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Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

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

CONFERENCE ON "ENVIRONMENTAL SCIENCE, TECHNOLOGY AND MANAGEMENT"
8–11 July 2003
The Convention Center, Chulabhorn Research Institute
Bangkok, Thailand

This international conference was organized by the Center for Environmental Science, Technology and Management, which has been established as a Center of Excellence in the Higher Education Development Project of the Thai Ministry of University Affairs.

The conference was attended by 280 participants.

A welcoming address was given by *Khunying* Mathuros Ruchirawat, Chairperson of the Organizing Committee and Vice President for Research at the Chulabhorn Research Institute. The opening address was delivered by Dr. Pornchai Matangkasombut, President of Mahidol University.

The conference was organized as a springboard for strengthening and enhancing the research capability of the center which comprises 6 postgraduate programs that together contribute to interdisciplinary education and research in Environmental Science, Research and Management.

The program of the center is supported by a loan from the Asian Development Bank (ADB) and is

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CONFERENCE ON "ENVIRONMENTAL SCIENCE, TECHNOLOGY AND MANAGEMENT"
8–11 July 2003, The Convention Center, Chulabhorn Research Institute, Bangkok, Thailand

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implemented by a consortium of 4 collaborating institutions: Mahidol University, Burapha University, Chulabhorn Research Institute and Asian Institute of Technology.

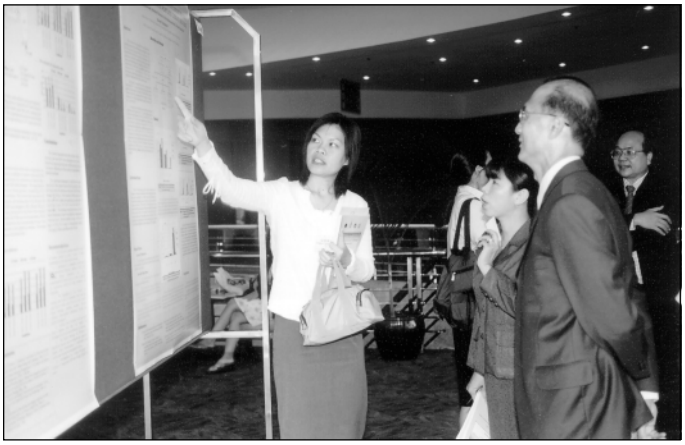
The conference program featured platform presentations by specially invited international and Thai specialists and academics, and poster presentations were organized by Thai researchers.

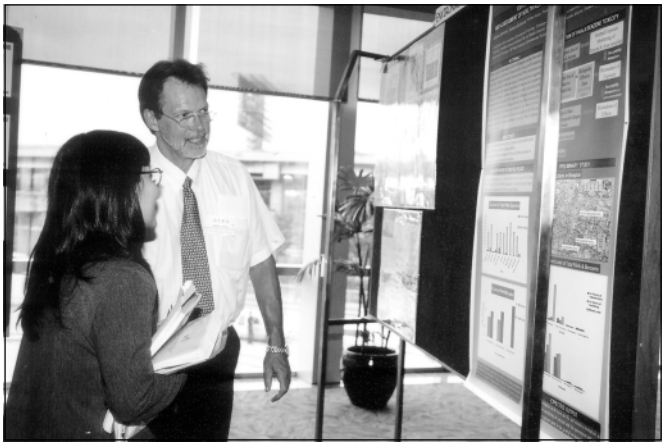
The opening remarks at the conference were followed by a roundtable discussion on "Issues and Challenges in Setting up Industrial Linkages for Research".

Plenary lectures were given by Professor Daniel Watts of the Center for Environmental Engineering and Science, New Jersey Institute of Technology, USA and by Professor Herman Autrup of the Department of Environmental Medicine, Faculty of Medicine, University of Aarhaus, Denmark. Other international presenters were Professor Heinz Eckhardt of the School of Civil Engineering, University for Applied Science FH Wiesbaden, Germany, Professor Chester W. Price, Department of Food Science and Technology, University of California, USA and Professor Alan Baker of the School of Botany, University of Melbourne, Australia.

The platform presentations that comprised the program of the first three days of the conference were divided into 6 main areas: Treatment and Technology, Petrochemicals, Bioremediation, Heavy Metals, Pesticides and Environmental Toxicology. In all there were 35 presentations.

The fourth and final day of the conference was devoted to poster presentations of which there were 68, divided into the categories of Bioremediation, Effects on Environment, Environmental and Natural Resources, Environmental Health, Heavy Metals, Pesticides, Technology, Treatment, and one miscellaneous category.





THE ROLE OF ARSENIC-METABOLIZING BACTERIA IN THE CONTAMINATION OF DRINKING WATER

Naturally occurring arsenic is very broadly distributed in many subsurface drinking water aquifers around the world and these natural sources of arsenic are of the greatest concern to human health on a global basis.

Arsenic can exist in four oxidation states: As(-III), As(0), As(III), and AS(V). Native (elemental) arsenic occurs rarely, whereas traces of toxic arsines can be detected in gases emanating from anoxic environments. The predominant form of inorganic arsenic in aqueous, aerobic environments is arsenate [As(V) as $H_2AsO_4^-$ and $HAsO_4^{2-}$], whereas arsenite [As(III) as $H_3AsO_3^0$ and $H_2AsO_3^-$] is more prevalent in anoxic environments. Arsenate is strongly adsorbed to the surface of several common minerals, such as ferrihydrite and alumina, a property that constrains its hydrologic mobility.

The contribution made by microorganisms to the biogeochemistry of arsenic in the environment is extensive as it involves various oxidation, reduction, methylation, and demethylation reactions of its main chemical species.

Understanding the role of microorganisms in the hydrologic mobility of arsenic in drinking water aquifers is a highly complex and unresolved environmental question of critical importance to the health of millions of people worldwide.

In Bangladesh alone, perhaps 30 million people drink well waters that contain elevated arsenic concentrations, and thousands of new cases of severe arseniasis (arsenicosis) occur annually in that country.

Several theories have been proposed to explain the subsurface mobilization of arsenic. These include

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HEALTH EFFECTS OF LONG-TERM EXPOSURE TO INGESTED ARSENIC

Long-term exposure to ingested arsenic may induce many health effects. Biologic gradients between ingested arsenic and skin and various internal cancers have been well-documented.

Other chronic health effects induced by arsenic have also drawn global attention, especially cardiovascular, neurologic, reproductive, and developmental hazards. Mortality and morbidity of vascular diseases, including peripheral vascular disease, cerebral infarction, and ischemic heart disease, have been associated with arsenic levels in drinking water in arseniasis-endemic areas.

Now a new study carried out in Taiwan has provided evidence indicating that the ingestion of arsenic may lead to the development of diabetes mellitus in arsenic-endemic areas of the country.

In the study, researchers used the National Health Insurance Database for 1999-2000 to derive the prevalence of non-insulin-dependent diabetes and related vascular diseases by age and sex among residents in southwestern arseniasis-endemic and nonendemic areas in Taiwan. The study included 66,667 residents living in endemic areas and 639,667 in nonendemic areas, all $\geq$ 25 years of age. The status of diabetes and vascular diseases was ascertained through disease diagnosis and treatment prescription included in the reimbursement claims of clinics and hospitals. The prevalence of non-insulin-dependent diabetes, age- and gender-adjusted to the general population in Taiwan, was 7.5% (95% confidence interval, 7.4-7.7%) in the arseniasis-endemic areas and 3.5% (3.5-3.6%) in the nonendemic areas. Among both diabetics and nondiabetics, higher prevalence of microvascular and macrovascular diseases was observed in arseniasis-endemic than in the nonendemic areas. Age- and gender-adjusted prevalence of microvascular disease in endemic and nonendemic areas was 20.0% and 6.0%, respectively, for diabetics, and 8.6% and 1.0%, respectively, for nondiabetics. The corresponding prevalence of macrovascular disease was 25.3% and 13.7% for diabetics, and 12.3% and 5.5% for nondiabetics.

The National Health Insurance Database used in this study consisted of reimbursement claims of all patients who had received care from contracted clinics and/or hospitals at least once in 1999-2000. Therefore, those who were not cared for by contracted hospitals or clinics during the study period were excluded from the database. However, more than 96% of insured people had received care from contracted hospitals and clinics. The prevalence estimated in this study was considered reasonably correct. The disease prevalence might be overestimated if patients are more likely to visit clinicians and to be included in the database than are unaffected people. Nonetheless, the odds ratio comparing arseniasis-endemic and nonendemic areas would be valid if the frequencies of visiting clinicians were the same between two comparison areas.

Considering the rural and urban differences in lifestyles and disease patterns, residents in the rural area were considered less likely to develop cardiovascular diseases as a result of decreased prevalence of risk factors from dietary intake, obesity, and physical activity. However, residents in the arseniasis-endemic area had a higher prevalence of cardiovascular disease despite the fact that the endemic area was more rural than was the nonendemic area in Taiwan. Thus, the vascular effect of ingested arsenic observed in this study was based on a conservative comparison.

This study demonstrated that residents in the arseniasis-endemic area had an increased risk of diabetes and its related vascular diseases compared with those in the nonendemic area. This study also found a larger contribution of ingested arsenic on the development of microvascular diseases than of diabetes. Future studies will be directed to mechanistic investigations of arsenic inducing non-insulin-dependent diabetes and atherosclerosis. Risk assessment of arsenic exposure for diabetes and the related vascular diseases should be integrated with the current scheme for cancer risk from arsenic.

Source: Environmental Health Perspectives, Vol. 111, No. 2, February 2003.

NICKEL RELEASE FROM EURO COINS

Nickel allergy is relatively common and it has long been known that contact with the metal over a period of time can cause a rash characteristic of allergic contact dermatitis. Thus under the European Union Nickel Directive, the amount of nickel in products that come into direct and prolonged contact with the skin is regulated. This directive includes the amount of nickel contained in coins.

However, in a recent study, researchers from the University Hospital and the Institute of Metallurgy, Zurich, Switzerland, have found that, because of a design flaw, 1-euro and 2- euro coins can generate an electrical current resulting in the release of amounts of nickel that exceed the permitted amount by a factor of between 240 and 320.

The source of the problem is the two different nickel alloys used in the coins, one comprising an outer ring, which surrounds a smaller disk made of the second alloy. In the presence of human sweat, the two alloys produce a small but corrosive electrical current that boosts the release of nickel to levels that exceed that of pure nickel under the same conditions.

Since the introduction of the coins in January 2001, there has been an increase in reported cases of nickel-contact allergy suggesting that people working with the euro with prolonged contact may be at risk.

Source: JAMA, Vol. 288, No. 14, October 2002.

Cancer Risks from Irradiated Dietary Fats

Food irradiation is considered a highly effective processing technology to improve and maintain food safety. Application of this process to food products effectively reduces the number of microbial pathogens, which are annually responsible for millions of food-borne illnesses worldwide. Furthermore, nutritional, genetic, and toxicological studies of shelf-stable chicken sterilized by ionizing radiation have failed to reveal any evidence of genotoxic effects in mice, rats, and rabbits.

However, it has been known for some 30 years that a family of compounds, the 2-alkylcyclobutanones (2-ACBs) is in fact produced by high-dose irradiation of synthetic triglycerides. Recent research into the effects of irradiation on food safety has detected the presence of 2-ACBs in irradiated fat-containing foods such as minced chicken, pork, lamb, beef, and mechanically recovered meats, as well as other fat-containing foods.

The 2-ACBs are formed during the irradiation process as a result of the radiation-induced cleavage of triglycerides. They have been detected exclusively in irradiated fat-containing foods and have not been found in nonirradiated foods treated by other processes such as freezing, heating or simple preservation treatments.

Concerns about the safety of 2-ACBs have been raised with regard to public health risk, despite the fact that only very small amounts are present in the human diet.

A study has been carried out to determine whether 2-ACBs modulate carcinogenesis in an experimental animal model.

The 2-ACBs used for the experimental study were 2-tetra-decylcyclobutanone (2-tDCB, derived from stearic acid) and 2-(tetradec-5'-enyl)-cyclobutanone (2-tDeCB, derived from oleic acid). These compounds were obtained as follows: the 2,2-dimethylhydrazone derived from cyclobutanone was treated with a base, and, after addition of the required primary alkyl halide (1-bromotetradecane for 2-tDCB and 1-bromotetradec-5-ene for 2-tDeCB), an acidic hydrolysis delivered the desired 2-ACB in a highly pure state.

Wistar rats received daily a solution of highly pure 2-tDCB or 2-tDeCB at a concentration of 0.005% in 1% ethanol as drinking fluid, while control animals received 1% ethanol. All animals received a single intraperitoneal injection of the chemical carcinogen azoxymethane (AOM) at weeks 3 and 4. At 3 months after AOM injection, no significant changes were observed in the total number of preneoplastic lesions in the colon of AOM controls and 2-ACB-treated animals. After 6 months, the total number of tumors in the colon was threefold higher in the 2-ACB-treated animals than in the AOM controls. The colon of four of six AOM control rats exhibited only one small tumor (≤6 mm^3). Multiple tumors were observed in four and three of six animals treated with 2-tDCB or 2-tDeCB, respectively. Medium ($6 < S < 25$ mm^3) and larger (> 25 mm^3) tumors were detected only in 2-ACB-treated animals. This is the first demonstration that a compound found exclusively in irradiated dietary fats may promote colon carcinogenesis in animals treated with a chemical carcinogen.

The relevance of these results for the risk assessment of human consumption of irradiated food remains to be elucidated. It must be emphasized that the daily amount of pure 2-ACB administered to rats corresponds to a pharmacological dose (3.2 mg/kg body wt), which is not comparable to the amount ingested by humans eating irradiated food products, which can be estimated to be ≤5-10 µg/kg body wt. In addition, these food products may also contain several components that may reduce the bioavailability of 2-ACBs. The benefits of food irradiation to protect public health against food-borne pathogenic bacteria are becoming increasingly recognized. In light of the expected extended application of food irradiation, however, it seems necessary to further clarify the potential toxicity of 2-ACBs and their contribution to a possible risk associated with human consumption of irradiated fat-containing food.

Source: Nutrition and Cancer, No. 44(2), 2002.

THE USE OF RICIN IN CANCER TREATMENT

Ricin, in recent years, has been associated with biowarfare. Less well known to the general public is the fact that ricin's cytocidal properties have also been exploited in cancer treatment in which the toxin is linked up with antibodies that target tumor cells. However, applications have been limited because of a side effect known as vascular leak syndrome resulting from endothelial damage that causes fluid to escape from the bloodstream into the lungs, muscles, brain, and other tissues of the body. Now, a group of researchers has demonstrated how a single point mutation in ricin toxin can eliminate vascular leak syndrome without compromising the toxin's enzymatic action.

This research has sought to block the disintegrin function of ricin by making mutations in the leucine-aspartate-valine (LDV) sequence and also in neighboring amino acids, as determined from the three-dimensional toxin structure. A handful of these mutants retained an acceptable level of enzymatic activity and cytotoxicity against the human $CD22^+$ lymphoma cell line Daudi. To determine which mutant would best avoid vascular leak syndrome, the researchers tested each one in a pulmonary vascular leak model. Native and mutant immunotoxin were each administered to mice, followed by radiolabeled albumin. The lungs of the mice were then counted for radioactivity to quantify the excess leakage of protein into the lungs. The mutation of amino acid 97 from asparagine to alanine was found not to cause significant leakage. A

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HEALTH RISKS FROM MANGANESE EXPOSURE

In Canada, the government completed phasing out leaded gasoline in 1990 as a measure to reduce air pollution in urban areas. This ban paved the way for more widespread use of a manganese based compound, Methylcyclopentadienyl Manganese Tricarbonyl (MMT), in gasoline.

The additive increases octane levels, which boosts engine performance and enables fuel to be burned more evenly. Health officials in Canada, which has allowed MMT in gas since 1976, reaffirmed 9 years ago that in their view, MMT is safe, and the MMT levels to which people are generally exposed are too low to cause harm. However, this view is not universally accepted.

As a nutrient, manganese is an essential component of several enzymes; a deficiency can lead to heart and bone problems and in children, stunted growth. The liver removes extra dietary manganese from the circulation, so ingested manganese is not a major concern. However, when manganese is inhaled, blood ferries it from the lungs to the brain, where it can readily cross the blood-brain barrier.

It's been known since 1837 that workers in manganese mines can develop manganism, a dreaded illness marked by Parkinson's like tremors, violent outbursts, and hallucinations. Victims have lesions in the globus pallidus and striatum of the basal ganglia, a part of the brain involved in fine muscle control. But it takes large amounts of manganese to trigger the disease: airborne concentrations as high as 100 or more milligrams per cubic meter. And recently, concerns have grown that welders exposed to manganese in fumes could be at risk for Parkinson's-like disease.

By comparison, manganese exposure from MMT is low: Canada, for example, allows no more than 18 milligrams of manganese from MMT per liter of gasoline, and only a fraction of this amount is thought to reach the air as manganese particles.

Uncertainty still remains, however, over estimates of how much manganese might be inhaled where MMT gas is sold, and a study carried out in the mid 1990s used personal monitors to record individual manganese exposure in 542 people in Toronto. This study found that exposures fell well below the threshold. One important question that remains, however, is whether these results would apply to cities with climatic conditions and traffic patterns that are substantially different from those in Toronto. Another fundamental concern is that while current regulations on airborne manganese may protect healthy people, certain vulnerable groups could still be at risk from existing levels of exposure.

Source: Science, Vol. 300, No. 5621, May 2003.

THE ROLE OF ARSENIC-METABOLIZING BACTERIA IN THE CONTAMINATION OF DRINKING WATER

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(i) the oxidation of As-containing pyrites, (ii) the release of As(V) from reduction of iron oxides by autochthonous organic matter (e.g., peat), (iii) the reduction of iron oxides by allochthonous organic matter (from dissolved organics in recharging waters), and (iv) the exchange of adsorbed As(V) with fertilizer phosphates. These are not necessarily mutually exclusive processes, but over time microorganisms probably play an essential role in both the direct reduction and oxidation of the arsenic species, as well as the iron minerals contained in these aquifers.

On the basis of what is now known of the microbial metabolism of arsenic in nature, it is possible to begin to formulate a model for what might be occurring in the aquifers of Bangladesh.

Perhaps the initial process is the oxidation of the original As(III)-containing minerals (e.g., arsenopyrite) during transport and sedimentation by pioneering chemolithoautotrophic arsenite oxidizers (CAOs) and heterotrophic arsenite oxidizers (HAOs) taking place over recent geologic time periods. This would result in the accumulation of As(V) onto surfaces of oxidized minerals like ferrihydrite. Subsequent human activity in the form of intensive irrigated agriculture, digging of wells, and lowering of groundwater tables would provide oxidants (e.g., oxygen, nitrate) that would further stimulate As(III) oxidation. This would cause a buildup of microbial biomass (and its associated organic matter) and the creation of anoxic conditions. This organic matter, in conjunction with other sources either from decomposing buried peat deposits or from that dissolved in seasonal recharge from agricultural surface waters, would in turn promote the dissimilatory reduction of adsorbed As(V) by dissimilatory arsenate-reducing prokaryotes (DARPs) and the eventual dissolution of adsorbent minerals like ferrihydrite. The end result of these processes acting in concert over time and accelerated by human activities would be the release of arsenic into the aqueous phase.

Preliminary evidence does indeed suggest the presence of an anaerobic, microbial arsenic cycle in the subsurface aquifers of Bangladesh. Thus, there is an immediate need for research to provide a fuller understanding of the role(s) of subsurface microbes in mobilizing arsenic in aquifers.

Source: Science, Vol. 300, No. 5621, May 2003.

Dioxins in the Environment Alter the Body's Responses to Oestrogens

Oestrogens are steroid hormones that help to regulate the growth, differentiation and function of reproductive tissues, as well as those of other organs such as the bones, brain and cardiovascular system. Key to these diverse effects is the activation of the oestrogen receptors ERα and ERβ — members of a superfamily of receptors found in the cell nucleus — by their hormonal ligands, which include 17β-oestradiol. The ligand-activated receptors bind to the control regions (promoters) of specific genes, where they recruit co-activators or co-repressors and the machinery that brings about gene expression. The receptors thereby control the transcription of target genes and elicit a cascade of cellular events.

Mammalian cells also contain a variety of receptors that can bind and respond to toxic compounds present in the environment.

Environmental contaminants affect a wide variety of biological events in many species. Dioxins are typical environmental contaminants that exert adverse oestrogen-related effects. Although their anti-oestrogenic actions are well described, dioxins can also induce endometriosis and oestrogen-dependent tumors, implying possible oestrogenic effects. However, the molecular mechanism underlying oestrogen-related actions of dioxins remains largely unknown. A heterodimer of the dioxin receptor (AhR) and Arnt, which are basic helix-loop-helix/PAS-family transcription factors, mediates most of the toxic effects of dioxins. Now a recent study carried out by Japanese and French researchers shows that the agonist-activated AhR/Arnt heterodimer directly associates with oestrogen receptors ER-α and ER-β. This association results in the recruitment of unliganded ER and the co-activator p300 to oestrogen-responsive gene promoters, leading to activation of transcription and oestrogenic effects. The function of liganded ER is attenuated. Oestrogenic actions of AhR agonists were detected in wild-type ovariectomized mouse uteri, but were absent in $AhR^{-/-}$ or $ER\alpha^{-/-}$ ovariectomized mice. The findings of this important study suggest a novel mechanism by which ER-mediated oestrogen signaling is modulated by a co-regulatory-like function of activated AhR/Arnt, giving rise to adverse oestrogen-related actions of dioxin-type environmental contaminants.

Source: Nature, Vol. 423, No. 6939, May 2003.

A ROBUST SPECIATION METHOD FOR DETERMINING ARSENIC SPECIES IN HUMAN URINE

Arsenic exists in many chemical forms with varying degrees of toxicity. The more inorganic the form, the greater the virulence. For example, arsenate (AsV) and arsenite (AsIII) are known carcinogens. Methylated arsenic compounds monomethyl arsenic acid (MMA) and dimethyl arsenic acid (DMA) are less toxic, and the organic arsenicals arsenobetaine (AsB) and arsenocholine (AsC), commonly found in seafood, are relatively innocuous. Once these compounds are ingested, they metabolize in different ways; inorganic arsenic compounds are metabolized to DMA and MMA, whereas AsB and AsC are unchanged and are evidenced by their existence in urine. Speciation analysis, typically involving the coupling of a liquid chromatographic method to a highly sensitive detection method with multielement capabilities, such as inductively coupled plasma mass spectrometry (ICP-MS), is necessary to provide information about individual arsenic species.

Now a recent application to develop a more robust speciation method has employed a mobile phase designed to separate the six arsenic species in human urine in a single chromatographic run. In order to ensure a high sample throughput, it was essential that the mobile phases should not deposit a significant amount of salt on the sampling interface of the mass spectrometer.

Baseline separation was achieved for all six species as well as for the internal standard (potassium hexahydroxy antimonate V) in a single chromatographic run of less than 30 min., using an ammonium carbonate buffer gradient (between 10 and 50 mM) at ambient temperature, in conjunction with cation- and anion-exchange columns in series. The performance of the method was evaluated with respect to linearity, precision, accuracy, and detection limits. This method was applied to determine the concentration of these six arsenic species in human urine samples *(n = 251)* collected from a population-based exposure assessment survey. Method precision was demonstrated by the analysis of duplicate samples that were prepared over a 2-year analysis period. Total arsenic was also determined for the urine samples using flow injection analysis coupled to ICP-MS. The summed concentration of the arsenic species was compared with the measured arsenic total to demonstrate mass balance.

It is claimed that the new method resulted in acceptable performance and significant improvement over existing methods. However, additional improvements could be made.

Although the detection limits are similar or superior to those in other studies reported in the literature, further improvements in sensitivity could lower the detection limits. It may also be beneficial to employ a "mixed-bed" stationary-phase column containing both cationic and anionic elements instead of two columns to perform the separation. This would reduce the column regeneration time and possibly the species separation time.

The primary advantage of the new method is its robustness, a feature that is highly desirable in exposure, toxicology and epidemiology studies that generate large numbers of samples over a long period of time, making it a viable choice for speciation of arsenic species in urine.

Source: Environmental Health Perspectives, Vol. 111, No. 3, 2003.

The 5th Princess Chulabhorn International Science Congress
Evolving Genetics and Its Impact on the World
16-20 August 2004

Princess Chulabhorn International Science Congress Program was initiated by Professor Dr. Her Royal Highness Princess Chulabhorn to provide a forum for the exchange of the latest information and the most recent advances in research among the international scientific community. Under this program, international congresses on selected topics in science and technology are organized every 4-5 years.

The Fifth Princess Chulabhorn International Science Congress (PC-V) "Evolving Genetics and Its Impact on the World" will be held in Bangkok, Thailand from August 16-20, 2004 to commemorate the sixth cycle (72 years) of the birth of Her Majesty Queen Sirikit, the auspicious occasion when the people of Thailand celebrate and pay tribute to Her Majesty the Queen. On this occasion, the opening of the Congress will be presided over by His Majesty King Bhumibol on August 16, followed by keynote lectures to be given by distinguished scientists.

The 21st century marks the progress in the new genomic technologies and the unveiling of the entire human genome which have greatly contributed to developments in health sciences and biotechnology. The congress will address ways in which the revolution in genetics and its aftermath help to provide opportunities in the studies of diseases, the interaction between genes and the environment, and development of biotechnology.

Organizing Committee

Chairperson

Professor Dr. Her Royal Highness Princess Chulabhorn

Secretary General

Khunying Mathuros Ruchirawat, Ph.D.

Program

The scientific program will be built around the central theme **"Evolving Genetics and its Impact on the World"** which will consist of 3 main areas:-

Genetics in Health and Medicine

This will focus on the dramatic impacts that genomic research has had on modern medicine and health. It will include genetic diseases, infectious diseases, cancer, organ-specific disorders, disease susceptibility, drug discovery, and proteomic studies of disease.

Genes and Environment Interaction

Scientific and technological developments have undoubtedly improved the overall quality of life but at the same time some applications have a potential negative impact on human health and the environment. It is becoming apparent that there is an environmental component to every disease. Exposure to environmental agents may alter genetic information, gene expression or gene imprinting. These changes may also result in increased susceptibility to disease later in life. This area will focus on gene-environment interactions, such as the effect of environmental insults on the genome, as well as the use of genomic data in toxicology and risk assessment.

Genes and Biotechnology

Genomic discoveries have revolutionised biotechnology, in all its various forms, including food and agricultural biotechnology, as well as modern advances in microbiological research.

In each of these areas, plenary lectures, symposia and poster sessions will be organized. Short courses and workshops focusing on selected topics will also be organized.

Symposia (partial list)

Cancer: Integrating genomics with clinical research and therapy

Genetics: Individual risk and therapy

Liver diseases: Epidemiology and toxicology of aflatoxin B_1

Aging and neurological disorders

Post-genomic drug development

Molecular biological techniques in environmental health research

Gene-environment interaction

Molecular epidemiology: Gene-environment interaction

The use of toxicogenomic data in risk assessment

New directions in microbial research

New genetic tools to facilitate solving of complex problems

Eukaryotic cell genetics and gene regulation

Topics for Poster Sessions

Genetic and environmentally related disorders:

- *Aging*
- *Cancer*
- *Environmentally associated disorders*
- *Liver diseases*
- *Neurological disorders*

Gene therapy

Post-genomic drug development

Molecular biological techniques/diagnostics

Genetic tools and transgenic animal models

Testing and genetic susceptibility

Gene regulation

Gene-environment interaction

Toxicogenomics

Pharmacogenomics

Agricultural biotechnology

Genetically modified products

Registration

Registration fee includes admission to all scientific sessions, the Opening Ceremony and Reception on August 16, 2004 and Farewell Dinner on August 20, 2004.

The spouse/guest registration fee is only for social activities (including opening ceremony and farewell dinner) and spouse program. It does not admit individuals to scientific sessions.

Registration Fee	**US$**
Participants	350
Accompanying Persons	100
Students	150

Call for Abstracts

You are invited to submit abstracts for poster presentation. The deadline for submission of hardcopy or on-line abstracts: **June 1, 2004**.

Further information will be given in the Second Announcement.

The Second Announcement

A Second Announcement including instructions for submitting abstracts, registration and accommodation forms will be mailed to those who return the attached pre-registration form or fill out the on-line pre-registration form.

Language

The official language of the Congress is **English**.

Additional information:

Please check PC-V website at *http://www.cri.or.th/~pc5*

The Secretariat

THE 5th PRINCESS CHULABHORN INTERNATIONAL SCIENCE CONGRESS

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Health Effects of Battlefield Uranium

Twelve years after "depleted" uranium was first used in weapons of war, there is still no consensus with regard to the health effects on members of the armed forces who are exposed to fall-out from the use of such weapons.

The US Department of Defense (DOD) maintains that weapons containing "depleted" uranium are as safe as other forms of live ammunition. The Institute of Medicine (IOM) has given qualified reassurance of this claim but states that available studies of potential health effects are too limited and have too many shortcomings to allow firm conclusions.

Uranium weapons are useful because they pack an unmatched punch—at a density 1.7 times that of lead, a shaft, or "penetrator" of uranium fired in rounds from an A-10 warplane or in shells from an M1A1 Abrams tank can pierce armor nearly impervious to conventional weapons. Because the high-density projectiles can be fired from long range, military officials say they help keep US soldiers out of harm's way. And uranium holds another advantage over other heavy metals: it is cheap and plentiful, as tons of it pile up at uranium enrichment and reprocessing plants each year.

But the added punch may carry a health toll. When a bullet or shell with a uranium penetrator smashes into armor, the shell peels away and the penetrator sharpens, spraying a cloud of uranium oxide dust—a chemically toxic, weakly radioactive heavy metal. Soldiers caught in the shrapnel can be peppered by pinpoint fragments, while those located further from the impact may still inhale the dust.

In 1999 the RAND Corporation, a nonprofit research organization founded by DOD, published a review of findings on the health effects of battlefield exposure to "depleted" uranium. While finding no evidence of adverse health effects, the authors recommended continued long-term clinical and epidemiological research.

An IOM report from 2000 presented more specific conclusions. The authors state that the limited evidence available suggests that battlefield uranium exposure does not increase the risk for lung cancer or renal dysfunction. However, a dearth of robust studies stymied examination of other health concerns. The IOM panel wrote that there is insufficient evidence to evaluate possible links to lymphatic and bone cancers, nervous system diseases, nonmalignant respiratory diseases, and a host of the other health outcomes.

In 2002, a panel of scientists appointed by the Royal Society in London completed a two-part analysis. The panel examined worst-case scenarios, such as that of a soldier inside a vehicle hit by uranium munitions. In that case, the lifetime risk for lung cancer could be doubled (the lifetime risk of dying from lung cancer in the United States is 1 in 250; it is 1 in 6 for long-term smokers); kidneys could fail within days; and DNA might also be damaged. However, the panel was careful to point out that cancer rates among exposed veterans would be nearly impossible to distinguish from normal rates; and that they were unaware of any cases of kidney failure among Gulf War veterans.

Together, these reports from the RAND, the IOM, and the Royal Society raise more questions than they answer.

Today, hundreds of thousands of soldiers may face these unanswered questions anew. Despite official reassurances about the safety of uranium weapons, a cloud of uncertainty hangs over them; the acute and long-term dangers are simply not well understood.

Source: JAMA, Vol. 289, No. 13, April 2003.

THE USE OF RICIN IN CANCER TREATMENT

(Continued from page 4)

fivefold higher dose of this mutant (Asn97 → Ala; N97A) could be administered to mice without killing them. To determine whether the higher dose of RFB4-N97A would enhance antitumor activity, the researchers treated severe combined immune-deficiency (SCID) mice carrying Daudi cells with either a standard dose of RFB4-dgA, a fivefold higher dose of RFB4-N97A, or RFB4 as control. The survival with RFB4-N97A was longer than with RFB4-dgA (median ~90 versus ~75 days, P = 0.036). Thus, the researchers concluded that RFB4-N97A might be a better toxin than dgA for immunotoxin treatment in humans.

Replacement of the chemically produced dgA with a recombinant protein may simplify production of the toxin, and may also allow further improvements to it. The switch from dgA to N97A might be immediately useful in immunotoxins targeting CD19, CD25, and CD30, which in humans are also associated with vascular leak syndrome. This work may also stimulate the development of ricin immunotoxins targeted to other antigens.

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