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

INTERNATIONAL YEAR OF CHEMISTRY 2011

HRH Princess Chulabhorn was one of the researchers from 16 different countries who were honored with the presentation of the Distinguished Women in Chemistry/Chemical Engineering Award at the August 2, 2011, International Union of Pure and Applied Chemistry meeting in Puerto Rico.

The event was part of the International Year of Chemistry 2011, a yearlong celebration of chemistry and its contribution to science and society.

Events organized throughout the year celebrate the 100th anniversaries of the founding of the International Association of Chemical Societies and of the Nobel Prize in Chemistry awarded to Mme. Marie Sklodowska Curie – providing an opportunity to recognize the contribution of women researchers to chemistry.

On this landmark occasion, HRH Princess Chulabhorn delivered a keynote address entitled *"A Journey of a Female Thai Chemist"*.

In her address, Her Royal Highness stated that all available data indicate that in almost all countries in the world today women are underrepresented in science. This has been the case throughout history, and although this situation may now be changing, the change is slow. Examples of successful women scientists are rare due to lack of opportunity and encouragement rather than lack of ability and dedication.

Fortunately, in Thailand, gender discrimination is no longer a major issue for female chemists. Indeed, in Thailand women are not at all underrepresented in science in general and chemistry in particular.

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INTERNATIONAL YEAR OF CHEMISTRY 2011

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Her Royal Highness cited the example of the talent of the country's high school students: in the International Chemistry Olympiad, as well as in the Olympiads in other branches of science, female students, although smaller in number than their male colleagues, are no less a significant part of Thailand's success throughout the past two decades of these international events.

Her Royal Highness concluded her address by stating, "With the strong presence of female students in international academic competitions, we believe that these female students will one day become a significant force to drive Thailand to the forefront in science and technology for a bright and sustainable future."

Metabolites of Arsenic and Increased DNA Damage of p53 Gene in Arsenic Plant Workers

Recent studies have shown that monomethylarsonous acid (MMA) is more cytotoxic and genotoxic than arsenate and arsenite, which may be attributed to the increased levels of reactive oxygen species.

A new study has used hydride generation-atomic absorption spectrometry to determine three arsenic species in the urine of workers who had been working in arsenic plants. The researchers calculated primary and secondary methylation indexes.

Methylation and reduction reactions are involved in arsenic biotransformation. In humans, methylated and dimethylated arsenic are mainly found as metabolites in urine. It has become obvious that methylation of inorganic arsenic is not necessarily a detoxification process, but paradoxically both a detoxification and activation process. Several studies have shown an association between increased fraction of MMA in urine, probably reflecting the highly toxic MMA^{III} in the tissues, and increased risk of various arsenic-related adverse health effects.

The cytotoxic and genotoxic effects of arsenic greatly differ among their chemical species. Recent studies show that most mammalian species rapidly convert inorganic arsenic (iAs) to methylarsenic species (MAs) and dimethylarsenic species (DMAs). There are data that demonstrate that MMA, one of the methylated metabolites, result in the induction of DNA damage. It is the increased levels of reactive oxygen species that play a role in MMA^{III} induced DNA damage.

Mutations of the *TP53* tumor suppressor gene have been found in nearly all tumor types and are estimated to contribute to more than 50% of all cancers. Among the 393 codons of the human *p53* gene, 222 are targets of 698 different types of mutations. The sites of *p53* gene mutation are mainly exons 4-11. Some studies showed that, for different genotoxic compounds, base sites attacked are characteristic of themselves in *p53* gene. For arsenic, exons 5 and 8 are main regions attacked. Mutagenesis is a multistage process. Substitution mutations can be induced by base modified through alteration of pairing property.

DNA damage blocks DNA polymerase progression and increases miscoding. The effects of specific lesions on *taq* DNA polymerase fidelity and amplification efficiency have been assessed. The mean modified efficiency (MME) as a more precise method for determining PCR amplification efficiency of damaged templates was introduced. Because the MME method can detect small reductions in amplification efficiency, it may be useful in comparing the extent of damage in environmentally degraded or archival DNA specimens.

A previous study has shown that base modification in exon 5 of *p53* gene can be induced by arsenic, and the damage level of exon 5 is a useful biomarker to assess adverse health effect levels caused by chronic exposure to arsenic. In this present study, researchers attempt to determine what metabolite of arsenic may cause increased damage of exons 5, 6, or 8 of *p53* gene, and what arsenic metabolism pattern most easily causes the damage.

This study used hydride generation-atomic absorption spectrometry to determine three arsenic species in urine of workers who had been working in arsenic plants, and calculated primary and secondary methylation indexes. The damages of exon 5, 6, 8 of *p53* gene were determined by a recently developed method. Results show that the concentrations of each urinary arsenic species, and damage indexes of exon 5 and 8 of *p53* gene in the exposed population were significantly higher, but SMI was significantly lower than in the control group. Closely positive correlation was found between the damage index of exon 5 and primary methylation index (PMI = MMA/iAs), MMA, DMA, but there was closely negative correlation between the damage index of exon 5 and secondary methylation index (SMI = DMA/MMA). These findings suggested that DNA damage of exon 5 and 8 of *p53* gene existed in the population occupationally exposed to arsenic. For exon 5, important factors may include the model of arsenic metabolic transformation, the concentrations of MMA and DMA, and the MMA may be of great importance.

The study supports the argument that modified bases alter base pairing properties which lead to substitution mutations. MMA and damage of exon 5 of *p53* gene may be useful biomarkers to assess adverse health effects caused by chronic exposure to arsenic in humans.

Source: Toxicology and Applied Pharmacology, Vol. 254, Issue 1, Pages 41-47, July 2011.

POTENTIAL SOURCES FOR HUMAN EXPOSURE TO BISPHENOL-A

Bisphenol-A (BPA) is a high production volume chemical; its production volume amounted to 3.8 million tons in 2006. Almost 65% of the BPA is polymerized to the resistant plastic polycarbonate (PC) and almost 30% is polymerized to epoxy resins, which still leaves some 0.2 million tons for additional applications.

Due to its wide spread use in consumer goods and commodities, BPA is ubiquitously present in the environment and in humans. BPA has been detected in a large number of environmental compartments (e.g. surface- and wastewater, sediments and biota).

Health effects related to BPA have been extensively investigated, however, they are not fully understood yet and their interpretation is sometimes controversial. Also governmental decisions are sometimes contradictory. At the same time, Canada was the first country in the world listing BPA as a toxic substance, and the European Food Safety Authority (EFSA) could not identify new studies which would call for a revision of the current BPA tolerable daily intake of 50 µg/kg bw/day. However, the Health and Consumer Commissioner said the EFSA advice had thrown up "areas of uncertainty" which meant infant exposure to the chemical should be minimized and this led to a ban of PC baby bottles.

Though humans in the industrialized world are daily exposed to BPA, the totality of sources for human exposure is still insufficiently clarified. While exposures through PC bottles and epoxy resin coated food and beverage cans have been extensively discussed in the literature, the currently observed exposure cannot be explained by dietary exposure alone. The importance of the non-food and non-oral exposure route has also gained research interest, while some studies have already confirmed a contribution of alternative exposure pathways, e.g. dermal absorption.

This review summarizes the numerous applications of BPA and the potential sources for human exposure. The exposure to humans is believed to occur mainly through food contamination from PC bottles, as well as through food and beverage cans coated with epoxy resins. However, there seems to be a discrepancy between exposure assessments based on biomonitoring data and those based on food/drink concentrations. Several recent studies indicated also the importance of non-food sources. Although the main use of BPA is polymerization to PC and epoxy resins, it can also be used as an additive, from which it may be easily released. Several studies have already provided scientific evidence for the contribution of sources for dermal BPA absorption such as thermal paper where BPA is used as an additive. Polymeric applications of BPA require further investigation regarding the amounts of BPA present, as well as the factors affecting its release and potential dermal or non-dermal exposure from these sources. It is clear that not all sources of BPA have been identified.

Through the recycling of thermal paper, BPA is expected in recycled paper products. One study found BPA in toilet paper made from recycled paper in concentrations between 3.2 and 46.1 µg/g dry matter and in waste paper in concentrations between 0.09 and 4.23 µg/g dry matter. This implies that toilet paper can be an important source of BPA emission to waste water. Moreover, BPA was found to occur in aquatic systems and landfill leachates. Another study found the BPA levels in paper and cardboard containers used for take-away food to range from 0.05 to 1817 ng/g at a detection frequency of 45%. BPA could also be detected in kitchen roll from recycled paper (0.6-24 µg/g), while kitchen roll from virgin paper contained no or negligible BPA concentrations.

Since epoxy pipe-linings are widely used for the rehabilitation of drinking water pipes, concern was raised about the presence of BPA in tap water, and researchers detected BPA in tap water from six different drinking water plants in Guangzhou, China in concentrations between 15 and 317 ng/L.

Although BPA has a low vapor pressure, absorption into the core portion of airborne particles was suggested and therefore inhalation of BPA can occur. For the normal population, inhalation is expected to have a minor contribution. However, for an occupationally exposed population, inhalation can have a significant contribution. For comparison, mean indoor air levels in child daycare centers in North Carolina, US were below 1 ng/m^3, while a concentration of 208 ng/m^3 was measured in an air sample from a plastic workplace. Higher urinary BPA levels were already reported for epoxy resin sprayers compared to workers whose work did not involve use of BPA-containing materials.

Exposure assessments for BPA have mainly focused on oral intake through epoxy resin coated food cans or PC bottles. Some recent findings highlight the importance of non-food sources or non-oral exposure. Several studies already provided scientific evidence for the dermal absorption of BPA present in thermal paper. Yet, the use of BPA in several polymers, the amounts of free BPA present, factors affecting its release, and potential dermal or non-dermal exposure from various sources are not well known. The additive applications also need further investigation.

Source: International Journal of Hygiene and Environmental Health, Vol. 214, Pages 339-347, September 2011.

Exposure to Paraquat and Maneb Increases Risk of Developing Parkinson's Disease

Epidemiological and *in vivo* studies have demonstrated that exposure to the pesticides, paraquat (PQ) and maneb (MB), increase the risk of developing Parkinson's disease (PD) and cause dopaminergic cell loss, respectively.

PQ is a well-recognized cause of oxidative toxicity. It is one of the most widely used herbicides in the world and is quick acting and nonselective.

Over the past two decades, epidemiological studies have reported an increased risk of developing PD in residents of rural areas that have been exposed to pesticides.

These observations have led to development of an environmental hypothesis of PD in which chemical agents present in the environment are proposed to selectively damage dopaminergic neurons in the substantia nigra pars compacta, thus promoting the progression and development of PD.

PQ toxicity is caused by oxidative stress due to redox cycling, a process in which it accepts an electron from an appropriate donor and subsequently reduces O_2 to produce superoxide anion radical and regenerates. Superoxide and related reactive oxygen species (ROS) cause toxicity by radical and nonradical mechanisms, with glutathione and thioredoxin antioxidant systems being critical for protection. Additionally, mitochondria are a major source of PQ-induced ROS production in neurons.

The fungicide MB, a manganese-containing ethylenebis (dithiocarbamate) compound, is used to treat numerous plant pathologies. Information regarding the mechanism of toxicity of this environmental toxicant is limited, but MB alters the toxicokinetics of PQ in mice, inhibits complex III of the mitochondrial electron transport chain in isolated mitochondria from rat brain, and causes mitochondrial dysfunction in primary mesencephalic neuron culture. Because complex III is a major site of ROS production in mitochondria, MB could potentiate mitochondrial ROS production and exacerbate PQ toxicity.

The purpose of this study was to determine if MB potentiates oxidative stress caused by PQ, thus providing a mechanism for enhanced neurotoxicity by the combination. The results show that PQ alone at a moderately toxic dose (20-30% cell death in 24h) caused increased ROS generation, oxidation of mitochondrial thioredoxin-2 and peroxiredoxin-3, lesser oxidation of cytoplasmic thioredoxin-1 and peroxiredoxin-1, and no oxidation of cellular reduced glutathione/oxidized glutathione (GSH/GSSG). In contrast, MB alone at a similar toxic dose resulted in no ROS generation, no oxidation of thioredoxin and peroxiredoxin, and an increase in cellular GSH after 24h. Together, MB increased GSH and inhibited ROS production and thioredoxin/peroxiredoxin oxidation observed with PQ alone, yet resulted in more extensive (>50%) cell death. MB treatment resulted in increased abundance of nuclear Nrf2 (redox-sensitive transcription factor) and mRNA for phase II enzymes under the control of Nrf2, indicating activation of cell protective responses. The results show that MB potentiation of PQ neurotoxicity does not occur by enhancing oxidative stress and suggests that increased toxicity occurs by a combination of divergent mechanisms, perhaps involving alkylation by MB and oxidation by PQ.

Source: Toxicological Sciences, Vol. 121, Issue 2, Pages 368-375, June 2011.

LONG-TERM EFFECTS ON HUMORAL IMMUNITY AMONG WORKERS EXPOSED TO TCDD

Epidemiological studies have shown inconsistent effects on immunological parameters in subjects exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).

Studies have shown a possible relationship between occupational exposure to chlorophenoxy herbicides, chlorophenols and their contaminants (eg, dioxins and furans) and risk of several cancers including soft tissues sarcomas, non-Hodgkin's lymphoma (NHL) and lung cancer. Manufacture of some chlorophenoxy herbicides (eg, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)) has been prohibited in many countries because of possible contamination with polychlorinated dibenzo-p-dioxins (PCDDs), including the highly toxic TCDD. TCDD is an unwanted by-product of numerous chemical reactions involving chlorine compounds and is highly persistent in the environment and biological organisms.

Immunotoxicity related to TCDD has been described in several animal studies. Results of human epidemiological studies on this topic, however, have been largely inconsistent. For example, several epidemiological studies, but not all, have shown perturbations in immunoglobulin levels in TCDD exposed subjects. Immune suppression increases susceptibility to various infectious diseases and lymphoproliferative diseases such as lymphoma. It is well known that severe immune deficiency in humans increases the risk for NHL. Moreover, NHL has been associated with exposure to chlorophenoxy herbicides or chlorophenols in several case-control and some recent cohort studies, particularly with TCDD exposure. Therefore, one could hypothesise that the possible link between NHL and TCDD might be governed by TCDD related perturbations (ie, suppression) of the immune system.

Besides possible effects on immunological parameters, several animal and *in vitro* studies have suggested that TCDD may exacerbate atopic conditions, in particular atopic dermatitis. However, to date only a few investigations have studied TCDD

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THE ANTIOXIDANT PROPERTY OF VITAMIN E IN ENDOSULFAN AND CHLORPYRIFOS TOXICITY

Of the various pollutants present in the atmosphere, heavy metals and pesticides are considered toxic to livestock as well as human beings. However not all pesticides are actually toxic for humans or other non-target species. In this regard, a study was carried out into the antioxidant property of vitamin E in endosulfan and chlorpyrifos toxicity.

Endosulfan is an organochlorine insecticide and acaricide, and acts as a contact poison in a wide variety of insects and mites. It is easily absorbed by the stomach, lungs and through the skin, which means that all routes of exposure can pose a hazard. It enhances the effect of estrogens and acts as an endocrine disruptor, causing reproductive and developmental damage in animals and humans, as well as cancer. Recent studies indicate that pesticide intoxication produces oxidative stress by the generation of free radicals and by inducing tissue lipid peroxidation in mammals and other organisms. Researchers have reported the oxidative stress inducing effects of endosulfan, with an increase of lipid peroxidation and a significant alteration in glutathione (GSH) redox cycle in cerebral and hepatic tissues of rats.

The organophosphorus (OP) insecticide, chlorpyrifos, is widely used for a variety of agricultural and human health applications. OPs produce a wide range of toxicity in mammals by inhibiting acetylcholinesterase (AChE), and the consequent accumulation of the neurotransmitter acetylcholine (ACh) in synaptic junction leads to excessive stimulation of postsynaptic cells causing cholinergic toxicity. In fact, one of the molecular mechanisms of the toxicity of some pesticides seems to be lipid peroxidation. As a consequence, these compounds can disturb the biochemical and physiological functions of the red blood cells (RBCs). The susceptibility of RBC to oxidative damage is due to the presence of polyunsaturated fatty acid, heme iron and oxygen, which may produce oxidative changes in RBC.

Major contributors to non-enzymatic protection against lipid peroxidation are vitamin E and vitamin C, well-known free radical scavengers. Vitamin E is a lipid soluble, chain-breaking antioxidant playing a major protective role against oxidative stress and prevents the production of lipid peroxides by scavenging free radicals in biological membranes. Some investigators reported that administering vitamin E may be useful in controlling the toxic effect of insecticides and chemicals. With these points in mind, the present study was planned to establish the antioxidant role of vitamin E on oxidative stress induced in rat RBCs by pesticides.

Ten male healthy rats weighing about 100-200 g were used in the study. About 3 ml peripheral blood was obtained from ocular vein/heart puncture of rats, using ethylenediaminetetraacetic acid (EDTA)-sodium salt as the anticoagulant for assays. Blood was centrifuged at 2000 rpm for 10 min. Plasma and buffy coat was removed. Subsequently, the cells were washed three times with phosphate buffered saline, pH 7.2. The final red cell suspension was taken in test tubes for chlorpyrifos, endosulfan and vitamin E treatment, each in triplicate set. Pesticides and vitamin E (chlorpyrifos, endosulfan, vitamin E, chlorpyrifos and vitamin E, and endosulfan and vitamin E) were dissolved in dimethyl sulfonic acid (DMSO) and the solution was made up 100 ppm stock solution of each group, respectively. The above combinations were mixed and the desired 1 ppm concentration was made in all groups (DMSO 5% of total volume and test was performed in triplicate set). Also, 5% DMSO was dissolved/mixed in control group. The tubes were incubated for 3 hours at 37^{o}C in a shaking water bath. At the end of incubation, the tubes were removed and subjected to biochemical analysis.

Data pertaining to hemoglobin (Hb) concentration and enzyme activity show there was significantly higher Hb level in the endosulfan exposed group and lowest level was found in the control group (without exposure and treatment) erythrocyte cell lysate. The level of lipid peroxides (LPO) in cell lysate was significantly greater in the group exposed to endosulfan and chlorpyrifos, and lowest in the control group. The LPO level in cell lysate reduced significantly in vitamin E treated groups as compared to their respective non-treated pesticide exposed group. The superoxide dismutase (SOD) activity was significantly lower in endosulfan and chlorpyrifos exposed groups. Rats' erythrocytes exposed to endosulfan and chlorpyrifos at 1 ppm concentration and on treatment with vitamin E showed greater SOD activity compared with non-treated pesticide exposed group. It was with duration treatment (3 hrs) vitamin E treatment improved SOD activity with duration treatment in both pesticide groups. However, vitamin E treatment in both pesticide exposures increased catalase (CAT) activities in erythrocytes. The CAT activity in erythrocytes decreased gradually following both the pesticide exposures. The glutathione-S-transferase (GST) activity in erythrocytes increased significantly in pesticide exposed groups as compared to their respective vitamin E treated group. The GST activity was significantly higher in endosulfan and chlorpyrifos exposed groups.

These studies comprise a part of comparative toxicology studies aimed to identify the biochemical and physiological alterations in RBCs exposed to two different pesticides. The approach is known to help in understanding the mechanisms of toxic action due to xenobiotics.

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Effects of Subchronical Exposure to Low Doses of Heavy Metals in Rats

Lead (Pb), cadmium (Cd) and thallium (Tl) are ubiquitous air and water pollutants and are associated with a multitude of adverse health effects.

The main affected target organs per metal are the central nervous system, as well as the haematological, skeletal and gastrointestinal systems for Pb, kidney, lung, skeletal system, placenta and also central nervous system for Cd and epidermal, gastro-intestinal, renal, peripheral and central nervous systems for Tl. The severity of damage depends on the time and level of exposure, plus the rate of absorption, age and individual susceptibility. Although several adverse health effects of heavy metals have been known for a long time, excessive human and environmental exposure to these elements continues.

A variety of mechanisms have been attributed to heavy metal-induced toxicity and they have often been related with the generation of reactive oxygen species (ROS), because the increase of ROS production involves an imbalance between free radical generation and depletion of antioxidant defense systems. Increase of ROS usually leads to oxidative stress, which results in alteration of the electron transport chain, followed by oxidative deterioration of biological macromo-lecules with subsequent cellular damage in organs and tissues, including muscle tissue. It has been reported that muscle contractions cause an increase in ROS because muscle requires a large amount of adenosine triphosphate (ATP), which is almost entirely generated by mitochondrial oxidative phosphory-lation. The mitochondrial electron transport chain contains several redox centres that may leak electrons to molecular oxygen, serving as the primary source of superoxide production in most tissues. Studies indicate that complex I (NADH: ubiquinone oxidoreductase) and complex III (ubiquinol:cytochrome C oxidase) are regarded as important sites of superoxide production.

It is widely recognized that various types of muscle fibres show differences in morphological, con-tractile, and biochemical properties. A major subdivision can be made using standard histochemical methods. Type I fibres are slow, contracting and relaxing fibres; whereas type II fibres are fast, have a high oxidative capacity and are needed for generating the high power and shortening velocity required for rapid motor activity. These fibres can be divided into several subgroups. Rat lower hindlimb muscles, except soleus, are dominated by “fast” fibres, and the pattern of “slow” type I fibre regionalization was earlier reported; likewise, structural and functional characteristics of muscle fibres can be modified in response to several physiological and pathological condi-tions.

Little has been reported about muscle damage by effects of heavy metals in humans and/or animals. An early study reported myopathic changes, which include fibre necrosis, fibre and central nucleation that involves axon degeneration of nerve in humans exposed accidentally to Tl. This result correlates with an experimental study in which muscle fibres from rats exposed to Tl show loss of their transverse striation, phagocytic infiltration, hyaline degeneration and progressive muscular atrophy. Likewise, it has been reported that workers exposed to Pb complain of muscle weakness, cramps and joint pain. It has also been reported that Cd produces myocardial oedema, degeneration and necrosis secondary to ischaemia. In the present work, his-tochemical alterations produced in skeletal muscle of rats exposed subchronically to low doses of heavy metals (Pb, Cd and Tl) were examined in detail.

The results showed that the administration of heavy metals via drinking water for 90 days induces slight changes in the activity of enzymes of complexes I and IV of the respiratory chain and produces a decrement in the percentage of fibre type I (Pb group) and an increase of fast-fatigue resistance (FFR) (Pb and Tl groups) on rat muscle. Studies in animals and humans exposed to Pb, Cd, and Tl have reported that these metals are able to increase the generation of ROS in different tissues, mainly due to a conjugation of the increment of lipid peroxidation and the decline of the antioxidant defense system. Mitochondria have largely been demonstrated to be the major source of ROS generation and alteration on enzymatic function (for example, complexes I and IV of respiratory chain) can produce alterations on the morphology of the structure or these organelles. In this study, researchers suggest that increments in oxidative stress, generated mainly by the mitochondrial pathway, can produce cellular damage and alter the activity of mitochondrial oxidative phosphorylation enzymes in the muscular fibres. It is also possible that these changes in energy metabolism are mediated by a lack of oxygen, which can induce muscle fibre type transformation. It has been observed that excess of ROS production in muscle, which is generated during excessive exercise, causes oxidative stress and damages cellular components because muscle contraction requires a large amount of ATP, which is generated by mitochondria.

Environmental exposure to Tl occurs at low concentrations; it is rapidly and completely adsorbed, distributed and retained in all tissues with rather slow elimination. Several reports have discussed the role of ROS formation in different tissues exposed to Tl and the induction of oxidative damage. It has been proposed that Tl uncouples mitochondrial electron transport, so inducing loss of mitochondrial transmembranal potential. This, in turn, increases the oxidant content in mitochondria with subsequent release of cytochrome C which impairs mitochondrial functioning, which is considered an event that precedes mitochondrial damage. The study found a significant increase in the number of ragged red fibres in the group of rats treated with Tl; these fibres are distinctive in skeletal muscle and are present when there are biochemical defects which involve the respiratory chain, and are considered markers of mitochondrial damage. This suggests that both complexes I and IV of the mitochondrial respiratory chain are vulnerable to low Tl intoxication thus altering the activity of these enzymatic complexes.

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LONG-TERM EFFECTS ON HUMORAL IMMUNITY AMONG WORKERS EXPOSED TO TCDD

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exposure in relation to prevalence of atopic diseases in humans.

Now in a new study researchers have investigated changes in humoral immunity and prevalence of atopic diseases among workers from a Dutch historical cohort occupationally exposed to chlorophenoxy herbicides and contaminants including TCDD.

45 workers who had been exposed to high levels of TCDD in the past and 108 non-exposed workers, 39 from the same factory as the exposed subjects (internal control group) and 69 from a comparable factory but without TCDD exposure (external control group), were included in the study. Blood immunoglobulin (Ig) and complement factor (C) concentrations and specific IgE antibodies to a panel of common allergens were measured using quantitative nephelometry or ELISA. TCDD plasma levels were measured and back-extrapolated to the time of last exposure (TCDDmax) using a one-compartment first order kinetic model.

The results showed a borderline significant negative association between both current and predicted TCDD levels and C4 was found in multivariate analyses. History of eczema was significantly associated with current TCDD levels in both crude and adjusted models.

The study showed that plasma TCDD levels were not associated with markers of humoral immunity with the possible exception of a borderline significant decrease in C4 levels. Given the observed heterogeneity in results from different studies, it can be hypothesised that perturbation of the humoral immune response due to TCDD exposure, if it occurs at all, may be subtle. However, the immune system is complex with both humoral and cellular components playing an important role. Therefore, more in-depth characterisation of both the humoral (eg, cytokine expression profiles) and cellular components might provide additional insights into the possible immunological effects of TCDD in humans.

Source: Occupational and Environmental Medicine, Vol. 68, Issue 6, Pages 419-424, June 2011.

THE ANTIOXIDANT PROPERTY OF VITAMIN E IN ENDOSULFAN AND CHLORPYRIFOS TOXICITY

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There are several pathways by which the pesticide is thought to induce oxidative stress. It inhibits the mitochondrial electron-transfer chain reaction, leading to accumulation of semi ubiquitous, which enables it to transfer one electron to molecular oxygen to form superoxide radicals. Further, it may also interfere with cellular antioxidant defense system via alteration in activities of antioxidant enzymes, viz., SOD and CAT and status of GSH. LPO level in rat erythrocytes treated with vitamin E was comparable to that of control, suggesting that endosulfan and chlorpyrifos act as catalysts in the oxidative deterioration of biological macromolecules and this effect could be minimized by treatment with antioxidants.

These indirectly suggest an increased production of oxygen free radicals in erythrocytes. Highly reactive oxygen metabolites, expecially hydroxyl radicals, act on unsaturated fatty acids of phospholipid components of membranes to produce malondialdehyde (MDA), a lipid peroxidation product. Chlorpyrifos has been reported to induce oxidative stress, as shown by enhanced MDA production. The use of vitamin E in conjunction with chlorpyrifos affected such an elevation in the level of MDA, bringing it within the normal limits. The normalization of LPO following vitamin E treatment is very likely due to its antioxidant properties.

The results revealed that endosulfan and chlorpyrifos caused a statistically significant decrease in SOD activity in rat erythrocytes compared to the control value. Supplementation of vitamin E to endosulfan and chlorpyrifos treated groups of rat erythrocytes normalized the levels of SOD. Treatment with vitamin E alone did not result in significant alteration in SOD activity compared to control treatment. The decrease in the activity of SOD in chlorpyrifos-intoxicated animals may be attributed to the consumption of this enzyme in converting O_2^- to H_2O.

In comparison to the control group, the activity of GST was significantly higher in chlorpyrifos treated rat erythrocytes. Considering that GSTs are detoxifying enzymes that catalyze the conjugation of a variety of electrophilic substrates to the thiol group of GSH, producing less toxic forms, the significant increase of GST activity in the rat erythrocytes after exposure to endosulfan and chlorpyrifos may indicate sufficient detoxification of pesticide in rat erythrocytes while the use of vitamin E with pesticide approaches the control group.

CAT is ubiquitously present in a wide range of aerobic cell types, with the highest activities in mammals being found in liver, kidney and RBCs. Endosulfan and chlorpyrifos caused significant decrease in CAT activity in erythrocytes of rats in this study. In comparison, vitamin E with endosulfan and chlorpyrifos treated erythrocytes maintained the levels of CAT at the normal values.

In conclusion, treatment with vitamin E potentially reduced the free radicals in erythrocytes and ameliorated the oxidative stress as evidenced from lower concentrations of LPOs and GST and higher activities of SOD and CAT in erythrocytes. The efficacy of vitamin E in ameliorating pesticide-induced oxidative stress was higher for chlorpyrifos than for endosulfan.

Source: Toxicology International, Vol. 18, Issue 1, Pages 73-76, Jan-Jun 2011.

PROTECTIVE EFFECTS OF ZINC AND SELENIUM AGAINST BENZENE TOXICITY IN RATS

Benzene is an important pollutant compound, present in both occupational and general environment. It is used as a constituent in motor fuels, as a solvent for fats, waxes, resins, oils, inks, paints, plastics, rubber, in the extraction of oils from seeds and nuts, and in photogravure printing.

Workers employed in industries that manufacture or use benzene are exposed to its highest levels. The known toxicity of benzene implicates the production of oxygen radicals or reactive oxygen species (ROS). ROS play an important role in the etiology of many diseases and aging that is associated with a high risk of micronutrient deficiency; it may also affect nutrient intake, increase the need for specific nutrients, and/or interfere with their absorption, storage, and utilization. As a response to the production of ROS, the human body develops antioxidant mechanisms, these include enzymes that have antioxidant activity. These are enzymes that provide cellular protection against damage due to superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px). Animal studies have shown that antioxidant enzyme levels are variable depending on the availability of antioxidants in diet. To achieve proper function of these enzymes, adequacy of some micronutrients such as zinc (Zn) or selenium (Se) is essential. Zn is a critical component of biomembranes. It is essential for proper membrane structure and function, activity of numerous enzymes and plays an important role in regulation of cellular glutathione that is vital to cellular antioxidant defenses. Evidence also suggests that additional selenocompounds would be beneficial in some health conditions.

The present study investigates the protective role of Zn and Se in attenuating benzene-induced toxicity in rats. Male Sprague-Dawley rats were injected with benzene (0.5 mL/kg body weight ip) and received a diet supplement containing Zn and Se. Several hematological and biochemical parameters (representing antioxidant status) were estimated. Histopathological examinations were performed. Results showed that food intake and body weight gain of benzene-injected rats were significantly lower than that of the control rats. Benzene-injected rats showed increased plasma malondialdehyde (MDA) and decreased activity of GSH-Px, catalase, SOD enzymes, as well as reduced glutathione (GSH) when compared to the control group. Histopathological investigations revealed structural changes in benzene-injected rats' liver. Supplementation with Zn and Se resulted in a significant decrease in MDA, elevation in GSH, GSH-Px, SOD and catalase levels.

The present study suggests that feeding a diet supplemented with Zn and Se prevents benzene toxicity.

The results show that benzene caused an increase in the level of lipid peroxidation products (MDA), decrease in the activity of antioxidant enzymes in blood and induced hepatic injury. Zn and Se supplementation provides protection against benzene-induced oxidative stress as concluded from the decreased levels of MDA, while the activities of antioxidant enzymes in blood were increased. Therefore, Zn and Se may diminish the occurrence of necrosis, fibrosis and cirrhosis induced by benzene. Based upon these results, this study suggests that the combined effect of Zn and Se provide protection against benzene toxicity.

Source: Toxicology and Industrial Health, Vol. 27, Issue 6, Pages 537-545, July 2011.

Effects of Subchronical Exposure to Low Doses of Heavy Metals in Rats

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The results reported in this study, which were obtained by histochemical methods, showed slight changes on the activity of respiratory chain enzymes and a significant increase of FFR of muscular fibres on rats exposed to low-doses of Tl, Cd and Pb, for 90 days. These data suggest that histochemical changes can be associated with a potential increment of free radicals due to heavy metal chronic exposure. Further studies with elevated doses and other exposure times are required in order to evaluate the severity of the effects of heavy metals on muscular fibres.

Source: Environmental Toxicology and Pharmacology, Vol. 32, Issue 1, Pages 107-112, July 2011.

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