins in the urine), is an indication of kidney dysfunction.

The researchers found no associations between lead and low bone mineral density or tubular proteinuria. In the case of cadmium, however, the researchers found a clear relationship between blood concentrations and both conditions. That relationship was particularly strong for tubular proteinuria.

Even when the occupationally exposed participants were excluded,

the subgroup with the highest blood cadmium concentrations had a fourfold increased risk of having tubular proteinuria, compared with the subgroup with the lowest blood cadmium concentrations. It is also interesting to note that even 15 years after the cessation of exposure, cadmium-exposed workers showed a stronger association between blood cadmium and tubular proteinuria than between urinary cadmium and tubular proteinuria, indications that there may be a dose-response relationship involved.

Source: Environmental Health Perspectives, Vol. 110, No. 7, July 2002

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