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INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

HRH Princess Chulabhorn Opens Jakarta Executive Seminar and Training Course on Environmental Toxicology

In collaboration with the Hazardous Waste and Substance Management Environmental Impact Management Agency (BAPEDAL), Jakarta, Indonesia, the Chulabhorn Research Institute organized a 10 day training course in Jakarta for Indonesian personnel which was opened on 30 October 2000 by Her Royal Highness Princess Chulabhorn, President of the Chulabhorn Research Institute.

In her opening address at the Executive Seminar which preceded the training course, Her Royal Highness stated that the meeting was a landmark event since it set out to address issues that affected the entire Southeast Asia region, both in terms of pollution control and sustainable industrial development.

Her Royal Highness noted that the rapid industrial expansion that had occurred in recent years in Indonesia, as in many other countries in the region, had led government agencies and the industrial sector to re-examine more critically than ever before the effect of development on long-term economic plans for sustainable

(Continued on page 2)

HRH Princess Chulabhorn Opens Jakarta Executive Seminar and Training Course on Environmental Toxicology

(Continued from page 1)

growth and improvements in the people's quality of life, through protection of the environment.

The Chulabhorn Research Institute's UNDP-supported human resource development program in Environmental Toxicology provided specialized training in all aspects of pollution control and management.

On this occasion, Her Royal Highness acknowledged the work of the Hazardous Waste and Substance Management, Environmental Impact Management Agency, Indonesia, for coordinating the training course and for their active participation in CRI's capacity building program over the last three years.

The training course, which was attended by 39 Indonesian personnel, was taught by specialists from Canada, Italy, UK and US as well as by faculty members from the Chulabhorn Research Institute.

The Need for Caution in the Use of Herbal Medicine

A recent report by researchers in Belgium indicates that a Chinese herb, Avistolochia fangchi, previously linked to incidences of kidney failure may also cause cancer.

Patients at a Belgian weight-loss clinic were given this herb in error. Staff at the clinic had prescribed the herb *Stephania tetrandra,* but the pills that patients received also included aristolochia, possibly because of a manufacturing error. On average, the patients took the two herbs for about a year.

Of the patients who accidentally received the herb, 18 developed cancers of the urinary system, according to the report. These 18 patients had already experienced severe kidney failure as a result of taking another combination of two Chinese herbs *(S tetrandra* and *Magnolia officinalis)* and needed kidney dialysis or kidney transplants.

The researchers became aware of the extent of the cancer risk after discovering a urinary system cancer in a patient undergoing transplantation. Other patients being treated for kidney disease related to treatment with Chinese herbs were offered preventive removal of the kidneys and ureters. In the 39 patients who accepted this offer, 18 cancers were discovered, representing a cancer rate of 46 percent.

In 19 of the 21 patients without cancer, mild to moderate precancerous abnormalities were found in the ureters or kidneys, according to the report.

All the affected kidneys showed evidence of exposure to aristolochic acid, the harmful ingredient in *A fangchi,* and lower levels were found in some of the ureters. Only four samples contained evidence of exposure to ochratoxin A, a possible carcinogen sometimes found in *S tetrandra.*

The risk of cancer was greater for patients who had taken larger amounts of *A fangchi,* the investigators noted. Eight of 24 patients who took 200 grams or less had urinary system cancer, compared with 10 of 15 patients who took 201 grams or more.

Cases of kidney failure from aristolochia have also been reported in France, Britain, Spain, Japan, Taiwan, and the United States reinforcing the need for caution in the use of natural herbal medicine.

Source: BMJ Vol. 320 June 2000.

Health effects of excessive intake of Flavonoids

Plant flavonoids are common dietary components that have many potent biological properties. Early studies investigated their mutagenic and genotoxic activity in a number of in vitro assays. Recently there has been renewed interest in flavonoids because of the antioxidant and estrogenic effects ascribed to them. This has led to their proposed use as anticarcinogens and cardio protective agents. There has been a dramatic increase in recent years in consumption of flavonoids as dietary supplements but unfortunately the potentially toxic effects of excessive flavonoid intake have been largely ignored.

A number of epidemiological studies suggest that a decreased risk of heart disease and cancers of the breast, prostate, lung, colon, and stomach is associated with increased consumption of fruits, vegetables, and soy products. Populations at lowest risk are Asians and vegetarians. Based on the average daily intake of flavonols (68 mg) and isoflavones (20-240 mg) in Asian populations, dietary exposures at these doses are not likely to cause adverse health effects. To date, no human data on the long-term effects of high-dose supplementation are available. The level of flavonoids required to induce

(Continued on page 8)

DIETARY CAFFEINE AND PARKINSON'S DISEASE

A prospective study has revealed a significant inverse association between coffee consumption measured during midlife and incident Parkinson's disease (PD) with a dose-response relationship.

The study is based on an earlier longitudinal study from the Honolulu Heart Program and presents an expanded analysis of the relationship between consumption of coffee and dietary caffeine and risk of PD within the same cohort but with longer follow-up and nearly twice the number of incident PD cases than were previously available.

The median age of the 8004 men at study enrollment (1965-1968) was 53 years (range, 45-68 years). The median length of follow-up was 27 years, minimum follow-up was 0.8 years to the first death, and maximum follow-up was 30 years from the baseline examination. Among the men, 102 developed PD over the 30 years of follow-up. The median age of PD diagnosis was 73.6 years (range, 54-89 years), and the median interval between baseline examination and PD onset was 16.6 years (range, 2-30 years).

Coffee drinkers had significantly lower incidence of PD than nondrinkers ($P<.001$). This effect was apparent when examining incidence of PD based on 30 and 24 years of follow-up according to amounts of coffee consumed at the time of study enrollment and at the 1971 examination. At each examination, increasing amounts of coffee consumed were associated with decline in PD incidence ($P<.01$).

Although the protective effect of dietary caffeine showed a similar dose-response pattern for both drinkers and nondrinkers of coffee, it was significant only in coffee drinkers. The lack of a significant association in noncoffee drinkers may have been due to a small sample size.

Cumulative incidence curves for PD over time by amounts of coffee consumed and by caffeine intake from non-coffee sources reveal the magnitude of dose effect between exposure categories. For men who were nondrinkers of coffee and those who consumed 28 oz or more per day, differences in the cumulative incidence of PD became apparent as early as 10 years into follow-up. A similar divergence is apparent between men who consumed the least and the most amounts of caffeine from noncoffee sources.

The association between coffee intake at study enrollment and risk of PD remained statistically significant for men whose diagnosis of PD occurred before ($P=.005$) and after 1991 ($P=.01$).

Coffee intake determined at study enrollment was also significantly associated with PD that occurred in the first ($P=.048$) and second ($P=.002$) 15 years of follow-up. In both instances, risk of PD declined with increasing amounts of coffee consumed.

Source: JAMA Vol. 283 No. 20 May 2000.

ARSENIC POISONING ON THE INDIAN SUBCONTINENT

At a recent conference on public health held at Harvard University, the vice president of the Bangladesh Public Health association reported that more than 7000 people in Bangladesh have already been diagnosed with symptoms of arsenic poisoning, but that in fact half of the country's entire population may be at risk, since an estimated 60 million regularly ingest arsenic through drinking contaminated groundwater. The source of the arsenic is geological. The alluvial sediments which cover much of the country are rich in iron pyrites, which contain arsenic, and hydrologists have suggested that excessive groundwater depletion causes arsenic to be released from pyrite decomposition.

However, the dose-response relation is still an unresolved research issue. Previous studies in Taiwan have indicated that some forms of cancer might be the result of a cumulative effect of arsenic poisoning that reveal themselves after 15 to 20 years of ingestion of arsenic contaminated water.

In Bangladesh, there have been cases of squamous cell carcinoma that seem to be attributable to arsenic ingestion that have occurred within 10 years of exposure. Arsenic contaminated groundwater and the associated toxicity has also been previously reported from Argentina, China, Mexico, Taiwan, and Thailand, but the number of people exposed to the risk is very much greater on the subcontinent.

Source: BMJ Volume 320 March 2000.

LOW-COST ACTIVATED CARBON ABSORBANTS DEVELOPED FOR MANAGEMENT OF INDUSTRIAL EMISSIONS

A team of researchers at Illinois State Geological Survey in the United States has succeeded in producing low-cost, activated-carbon absorbents from any type of waste material. In particular, used tyres and waste nut shells can both be processed to make porous, carbon-based absorbent materials that are capable of removing elemental mercury and mercuric chloride components from the gas flue produced when coal is burned in a power station. Currently, coal-fired power plants are one of the largest anthropogenic sources of mercury emissions.

Recycling waste products to make absorbers is potentially much cheaper than producing conventional absorbers. Tyres in particular are highly cost effective because of their substantial sulphur content. Pistachio shells have also been found to be effective mercury absorbers.

The research team of environmental engineers are continuing their work on recycled absorbers using fly-ash and the by-products of corn processing, confident that there is a big market for new products to manage industrial emissions.

Source: Chemistry & Industry No. 16 August 2000.

Biofuels – a viable alternative to crude oil

Transport and industry rely very largely on diesel oil as an energy source. However growing environmental awareness and increasing costs of crude oil have led to an intensified search for alternative sources of energy and researchers have focussed attention on biofuels, plant-based fuel sources, particularly for use in diesel engines.

Rapeseed oil is the main raw material used in bio-diesel production, followed by sunflower oil and soybean oil. Other raw materials include palm oil, linseed oil, beef tallow and used cooking oil.

Bio-diesel is commercially produced through the transesterification of vegetable oils or fats with alcohol. The ester interchange—replacement of the alcohol components, glycerol, by methanol—takes place quite easily at low temperatures (50-70°C), under atmospheric pressure, in excess methanol and with an alkaline catalyst such as sodium hydroxide. However, these mild reaction conditions require an oil to be neutralised by alkaline refining or steam distillation. It is also possible to convert crude palm oil with varying amounts of free fatty acid in a continuous process, by combining the esterification and transesterification processes, as developed by the Malaysian Palm Oil Board (MPOB). This has been successfully demonstrated in a 3000t/ a pilot plant.

Perhaps the most systematic and thorough evaluation of biofuel as a diesel substitute was conducted in Malaysia. Between 1984 and 1995, biofuel from palm oil was extensively evaluated in bench endurance tests and vehicle field trials, involving a wide range of diesel engines, such as lorries, taxis, tractors, stationary engines, generators and water pumps. In Kuala Lumpur, Malaysia, bio-diesel was used to fuel 30 buses between 1992 and 1995. Each bus travelled 300,000 km — the exhaustive field trial distance recommended by the engine manufacturer. Ten buses were run on bio-diesel from palm oil, ten on 50:50 blends with diesel, and a further ten, powered by petroleum diesel, were used as a control group.

Another fleet of six buses, three running on 100% palm oil bio-diesel and three on 100% petroleum diesel, were tested at about the same time but with a different lubricating oil. Each of these buses travelled between 200,000 and 250,000 km. The field trial has yielded encouraging results. Throughout the period, no technical problems were reported, where the engines had been maintained according to service manuals, and the operators were not able to detect any difference in terms of general engine performance.

All the indications are that bio-diesel has an important role to play as an industrial energy source in the future. Not only is it renewable but it is less polluting than diesel oil. However international standards are needed to ensure the quality of the fuel. Although bio-diesel may not replace petroleum diesel, it is estimated that in the near future 10 percent of world diesel consumption could be substituted by bio-diesel.

Source: Chemistry & Industry No. 16 August 2000.

EXPLORATION OF THE "PAIN" PATHWAY IN MICE

Neuroscientists from the University of California, San Francisco, USA, and the University of Würzburg, Germany, have genetically altered mice to remove the receptor that responds to heat and some substances that normally cause sensations of pain. These substances include capsaicin, the active ingredient in chili peppers and other so-called vanilloid compounds.

It had previously been demonstrated that neurons containing the capsaicin receptor vanilloid receptor I (VR1) responded to capsaicin and other painful stimuli in culture, but it was only after the decision taken by the team of neuroscientists to inactivate the VR1 gene that it was discovered that the resulting mice are impervious to capsaicin-induced pain.

Capsaicin injected into the hind paw of a normal mouse causes the animal to lick and shake the tender paw. However, the mutant mice barely reacted to the injection, and their paws did not swell or become inflamed as much as they do in normal mice. When researchers laced the drinking water of normal mice with capsaicin, the normal mice took one sip, rubbed their snouts, and stayed clear of the water bottle. The mutant mice, however, showed no such reluctance.

The mutant animals also tolerated high heat better, including having their tails immersed in a hot water bath and their paws put in contact with a hot plate. The animals did eventually react in both tests, showing that sensitivity was lessened, not eliminated. This suggests that other heat-sensing channels play a role as well.

Another type of test indicates that VR1 plays a role in the extra sensitivity to heat usually displayed by inflamed tissues. Mustard oil painted onto the paws of normal mice causes them to become inflamed and very sensitive to heat—just as sunburned skin is seared by warm water or sunshine. But in the mice lacking VR1, the mustard-oil treatment did not enhance the response to heat, although the animals still displayed the hypersensitivity to touch that develops in inflamed tissues. Because touch-sensitive pain must be triggered by other neuronal responses, the finding suggests that blocking VR1 would not relieve a common, painful condition—extreme sensitivity to touch, such as that accompanying shingles.

However, such inhibitors may help combat another type of especially troubling pain, the chronic internal pain that can accompany tissue damage. The neuroscientists conducting this research suspect that VR1 receptors might contribute to such pain. They found, for example, that neurons carrying the receptors can be excited by the acidic environment produced by inflammation. But neurons from VR1 – deficient mice bathed in an acidic solution did not react as vigorously as neurons from normal mice did. Thus, the researchers hope that blocking the VR1 receptor might help relieve chronic internal pain.

Source: Science Vol. 288 April 2000.

EFFECTS OF GLOBAL WARMING ON THE SPREAD OF MALARIA

Predictions of global climate change are often accompanied by forecasts that vector-borne diseases such as life threatening cerebral malaria, caused by *Plasmodium falciparum* transmitted by anopheline mosquitoes, will spread into cooler parts of the globe which are at present relatively free from *falciparum* malaria. As with many other vector-borne tropical diseases, the epidemiology of malaria remains poorly understood although *falciparium* malaria, the most severe form of the human disease, causes most of the approximately 1 million deaths worldwide that occur annually.

However, absolute mosquito abundance has not yet been related to multivariate climate.

Nevertheless, the problem of malaria has led to its being included in most predictions about the impact of climate change on the future distribution of vector-borne diseases. These studies, which draw on the forecasts of future climate from various global circulation models (GCMs), generally use only one or at most two climatic variables to make their predictions. Biological models for malaria distribution are based principally on the temperature dependence of mosquito blood-feeding intervals and longevity and the development period of the malaria parasite within the mosquito, each of which affects the rate of transmission.

However, in an alternative statistical approach combining several climatic variables, it has now been predicted, reassuringly for those who live in temperate zones, that the future distribution of the parasite *Plasmodium falciparum* is unlikely to change appreciably as a result of global warming. This is because global warming is not only about rises in temperature but, more precisely, it is about temperature, rainfall, and humidity co-varying spatially and temporally, and the impact of these variables on the numerous components of the vector and pathogen life-cycle.

For malaria, these components are not just limited to the temperature-sensitive incubation period of parasites in mosquitoes, but include the abundance, longevity, choice of host, and blood-feeding frequency of the vector, its susceptibility to the parasite, and a plethora of other factors that affect the host-parasite-vector interaction.

Source: Science Vol. 289 September 2000.

THE ROLE OF ZINC IN INCREASING IMMUNORESISTANCE TO INFECTION IN THE ELDERLY

Infections can cause mortality in the elderly when the immune response is damaged. Zinc has a leading role in the correct functioning of the immune response throughout the life of an organism. It affects the immune system in many ways because of its widespread role in the activity of enzymes, peptides, transcription factors and cytokines that are involved in the various physiological steps of immune development and reactivity.

Zinc influences immune cells directly by increasing the activity of multiple enzymes required for DNA replication and transcription. It affects membrane stability by competing with thiols to prevent peroxidative damage. In addition, zinc protects against oxidative stress induced by pro-inflammatory cytokines and subsequent activation of nuclear factor kB(NF-kB) and activator protein 1 (AP-1) transcription factors.

Protection occurs because several transcription factors contain zinc-finger-like domains, which are required for DNA replication, that are influenced by changes in the intracellular pool of zinc. In addition, the activity of some zinc-dependent enzymes (including nucleoside phosphorylase and thymidine kinase) is impaired during aging. This causes the cell membrane to become hard and vulnerable to reactive oxygen species and leads to subsequent oxidative damage and cell death.

The antioxidant role of zinc and the possible homeostasis between zinc-bound metallothioneins (MTs), inducible nitric oxide synthase (iNOS) and poly ADP-ribose polymerase (PARP) have been demonstrated.

Zinc has a crucial role in the maintenance of immunoresistance to infection in aging. Among the mechanisms proposed to account for this, interaction between MTs, iNOS and PARP, each of which is controlled by pro-inflammatory cytokines, is of interest because the activity of these proteins depends on zinc turnover, which is altered in aging. In this model, PARP might induce death of immune cells, rather than DNA repair. Zinc supplementation in aging might restore the DNA repair function of PARP. Polymorphisms within the human genes encoding PARP, iNOS and MT are currently under investigation. Study of the genetics of this system might give insight into possible genetic markers of aging and identify new biological tools to better understand the role of zinc in immunoresistance to infection.

Source: TiPS Vol. 21 June 2000.

HEALTH HAZARDS OF CHROMIUM

Chromium occurs in three main forms: Metallic chromium (Cr [0]) used to make steel and other alloys, trivalent chromium (Cr [III]) which occurs naturally in soil and plants, and hexavalent chromium (Cr[VI]) which is produced industrially when Cr(III) is heated in the presence of mineral bases and atmospheric oxygen, as for example in metal finishing processes.

It is this third form of chromium that has proven to be of the greatest occupational and environmental health concern.

Cr(VI) can enter the body when people breathe air, eat food, or drink water containing it. Cr(VI) is also found in house dust and soil, which can be ingested or inhaled. Of the various forms of chromium, Cr(VI) is the most toxic.

Certain Cr(VI) compounds have been found to be carcinogenic in humans, but the evidence to date indicates that the carcinogenicity is site-specific--limited to the lung and sinonasal cavity--and dependent on high exposures, such as might be encountered in an industrial setting. Cr(VI) can cause a wide range of other health effects. Inhaling relatively high concentrations of some forms of Cr(VI) can cause a runny nose, sneezing, itching, nosebleeds, ulcers, and holes in the nasal septum. Short-term high-level inhalational exposure can cause adverse effects at the contact site, including ulcers, irritation of the nasal mucosa, and holes in the nasal septum. Ingestion of very high doses of Cr(VI) can cause kidney and liver damage, nausea, irritation of the gastrointestinal tract, stomach ulcers, convulsions, and death. Dermal exposures may cause skin ulcers or allergic reactions (Cr[VI] is one of the most highly allergenic metals, second only to nickel). And studies of mice fed high doses of Cr(VI) have shown reproductive effects including reduced litter size and decreased fetal weight.

There is a great deal of controversy about the relative health effects of the various routes of exposure for Cr(VI). According to the International Agency for Research on Cancer (IARC), ingested Cr(VI) is largely converted to Cr(III) in the stomach, a fact that many chromium experts believe prevents ingestional exposure from posing significant health

dangers, since Cr(III) is not readily absorbed into the body. The saliva, gastric juice, intestinal bacteria, blood, liver, epithelial lining fluid, pulmonary alveolar macrophages, peripheral lung parynchema, and bronchial tree have all been associated with eliminating Cr(VI) from the body.

Cr(VI) compounds are emitted into the air, water, and soil by a number of different industries. In the air, chromium compounds are present mainly as fine dust particles that eventually settle over the land and water.

The Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) establish permissible exposure limits (PELs) and recommended exposure limits (RELs), respectively, for hazardous substances in the workplace. PELs are based on the feasibility of controlling the exposure in question within the workplace, while RELs are based on requirements for preventing occupational disease. Although employers are legally bound only by PELs, they are encouraged by NIOSH to follow whichever limit is the more protective. The PEL for Cr(VI) in workplace air during an 8-hour work day, 40-hour work week is 100 ?g/m3, while the REL for carcinogenic Cr(VI) compounds in workplace air is much lower: only 1??g/m3.

It has been estimated that workers in some 80 different professional categories may be exposed to Cr(VI). Various Cr(VI) compounds are used in leather tanning, the production of textiles, dyes, and pigments, and chrome plating. Other sources of chromium emissions include oil and coal combustion, stainless steel welding, steel production, cement plants, industrial paint and coating manufacture, and cooling towers, which use Cr(VI) as a rust inhibitor for their submerged moving parts.

After a century of widespread use, steps are being taken to curb the use of Cr(VI) in industry, but for many manufacturing processes Cr(VI) remains the chemical of choice, thanks to its powerful anticorrosive properties. Research on Cr(VI) is ongoing, but there are still many questions to be answered about the human health effects of this industrial heavy weight.

Source: Environmental Health Perspectives Vol. 108 No. 9 September 2000.

Health risks of low-level mercury exposure: the debate continues

Mercury, which is released into the environment largely from coal-burning power plants, is converted by bacteria into methylmercury that accumulates in the aquatic food chain. Humans are thus exposed to mercury when they eat fish.

The neurotoxic effects of methylmercury are well known: it can cause sensory and motor problems in adults and mental retardation in children exposed to high levels in the womb. However there is still uncertainty and considerable debate about whether low levels are harmful.

Five years ago the Environmental Protection Agency (EPA) in the United States proposed reducing the safe level for mercury exposure to 0.1 micrograms per kilogram of body weight per day. This decision, based on data from a 1971 poisoning incident in Iraq, ran counter to the views of other U.S. federal agencies such as the Food and Drug Administration (FDA) whose standard was five times higher.

These critics, from both industry and other government agencies, argued that EPA should base its decisions on new findings of studies of mercury's low level health effects. However, when EPA did this, they were also challenged.

The critics cite a study that has found no damage to neurological development in 700 5 1/2-year-olds born to mothers who ate mercury-contaminated fish in the Seychelles Islands in the Indian Ocean. The latest results of this ongoing study were published in 1998. EPA, in turn, has relied on a Danish study of children in the Faroe Islands in the North Atlantic, which did find neurological harm at low-level exposures. The critics contend that this study is flawed because the mercury-tainted whale meat that the Faroe islanders ate also contained polychlorinated biphenyls (PCBs) and other pollutants known to affect neuro-development

To the critics' surprise, a panel of the National Academy of Sciences placed more faith in the Faroe Islands study. At the panel's request, the Danish investigators excluded the data for children who were also exposed to high PCB levels; the remaining subjects still showed neurological effects from exposure to low levels of mercury.

FDA and other agencies must now decide whether to adjust their safety levels for mercury. They say they plan to weigh all the evidence—including the latest results, expected in 2001, from the Seychelles children.

Source: Science Vol. 289 No. 5478 July 2000.

Exposure to radon gas in homes and adult acute leukemia

A case-control study of adult leukemia resulting from possible carcinogenic effects of exposure to low doses of ionising radiation has been carried out in the United Kingdom.

The study region covered the southwest, north, and northwest of England and included a wide range of radon levels. All confirmed cases of acute leukemia diagnosed in residents aged 16-69 years in the study region were collected over a five year period starting in 1991.

Cases were matched with controls of the same sex, born within 2 years of their matched cases, randomly selected from the list of patients of the family physician with whom a case was registered.

A pseudo diagnosis date was used for controls, which was the date at which the control was the same age as the matched case at diagnosis.

The number of cases enrolled for the study was 807 with 1593 matched controls. Participation rate was 76% for cases and 65% for controls.

At interview permission was requested to measure radon gas in homes in which the participants lived at diagnosis or pseudo diagnosis. One passive detector was placed in the living room and a second in the bedroom. These were returned after 6 months with overall measurements taken 76% of homes of cases and 80% homes of controls. Since domestic levels of radon gas vary seasonally, standard methods were used to correct the 6-month measurement and to produce an estimate of yearly average exposure.

The results showed no association between acute leukemia and radon, which was a pattern consistent for subtypes of leukemia (lymphoid and myeloid) and for an unmatched analysis. Participation rates in the radon groups of the study were similar for cases and controls. Adjustment for deprivation did not affect the estimates of risk for radon, which suggests that the results are not an artifact of participation rates. This conclusion was further supported by the similarity in risk estimates for the north and southwest regions separately.

The findings of the study offer reassurance that domestic exposure to the low levels of radon in the United Kingdom poses no public health risk for acute leukemia.

Source: The Lancet Vol. 355 May 2000

Health effects of excessive intake of Flavonoids

(Continued from page 2)

mutations and cytotoxicity may not be physiologically achievable through dietary sources. However, the use of supplements, particularly antioxidant formulas and herbal mixtures that are commonly recommended in terms of gram rather than milligram doses, could result in exposure to potentially toxic levels. For example, typical manufacturers' recommended doses of quercetin supplements range between 500 and 1000 mg per day, which is 10 to 20 times what can be consumed in a typical vegetarian diet. This suggests that unregulated, commercially available flavonoid-containing supplements may have biologic activity that can adversely affect human health.

A significant number of studies provide evidence that the biologic activities of flavonoids may play a dual role in mutagenesis and carcinogenesis. They can act as antimutagens/promutagens and antioxidants/pro-oxidants, which is largely dependent upon the levels consumed as well as the physiological conditions in the body. Exposure to increased levels of flavonoids, whether through the diet or by supplementation, may potentially overwhelm the system, leading to the formation of reactive oxygen species, and ultimately DNA damage. Furthermore, these effects may be enhanced in fetal development where there is rapid cell growth, which may increase sensitivity to phytochemical exposure. Indeed, little is actually known about the toxicology of excess flavonoid intake, while beneficial attributes are commonly overemphasized.

Source: Free Radical Biology & Medicine Vol. 29 April 2000.

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