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"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

HRH PRINCESS CHULABHORN RECEIVES SPECIAL AWARD BY THE WORLD ACADEMY OF ART AND SCIENCE

This prestigious international award was granted to Her Royal Highness Princess Chulabhorn in recognition of her contributions to science.

The award was conferred at the General Assembly of the World Academy of Art and Science in Hyderabad, India, on 18 October 2008.

In accepting this honor before a congregation of distinguished members of the Academy, Her Royal Highness stated, "I wish to express my sincere thanks and appreciation to all those who contribute to the work of the Chulabhorn Research Institute in Thailand, including the network of collaborating agencies, institutes and individuals throughout the world, who assist in our work".

In her address to the General Assembly, Her Royal Highness described the role of science and technology in the protection of the environment, a critical issue in the 21st century. Her Royal Highness emphasized the fact that, "while advances in science and technology drive economic and social development, human activities also have a significant impact on the environment and ecosystem. Indeed, the human impact on our planet, if left unchecked, may threaten the finite resources on which we depend for life itself."

This year, the program of the four day meeting of the General Assembly had the theme "The Anthropocene Crisis: Perils and Possibilities of the 21st Century".

Topics covered in the plenary sessions were Defining the Anthropocene Epoch; Dealing with Climate Change: Progress and Stasis; Change and Change Agents; and Planetary Transitions: A New Paradigm.

IN VITRO AND *IN VIVO* REDUCTION OF SODIUM ARSENITE INDUCED TOXICITY BY AQUEOUS GARLIC EXTRACT

Epidemiological studies of populations from arsenic exposed areas confirm a wide variety of adverse health outcomes linked to arsenic exposure. The earliest observed physical manifestations of arsenic toxicity are skin lesions including melanosis and hyper-keratosis, which can later lead to skin cancer such as Bowen's disease, basal cell, and squamous cell carcinomas. Evidence also suggests that ingested inorganic arsenic very likely causes various other forms of internal cancers. This has led the International Agency for Research on Cancer to classify arsenic as a group 1 human carcinogen. In addition, there is a considerable debate about several non-cancerous effects that may result from exposure to arsenic such as hypertension, diabetes, cardiovascular disease, anemia, neurologic disorder, and liver and kidney diseases. Toxic effects of arsenic are mediated primarily by triggering the production of reactive oxygen species (ROS), inhibiting the activity of enzymes like superoxide dismutase and catalase, leading to alterations in cells' intrinsic antioxidant defenses; and resulting in oxidative stress or disturbed antioxidant/pro-oxidant ratio. Arsenite also has a high affinity for sulfur-containing ligands and is known to disrupt the activity of certain enzymes such as pyruvate dehydrogenase, glutathione reductase and thioredoxin reductase.

As the prevalence of heavy metal exposure was increasingly recognized and identified in individuals seen in private practice clinics, the need for effective prevention or treatment simultaneously increased. The current approved clinical intervention method is to give chelating agents that form an insoluble complex with arsenic and remove it from arsenic-burdened tissues. British Anti-Lewisite (BAL), a dithiol compound, having a strong chelating affinity for arsenic has long been the drug of choice. But, the use of BAL is very much compromised due to its adverse side effects like mucosal burning sensations; increase in blood pressure; nausea and vomiting; headache; conjunctivitis; lacrimation; and chest pain. These disadvantages resulted in the development of analogs of BAL, i.e. meso 2,3-dimercaptosuccinic acid and sodium 2,3-dimercaptopropane 1-sulfonate. However, because of their hydrophilic or lipophobic properties, they neither cross the cell membrane nor capture intracellular arsenic. In order to address this problem most effectively, drugs with lipophilic properties should be tested against arsenic poisoning. However, a potentially effective remedy is still not available.

The beneficial health properties of garlic (*Allium sativum* L.), a major component of many Asian diets, its antioxidant activities, accredited to the biologically active lipophilic sulfur-bearing compounds like allicin, *S*-allylycysteine (SAC), diallyl-di-sulfide (DADS) and diallylsulfide (DAS) has encouraged researchers to look into its anti-arsenic activities. A few previous reports have been restricted only to the anti-clastogenic property of garlic against arsenic but have not delved deep into any detailed or mechanistic study. In a recent study, the relevant aspects of arsenic exposure are analyzed; as is the potential of aqueous garlic extract (AGE) in mitigating the damage of arsenic induced toxicity explored, both in *in vitro* and animal studies. The potential of AGE in normalizing arsenic induced oxidant stress is also evaluated, along with the arsenic chelating capacity of the organosulfur compounds constituting AGE.

Interestingly, the researchers found that AGE application led to a decrease in the parameters indicative of arsenic-mediated oxidative stress. An increase in reduced glutathione (GSH) concentration coupled with a concurrent decrease in blood myeloperoxidase (MPO) and ROS level is indicative of the curative potential of AGE. Chemo-prophylactic efficacy was also recorded with AGE with respect to lipid peroxidation and antioxidant enzymes in ovary, liver and kidney tissue. Recently, hypoglycemia with decreased liver glycogen, liver pyruvic acid has been demonstrated to be involved in short term exposure to inorganic arsenic.

Garlic and garlic extracts, used for millennia in folk medicine, are reported to provide protection against free radical damage in the body through their components' antioxidant activities. SAC, for example, is reported to suppress the formation of superoxides, while DADS and DAS all scavenge hydroxyl radicals, enhance *in vivo* endogenous antioxidant system and prevent oxidative stress. Hence, the probable mechanism underlying the protective effect of garlic could primarily be by virtue of the powerful anti-oxidant activity of garlic or its components as manifested by the competency to diminish arsenic-induced ROS and lipid peroxidation (LPO) generation. However, the activity of various sulfur compounds could not alone be responsible for the anti-oxidant activity of garlic; it is more likely the consequence of synergism of various compounds. With recent scientific findings, including the pharmacokinetics and metabolism of organosulfur compounds in garlic, revealing that allicin, the most abundant thiosulfinate may not be biologically active inside the body and stomach fluids can destroy the enzyme, alliinase, in raw garlic which is necessary to generate allicin; therefore, it is logical that compounds other than allicin can also be responsible for the benefits. SAC appears to be a very promising compound with good absorption and antioxidant activities. The pharmacokinetic studies of SAC demonstrated rapid absorption and almost 100% bio-availability after oral administration and hence this compound may have played an important role in garlic's antioxidant effects. Even DADS and DAS can also be potent candidates, which are reported to have chemo-preventive action against human cancers. The researchers are on the process of identifying the individual components of AGE participating in quenching of the free radicals.

Source: Food and Chemical Toxicology, Vol. 46, Issue 2, February 2008.

Genotoxic Effects of Dental Fillings in Humans

Dental fillings provide a major iatrogenic exposure to xenobiotic compounds, because the prevalence of restored surfaces is very high in developed countries, where millions of restorative procedures are performed annually. Biocompatibility is the principal requisite for a successful dental restorative treatment, but potential adverse effects on human health present a serious problem.

Amalgam, which was introduced more than 150 years ago, is the most frequently used material as a tooth filling restoration. In spite of the availability of new materials, today amalgam is still a popular restorative owing to its wide potential applications, easiness of manipulation, adequate mechanical properties and relatively low cost. Conventional dental amalgam is a mercury (Hg) and silver-based alloy that consists of ~50% Hg, 35% silver, 15% tin, plus copper and zinc in various amounts. Amalgam may also contain traces of cadmium, platinum and palladium. It is widely accepted that amalgams are the main source of human exposure to Hg and they contribute substantially to the load of this metal in human body tissues. Several investigations have shown that elemental Hg vapor can be released from hardened dental amalgam, and the urine metal concentration in non-occupationally exposed individuals is directly related to the number of filling surfaces.

Hg release in the oral cavity is a function of several factors, including temperature, chewing, brushing, biological corrosion due to bacteria, electrochemical corrosion, and saliva pH. The released Hg vapor is inhaled, absorbed by lung and gastrointestinal tissue and retained mainly in the kidney, brain and liver. Moreover, it has been observed that there is a direct absorption across the oral mucosa and by migration through teeth into tissues. The estimates of total daily intake of Hg vapor from amalgams range from 5 to 9 μg.

The toxicological consequences of long-term exposure to Hg from amalgam fillings are still a matter of debate in several countries. Despite the well-known neurotoxicity of Hg vapor, it is estimated that there are 190 million people in the US with amalgam restorations and that 70 million new restorations are placed annually.

Considering the high number of people continuously exposed for many years to the constituents of dental fillings, a recent biomonitoring study was undertaken to assess the potential genotoxicity of dental restorative material in lymphocytes of exposed subjects, as compared with matched controls. The high sensitivity of comet assay to oxidative DNA lesions, due to alkali-labile sites other than strand breaks, prompted the researchers carrying out the study to use this test for the purpose of biomonitoring.

Thus, the study examined 68 carefully selected subjects taking into account the major known confounding factors. In the 44 exposed subjects, the mean numbers of restored surfaces were 3.0 and 3.8 in males and females, respectively. Comet tail length, percentage of DNA in the tail, tail moment or Olive tail moment were two fold higher in the exposed group than in unexposed controls, with significant differences. No significant difference was observed between amalgam and composite fillings. Furthermore, as shown by multivariate analysis, the association between dental fillings and DNA damage was enhanced by the number of fillings and by the exposure time. Among the lifestyle variables, a moderate physical activity showed a protective effect, being inversely correlated to the DNA damage parameters evaluated. On the whole, the use of DNA-migration allowed the researchers to detect for the first time the potential adverse impact on human health of both kinds of dental filling constituents, the amalgams and the methacrylates. The main mechanism underlying the genotoxicity of dental restorative materials of various nature may be ascribed to the ability of both amalgams and methacrylates to trigger the generation of cellular reactive oxygen species, able to cause oxidative DNA lesions.

This biomonitoring study, using an exposure marker able to detect strand breakage, transient repair sites and alkali-labile sites, confirms the potential adverse impact of both dental filling constituents on human health. Considering the large number of people involved in this kind of iatrogenic exposure, further investigations are desirable.

Source: Mutation Research, Vol. 650, Issue 2, February 2008.

Safety Evaluation of Titanium Dioxide Nanoparticles

Many nanomaterials have been prepared and evaluated for their functions and physical and chemical properties. In particular, biocompatible materials, ultrafine microstructures, and molecularly recognized and signaling materials have been broadly studied as leading-edge and advanced materials: fullerenes and carbon nanotubes are typical examples. In addition, titanium dioxide and zinc oxide nanoparticles are used not only in materials but also in humans in UV-care cosmetics.

These nanomaterials may be categorized as non-biodegradable, and liposomes and nano- and micro-emulsions are found in labile nanoparticles.

This raises the question of whether nanomaterials are safe for humans.

Titanium and titanium dioxide are believed to be highly inert and safe, even when they are absorbed via the GI tract and skin. If they are inert and non-biodegradable, we should evaluate the titanium dioxide nanoparticles similarly to fullerenes, carbon nanotubes and asbestos. It was found from preliminary survey and experiments, however, that titanium is naturally contained in the

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The Risk of Oral Clefts from Exposure to Ozone and Other Air Pollutants

The prevalence of oral clefts varies broadly from 0.06% to 0.17% in Caucasian births. Both genetic and environmental factors play important roles in the etiology of oral clefts, and there is probably also genetic susceptibility to the effects of environmental exposures. Ozone (O_3) and carbon monoxide (CO) are toxic for the fetal development in rats and have been shown to produce skeletal malformation in animals. Air pollution may influence the development of skeletal malformation through various biologic mechanisms, including hemodynamic, anoxic events, oxidative stress, and toxicity to certain cell populations during pregnancy.

Previous epidemiologic studies have elaborated the effects of exposure to ambient air pollution during pregnancy on the risk of birth defects. A case-control study in Southern California found an association between CO exposure during the second trimester and the risk of ventral septal defects and between second-month O_3 exposure and the risk of aortic artery and valve defects, pulmonary artery and valve anomalies, and conotruncal defects. A population-based case-control study in Texas found that the risk for aortic artery and valve defects, pulmonary artery and valve anomalies, and conotruncal defects was related to second-month O_3 exposure. Both studies assessed also the relations between exposure to air pollutants and the risk of oral clefts, and reported weak positive, but statistically nonsignificant associations with O_3 exposure.

Now researchers have conducted a nationwide population-based case-control study in Taiwan to assess the effects of ambient air pollution exposure during pregnancy on the risk of cleft lip with or without palate (CL/P). The study focused on predominantly traffic-related pollutants such as nitrogen oxides (NO_x), CO, and O_3 and air pollutants mainly from other fossil-fuel combustion sources, such as sulfur dioxide (SO_2) and particles with an aerodynamic diameter of ≤ 10 µm (PM_{10}).

The study found that the risk of CL/P increased with increasing O_3 levels during the first and second month of pregnancy. The effect estimate indicating an approximately 20% risk increase per 10-ppb increase in O_3 level was stable with different combinations of air pollutants in the multipollutant models. The risk of CL/P was not related to two traffic-related pollutants (NO_x and CO) or two stationary fossil-fuel combustion-related pollutants (PM_{10} and SO_2). The results provide evidence that O_3 exposure in the most susceptible time periods in pregnancy may increase the risk of CL/P. This finding is consistent with animal toxicologic evidence of the effects of O_3.

A major challenge of this study was the imprecision of exposure assessment that was based on monthly municipal level air pollutant information. An earlier study reported that when using the municipal level exposure obtained from air pollution monitoring stations as a proxy for personal exposure, the effect estimates are in general smaller than those based on personal assessment of exposure. A plausible mechanism of information bias is that pregnant women may change residential area, which will lead to exposure misclassification. Any random migration between cases and controls might introduce nondifferential misclassification and decrease the accuracy of exposure assessment. This most likely underestimates the air pollution effects rather than introducing a positive bias in the associations.

In general, the assessment of the independent effects of different pollutants is difficult, because urban air pollution constitutes a complex mixture of several compounds. Typically, NO_x and CO concentrations are highly correlated because they both are predominantly from vehicle emissions. Similarly, PM_{10} and SO_2 are somewhat correlated, having stationary fossil combustion processes as important sources. In addition, PM_{10} may also be partly traffic related, because it is correlated with NO_x. O_3 is, as a product of photochemical oxidation, a secondary air pollutant generated in the troposphere from precursors of the vehicle emissions (nitrogen dioxide and hydrogen carbon), but the concentrations of O_3 are slightly negatively related to NO_x and CO concentrations. This enables somewhat more valid assessment of the effects of O_3 independent from other traffic-related pollutants. In the modeling, the researchers were able to control for one stationary fossil-fuel pollutant at a time as a potential confounder when assessing the effect of one of the traffic-related pollutants and vice versa.

The evidence of a positive association between the risk of CL/P and exposure to O_3, provided by the present study, is compatible with toxicologic studies one of which reported that high exposure to O_3 (> 1.26 ppm) during organogenesis reduced skeletal ossification. In rats, exposure to 0.4 ppm O_3 for 1 - 4 days lowered the serum retinol concentration by 85%, which supports the hypothesized adverse effects of O_3, because vitamin A deprivation during organogenesis is known to cause several congenital defects. The risk of CL/P was associated with the levels of O_3. The most susceptible time periods in pregnancy for the effects of O_3 were the first and second month of gestation. O_3 is a secondary pollutant in the atmosphere produced from traffic exhausts but scavenged by direct motor vehicle emissions. O_3 is a known strong oxidizing agent that can generate hydrogen peroxide, hydroxyl radicals, and superoxides. It could contribute to oxidative stress and causally influence the development of oral clefts.

The finding of a lack of association between the risk of CL/P and traffic-related (CO, NO_x) and combustion-related (SO_2, PM_{10}) air pollutant levels in the present study is consistent with the results from two previous studies in Southern California and Texas. The present study provides an original finding that the effect of exposure to outdoor air O_3 during the first and second month of pregnancy increases the risk of CL/P. Given that similar levels are encountered globally by large numbers of pregnant women, O_3 may be an important determinant of orofacial birth defects.

Source: Environmental Health Perspectives, Vol. 116, No. 10, October 2008.

Effects of Low-Level Lead Exposure on Retinal and Visual Functions

The adverse effects of low-level developmental lead (Pb) exposure on cognitive, auditory, and visual-motor function are well documented, but very few studies have examined the impact of low-level developmental Pb exposure on retinal and visual function in children. This lack of research is despite findings that retinal and visual cortical structural-functional abnormalities occur in animals after moderate-level and high-level developmental Pb exposure.

Persistent rod photoreceptor-mediated (scotopic) electroretinographic (ERG) and behavioral deficits occur in monkeys, rats, and mice after moderate-level and high-level postnatal Pb exposure (PLE). The scotopic ERG alterations are characterized by decreases in a-wave and b-wave ERG amplitude (subnormality), sensitivity, and temporal resolution. Similar ERG changes occurred in Pb-exposed workers and isolated retinas exposed to Pb^{2+}. In contrast, adult monkeys with high-level lifetime Pb exposure exhibited increased ERG b-wave amplitudes (supernormality). Moreover, a prospective epidemiologic study of children with lifetime low-level and moderate-level Pb exposure revealed that only gestational Pb exposure (GLE) showed a significant dose-dependent relationship with supernormal ERG a-waves and b-waves and increased b-wave sensitivity with no change in implicit times.

In experimental animals, supernormal scotopic ERGs are observed after the loss of retinal dopamine (DA) or zinc (Zn). For example, the destruction of dopaminergic amacrine cells by the neurotoxin 6-hydroxydopamine produced supernormal scotopic ERGs with normal implicit times. Similarly, animals administered nonselective dopamine receptor antagonists had supernormal scotopic b-waves with normal implicit times. A persistent decrease in retinal tyrosine hydroxylase immunoreactivity after lifetime Pb exposure in monkeys suggests that a loss of DA produced supernormal ERGs. Chelation of retinal Zn produced supernormal scotopic ERGs and increased b-wave sensitivity. Although no published reports have shown that scotopic ERG supernormality results from an increased number of rods, the log scotopic b-wave threshold and amplitude are linearly related to the number of rod photoreceptors and their rhodopsin content per eye. In a recent study, researchers hypothesized that GLE produced supernormal scotopic ERGs by one of these three relatively independent mechanisms: an increased number of rod photoreceptors, decreased retinal DA metabolism and/or decreased retinal Zn concentrations.

To determine the sites and mechanisms of the GLE-induced supernormal scotopic ERGs, researchers developed a new dose-response model of GLE, then conducted scotopic ERG studies and retinal histologic, morphometric, and neurochemical experiments in adult offspring. Low-level and moderate-level GLE produced supernormal scotopic ERGs, an increased neurogenesis of rods and rod bipolar cells (BCs), and decreased DA synthesis and utilization/release in the absence of retinal injury. GLE produced inverted U-shaped dose-response curves as the high-level GLE dose produced rod cell loss and thus ER subnormality.

In the present study, five novel results were obtained. First, a new and clinically relevant rat model of human equivalent GLE, an exposure period of increasing relevance and concern, was established. Second, low-level and moderate-level GLE produced supernormal scotopic ERGs in adult rats that are similar to the ERG findings in male and female children with GLE. Third, low-level and moderate-level GLE increased neurogenesis of rod phororeceptors and rod BCs without affecting M ller glial cells. Fourth, GLE produced inverted U-shaped dose-response curves, as the high-level GLE produced subnormal ERGs and rod cell loss. Fifth, GLE produced dose-dependent decreases in adult retinal DA synthesis and utilization/release.

One of the most important and clinically relevant findings is that low-level and moderate-level GLE produced supernormal ERGs in adult rats. The blood Pb concentrations in these two groups are similar to those measured in pregnant women whose children had supernormal ERGs. In contrast, high-level GLE produced subnormal ERGs similar to those observed with PLE. These ERG results are characteristic of inverted U-shaped dose-response curves often observed in Pb neurotoxicity studies. These findings show that scotopic ERG is a sensitive, noninvasive biomarker that identified and discriminated low-level and moderate-level GLE from high-level GLE.

Source: Environmental Health Perspectives, Vol. 116, No. 5, May 2008.

ENVIRONMENTAL FACTORS AND HEALTH RISKS RESULTING FROM PRIMITIVE METHODS OF E-WASTE RECYCLING

Electronic waste (e-waste) from discarded electronic products has become one of the fastest growing types of waste in countries around the world. A major environmental health problem has been caused by an increasing amount of this waste being illegally exported to developing countries for recycling and disposal.

For some 20 years, Guiyu, in Guangdong province in south China, has been the destination for unregulated e-waste.

Nearly 60-80% of families in Guiyu are engaged in e-waste recycling operations. These primitive family-run recycling centers use methods such as sorting, firing, incineration, acidic and alkaline baths, manual assembly, open burning of wires and cables, and strong acid leaching. These operations are usually carried out with no or very little personal protection equipment or pollution control measures. In open burning of materials, fly ash particulates laden with heavy metals and other toxic materials are usually emitted, resulting in increased human exposure, contamination of food, soil, and surface water. Several studies have reported the soaring levels of toxic heavy metals and organic contaminants in workplace environment, surrounding soil and water sources of Guiyu.

Lead and cadmium were widely used in electronic devices, for example, lead was used as a major component of solders and lead oxide in the glass of cathode ray tubes (televisions and monitors), while in lead-acid batteries and in some PVC cables as stabilizers. Lead can build up in the body through repeated exposures and have irreversible effects on the nervous system, particularly the developing nervous system in children. Cadmium was used in electronics in some switches and solder joints, and as cadmium compounds in rechargeable batteries, UV stabilizers in older PVC cables and "phosphor" coatings in older cathode ray tubes. In the same way as lead, cadmium can accumulate in the body, causing damage to the kidneys and bone structure through long-term exposure. Cadmium and its compounds are known human carcinogens, primarily through inhalation of contaminated fumes and dusts. Therefore, the body's lead or cadmium levels and their effects on children's health have become an important environmental health problem.

Because of the potential heavy metal contamination in the living environment of Guiyu, a study to determine the blood lead levels (BLLs) of local children was conducted in 2004 when results showed that 81.8% of children aged 1-6 years had high lead content in their blood. In order to reassess the situation, a further study has been carried out to evaluate the BLLs again and also the blood calcium levels (BCLs) in children aged 1-7 years. For purposes of comparison, a control group of children with a mean age of 4.6 years from the neighboring town of Chendian was selected for study.

Chendian is mainly a center for the manufacture of clothing, and local residents do not work in e-waste processing. The population, traffic density and socioeconomic status of residents in both Guiyu and Chendian were very similar.

The results of this latest study show that children living in Guiyu had significantly higher BLLs and BCLs compared with children living in Chendian. In Guiyu, 109 children from the selected group of 154 (70.8%) had BLLs levels in excess of 10 μg/dL and 31 children from the same group (20%) had BCLs in excess of 2 μg/L.

This compared with 48 children from a group of 127 in Chendian (38.7%) with BLLs in excess of 10 μg/dL and 9 children from the same group (7.3%) with BCLs in excess of 2 μg/L.

A further observation from the study was that the mean height of the Guiyu children was significantly lower than that of Chendian children.

The study concludes that the higher lead and cadmium levels in Guiyu children may be due to environmental contamination related to the e-waste recycling activities in the locality.

Although the BLLs of children had decreased somewhat compared with the earlier study conducted in 2004, it was still a threat to children's health around the e-waste recycling area. The study recommends that greater attention should be given to the health effects of primitive e-waste recycling and policies should be implemented that help reduce environmental lead and cadmium exposure.

Source: Environmental Research, Vol. 108, No. 1, September 2008.

HEALTH DISORDERS ASSOCIATED WITH BISPHENOL A CONCENTRATIONS

Bisphenol A (BPA) is one of the world's highest production-volume chemicals, with more than 2 million metric tons produced worldwide in 2003 and annual increase in demand of 6% to 10%. It is used extensively in epoxy resins lining food and beverage containers and as a monomer in polycarbonate plastics in many consumer products. Widespread and continuous exposure to BPA, primarily through food but also through drinking water, dental sealants, dermal exposure, and inhalation of household dusts, is evident from the presence of detectable levels of BPA in more than 90% of the US population.

Most studies of the health effects of BPA have focused on well-documented estrogenic activity, but reports have highlighted additional modes of action, including liver damage, disrupted pancreatic β-cell function, thyroid hormone disruption, and obesity-promoting effects. The potential for low-dose effects has added to the controversy about possible hazards and whether currently recommended exposure thresholds require revision.

Debate about the health effects of BPA in humans has been hindered by the lack of epidemiologic data of sufficient statistical power to detect low-dose effects. The US National Health and Nutrition Examination Survey (NHANES) 2003-2004 recently released the only large-scale data on urinary BPA concentrations. Because orally administered BPA is rapidly and completely excreted, urine is considered the body fluid most appropriate for assessment of BPA exposure. The highly water-soluble major BPA metabolite, BPA-monoglucuronide, is formed in the gut wall and liver and is rapidly removed from the blood by the kidneys, with terminal half-lives of less than 6 hours after oral administration.

Given the previous animal evidence, researchers carrying out a new study hypothesized that higher urinary BPA concentrations would be associated with adverse health effects, especially in the liver and in relation to insulin, type 2 diabetes, and obesity in humans. Because of the paucity of direct human evidence, however, analyses were undertaken of all 8 of the reported major diagnostic groupings available in the NHANES 2003-2004 data (including cardiovascular and respiratory conditions for which 3 questions each are available on subdiagnoses). The study also examined a preselected list of 8 blood-based clinical measures reflecting liver function, glucose homeostasis, inflammation, and lipid changes.

The study found that higher urinary concentrations of BPA were associated with an increased prevalence of cardiovascular disease, diabetes, and liver-enzyme abnormalities. These findings add to the evidence suggesting adverse effects of low-dose BPA in animals.

Independent replication is now needed to confirm the associations reported in the present study. Because the analyses are based on urinary concentrations of BPA, which reflect recent exposure, studies based on repeat measurements over weeks, months, or even years would improve the assessment of longer-term exposure. Given the many routes of exposure to BPA, direct measures of dermal contact or of contact with contaminated foods, beverages, and dusts would be very difficult to undertake. A further issue is that although the previous animal-model literature provides evidence of the mechanisms underlying effects on liver cells (and therefore liver enzymes) and insulin signaling (and therefore diabetes), the mechanisms underlying the effect on prevalence of cardiovascular disease are not obvious. If the associations reported in the present study are confirmed in independent studies, more work will be needed to identify the mechanisms of action linking long-term, low-dose BPA exposure to adverse outcomes in humans. Given the substantial negative effects on adult health that may be associated with increased BPA concentrations and also given the potential for reducing human exposure, the present findings deserve scientific follow-up.

Source: The Journal of the American Medical Association, Vol. 300, No. 11, September 2008.

Lead Levels and Neurobehavioral Development of Neonates in Guiyu, China

Guiyu is the major electronic waste (e-waste) recycling town in China. It has a total area of 52 Km^2 and local population of 133,000. Recycling and disposing of e-waste from developed countries has become a major industry in the town.

The processes and techniques used in Guiyu for recycling e-waste are often primitive and lacking in pollution control measures. Recycling plants in Guiyu burn plastics in the open fires to reduce waste volume, and printed circuit boards are heated over honeycomb-coal fires to melt solder and collect electronic components, or dipped into strong acids to recover precious metals. The waste acid is then dumped into nearby streams. The result is severe contamination of the workplace and adjacent environment with a range of toxic metals and persistent organic contaminants. It was found that dissolved metal concentrations were higher in Lianjiang and Nanyang River within Guiyu than the reservoir outside

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Safety Evaluation of Titanium Dioxide Nanoparticles

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body as well as in vegetables and soil, indicating that we may ingest titanium compounds daily despite no detailed information on the chemical structure of such compounds. In addition, size is very important for non-biodegradable nanoparticles. Titanium dioxide particles bigger than 100 nm have been used in several foods and toothpastes; thus this strategy to estimate the safety of titanium oxide nanoparticles needs to be modified.

In the present study, therefore, the titanium level in typical raw food materials was surveyed, and then titanium dioxide nanoparticles (primary particle size, ca. 15 nm; secondary particle size, ca. 220 nm) were intravenously injected into mice, and the tissue distribution and elimination kinetics of titanium were determined.

As a result, an unexpectedly high titanium concentration was observed in several foods. It was also detected in blood and tissues of healthy mice without administration of titanium dioxide nanoparticles. Then, forced *i.v.* injection of the nanoparticles was performed in mice. The titanium level was significantly increased in blood and tissues, but no increase was found in the brain after *i.v.* injection. Most titanium was concentrated in the liver after injection, but the liver level decreased over time (ca. 30% decrease in 1 month). These data show that titanium must be eliminated from the body, and suggest that an evaluation method for toxicity of titanium dioxide nanoparticles should be reconsidered.

Source: The Journal of Toxicological Sciences, Vol. 33, No. 3, August 2008.

Lead Levels and Neurobehavioral Development of Neonates in Guiyu, China

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of Guiyu. Lianjiang River was enriched with dissolved As, Cr, Li, Mo, Sb and Se, while Nanyang River had elevated dissolved Ag, Be, Cd, Co, Cu, Ni, Pb and Zn.

Previous studies have reported that the residents in Guiyu had high incidence rates of skin damage, headaches, vertigo, nausea, chronic gastritis, and gastric and duodenal ulcers. A study has also examined blood lead levels (BLLs) of children in Guiyu and found that in 81.8% of the selected group of 1 to 6 year olds, BLLs exceeded 100 μg/L.

Lead is highly toxic to humans and has irreversible effects on the nervous system, particularly on the developing nervous systems of children. Lead can freely cross the placenta via diffusion, and may lead to fetal abortion, or fetal death in extreme cases. Surviving infants may be born prematurely and have congenital malformation, intrauterine hypoevolutism, low birth weight, and small head circumference. Furthermore, intrauterine exposure to lead may create other severe injury problems during the early phase of nervous system development in children, with consequences that may include decreased intelligence quotient, impairment of memory, movement disorders, total or partial deafness and impaired cognitive and spatial functioning.

Now a new study has been carried out to measure the lead levels in neonates and to examine the correlation between lead levels and neurobehavioral development.

One hundred full-term neonates from Guiyu and fifty-two neonates from neighboring towns (control group) in the late summer of 2006 were selected for study. The lead levels in the umbilical cord blood (CBPb) and lead levels in meconium (MPb) of neonates were determined with atomic absorption spectrophotometry. The neonatal behavioral neurological assessment (NBNA) was conducted on all neonates. A questionnaire related to the exposure to lead of pregnant women was used as a survey of the neonates' mothers. Compared with the control group, neonates in Guiyu had significantly higher levels of lead, and the mean CBPb and MPb were 113.28 μg/L and 2.50 μg/g, respectively. The relatively high lead levels in the neonates of the Guiyu group were found to correlate with their maternal occupation in relation to e-waste recycling. Neonates with high levels of lead load have lower NBNA scores. There was a statistically significant difference in NBNA scores between the Guiyu group and the control group by *t* test. No correlation was found between CBPb and NBNA scores; however, a negative correlation was found between MPb and NBNA scores. There is a correlation between relatively high lead levels in the umbilical cord blood and meconium in neonates and the local e-waste recycling activities related to lead contamination. This study suggests that environmental lead contamination due to e-waste recycling has an impact on neurobehavioral development of neonates in Guiyu.

Source: Journal of Environmental Monitoring, Vol. 10, Issue 10, October 2008.

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