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RISK OF CHILDHOOD LEUKEMIA IN RELATION TO RESIDENTIAL EXPOSURE TO PERSISTENT ORGANOCHLORINE CHEMICALS

Childhood leukemia is the most common childhood cancer, with acute lymphocytic leukemia (ALL) accounting for about 80% of childhood leukemias in most Western countries. Incidence peaks at 2-5 years of age, indicating the importance of exposures early in life.

Incidence of ALL is highest in industrialized countries and rose significantly over the period 1975-2004 in the United States, Europe, and Japan, suggesting that environmental exposures or lifestyle changes may play an etiologic role.

Organochlorine insecticides e.g., dichlorodiphenyltrichloroethane (DDT) and chlordane and polychlorinated biphenyls (PCBs) became common environmental contaminants after World War II because of their widespread use, persistence in the environment, and bioaccumulation through the food chain. Because of concerns about detrimental effects on the environment and human health, uses of DDT, PCBs, and chlordane were banned in the United States in 1972, 1977, and 1988, respectively. However, these chemicals persist indoors in carpets, where they are protected from degradation by sunlight, moisture, and microorganisms. Ingestion of house dust is an important route of chemical exposure for young children, who spend most of their time indoors and frequently put their hands in their mouths. Concentrations of organochlorines in serum, breast milk, and dietary sources have decreased substantially since the 1970s; as a result, indoor sources can be a major contributor to exposure for children living in older homes, where these chemicals are frequently detected.

Epidemiologic studies have implicated residential and parental exposure to pesticides as risk factors for childhood leukemia. However, specific pesticides were not identified in most studies, which relied primarily on self-reports about pesticide use. PCBs are considered probable human carcinogens and cause perturbations of the immune system. PCB congeners commonly found in blood, adipose tissue, and house dust have been associated with increased risk of adult non-Hodgkin lymphoma (NHL) in cohort and case-control studies.

Now a new study evaluates the hypothesis that persistent organochlorine chemicals may increase the risk of childhood leukemia. In the study, residential carpet dust is used as an indicator of exposure.

The population-based case-control study of childhood leukemia was carried out in 35 counties of northern and central California in 2001 to 2006. The study included 184 ALL cases 0-7 years of age and 212 birth certificate controls matched to cases by birth date, sex, race and ethnicity. Carpet dust samples were collected from the room where the child spent the most time before diagnosis, using a specialized vacuum.

The study revealed increased risk of ALL with increasing concentrations of total

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DNA Damage in Human Populations Exposed to Electronic Waste – a Report of a Recent Study Conducted in Northern China

Jinghai County of Tianjin has a history of more than 20 years in disassembling imported mechanical and electronic waste (E-waste) products. In recent years, the scale has gradually increased, but family workshops are still involved in the majority of the work. The use of outdated (and unsafe) ways to deal with E-wastes can lead to exposure to a variety of substances harmful to human health such as cadmium, nickel, lead, mercury, and dioxins as well as to the pollution of air, water, and soil with these substances. The contaminants can then enter the human body by absorption, ingestion, and skin contact, leading to a variety of harmful effects. While the local government has undertaken various initiatives and established an environmental protection industrial park in order to minimize the harmful effects of pollution, the lingering effects of the previous 20 years of this industry still exist, and may have a cumulative effect within the population. In addition, many people are unaware of the effects of environmental pollution and do not take advantage of the government initiatives. Many small-scale operations still deal with the waste by manually disassembling and burning it, which may cause serious environmental pollution and may affect the health of both those involved in the waste processing and those who are exposed to its second-hand byproducts. E-waste pollution may contribute to elevation of blood lead level in children living in the local environment. But little is known on the cytogenetic effect to humans caused by the pollution of E-wastes.

Chromosome abnormalities are evidence of DNA damage, and chromosomal aberrations are involved in human aging and cancer. Through observations of the number, shape, and structure of chromosomes, an accurate picture of the degree of damage from pollutants may be obtained. The current study discovered that people living in the area of E-waste exposure present increases in the incidence of chromosome aberrations, especially the formation of acentric fragments and monomers.

Similarly, micronucleus assays, which evaluate genomic instability, can be applied to detect chromosomal breakage, rearrangement, loss or mal-segregation, and, to a certain extent, reflect the degree of damage to the chromosome or spindle. The micronucleus index in human cells has become one of the standard cytogenetic tests for monitoring populations at risk. This study showed that the presence of micronuclei in the exposed group was increased and that many binuclear cells contained two or more micronuclei. Many pollutants are electrophilic and can form covalent bonds with macromolecules, such as DNA, leading to their fragmentation. During subsequent cell division, some of the fragments are kept in the cytoplasm because they are unable to enter the nucleus of splitting cells, leading to the formation of a micronucleus. In addition, some electronic pollutants can interrupt spindle fibers, causing the separation of an entire chromosome after the mitotic cycle, also leading to formation of a micronucleus. Comet assay can quantitatively detect DNA damage at the single cell level and can accurately reflect the degree of genomic instability. Since it is a sensitive, simple, and rapid method, comet assay has been widely applied in toxicology and genetic studies in recent years. In this study, the DNA percentage in the comet tail, tail moment and Olive tail moment obtained by single cell gel electrophoresis in samples from subjects in the exposed group were significantly higher than those from the control group, indicating that there are DNA damage agents in the environment in which the exposed population lived. The mechanisms are still undefined, but DNA damage from E-wastes may be due to oxidative damage to nucleobases, induction of membrane lipid peroxidation, DNA methylation, and dysfunction of DNA repair, all of which can lead to human genetic damage.

Source: Environmental Science and Pollution Research, Vol. 16, Issue 3, May 2009.

RISK OF CHILDHOOD LEUKEMIA IN RELATION TO RESIDENTIAL EXPOSURE TO PERSISTENT ORGANOCHLORINE CHEMICALS

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PCBs and with specific PCB congeners in dust samples taken from the room in which the child spent the most time.

In contrast, dust levels of the persistent organochlorine pesticides DDT, DDE, chlordane, methoxychlor, and pentachlorophenol were not associated with increased risk.

However, the findings suggest that residential exposure to PCBs may represent a previously unrecognized risk factor for the development of ALL in young children.

Source: Environmental Health Perspectives, Vol. 117, No. 6, June 2009.

Steroid Metabolic and Biosynthetic Enzymes as a Target of Modulation by Lead and Polychlorinated Biphenyls

Steroid hormones are lipophilic, low-molecular weight compounds derived from cholesterol that play a number of physiological roles. The main steroid hormones, secreted by gonads and adrenal glands, are androgens, estrogens, progestinics, glucocorticoids and mineral corticoids.

Many different enzyme systems are involved in the synthesis, intracellular bioactivation and degradation of steroids including cytochrome P450 isozymes, uridine-5-diphosphate-glucuronyltransferases (UGTs) and sulfotransferases (SULTs).

SULTs are a large class of enzymes that transfer a sulfuryl group from the universal sulfonate donor compound 3'-phospho-adenosine-5'-phosphosulfate (PAPS) to an acceptor molecule, in liver, kidney, brain, testis, intestine, platelets, and adrenal and fetal tissues. They have an important function both in the activation and in deactivation of many chemical compounds and in phase II of the conjugation pathway for xenobiotics, endogenous compounds and drugs, generally leading to an increase in hydrophilicity and thereby facilitating increased excretion of conjugated molecules. Sulfonation can also produce biologically active metabolites; intracellular sulfonation of the adrenal androgen dehydroepiandrosterone (DHEA) in steroid target cells produces DHEA-S, a hormone that is known to play a role in a number of physiological functions. Sulfonated steroids may be stored as inactive hormones that can be reactivated by steroid sulfatases, providing a mechanism for regulating endocrine homeostasis.

In mammals, there are two classes of sulfotransferases: membrane SULTs and cytosolic SULTs; the latter metabolize xenobiotics, thyroid hormones, steroids and neurotransmitters. At least 44 cytosolic sulfotransferases have been identified in mammalians and 11 SULTs have been detected in humans. They can be divided into five SULT families sharing less than 40% similarity with each other; the first two represent the largest and most widely examined families. The SULT1 family consists of sulfotransferases that transfer sulfonate to phenolic drugs and catecholamines (SULT1A), estrogenic steroids (SULT1E, named also EST and estrogen sulfotransferases), thyroid hormones (SULT1B) and xenobiotics (SULT1C). Human SULT1E also shows significant activity as regards DHEA and catalyzes the sulfonation of iodothyronines, including the pro-hormone T4 and the active hormone T3. SULT2A1, also named HST-hydroxysteroid sulfotransferase, is the prototypical human hydroxysteroid sulfotransferase. It is commonly referred to as DHEA sulfotransferase, since DHEA is considered the major substrate. SULT2A1, however, has broad substrate specificity and will sulfonate a wide variety of steroids and sterols, in addition to DHEA, involving hydroxyl groups at different carbon locations and with different spatial orientations.

Similar to SULT2A1, SULT2B1 isoforms will sulfonate pregnenolone. However, in contrast to SULT2A1, they do not sulfonate androsterone, bile acids, testosterone, estrogens and cortisol. Exposure to exogenous compounds can cause alterations in the biosynthesis or deactivation of endogenous steroids by inhibiting SULTs. Some of these inhibitors are polyphenols such as quercetin, components in red wine, tea and coffee.

Lead (Pb) also interferes with the mechanisms of sulfoconjugation by means of an effect on SULTs. A drop of about 50% was observed in the sulfonated compounds in workers with a blood Pb concentration between 45 and 65 g/100 ml.

SULTs are also inhibited by several hydroxylated PCBs; a reduction of the sulfonation of 3-hydroxybenzo[a]pyrene, a major metabolite of benzo(a)pyrene (BaP) in humans and animals, has been observed. The same findings have been noted in hydroxylated metabolites of polychlorinated dibenzo-*p*-dioxin (PCDD) and dibenzofurans (PCDFs), polybrominated diphenylethers (PBDEs) and bisphenol A (BPA) derivates. The *in vitro* effects of the most effective PCDD-OHs and PCDF-OHs were observed at concentrations that may actually be the same range as those present in human tissue. It has been demonstrated by means of *in vitro* experiments that various halogenated phenols are inhibitors of SULTs.

In this study, the metabolism of steroid hormones was investigated in subjects exposed to Pb and PCBs and in a control group, to confirm the effects of Pb at lower concentrations than those previously observed and to determine whether PCBs interfere with steroid hormone synthesis and sulfonation.

The study concluded that steroid metabolic and biosynthetic enzymes may be target of modulation by PCBs and Pb, which may cause changes in endogenous hormone homeostasis and interfere with the xenobiotic phase II of detoxification. It is likely that different mechanisms are involved in the steroid hormone metabolism interference. If the synthesis of steroids and their sulfonation is considered, it is also evident that Pb and PCB only partially share the same hormone pathways. The interference on 17-ketosteroid sulfonation of Pb and PCB is probably a consequence of their action on the SULT2 family, and partially, only for DHEA, on the SULT1 family (SULT1E1). The reduction in glucocorticoid sulfonation may depend on SULT2 family inhibition activity.

Source: International Archives of Occupational and Environmental Health, Vol. 82, No. 5, April 2009.

Micronucleus Occurrence and Gene Polymorphisms in Workers Occupationally Exposed to Vinyl Chloride Monomer

Recent epidemiological studies have shown vinyl chloride monomer (VCM), which is widely used in industry in the form of polyvinyl chloride, to be a multi-organ and multi-system carcinogen that induces a wide range of tumors including hepatic angiosarcomas and other liver tumors, brain tumors, and lung cancer.

VCM is biotransformed by human liver cytochrome P4502E1 to generate alkylating intermediates chloroethylene oxide and chloroacetaldehyde, which react with DNA bases to form etheno DNA adducts, namely, 1,N(6)-etheno-adenine, 3,N(4)-ethenocytosine, and N(2)-3-ethenoguanine. These etheno DNA adducts are promutagenic and genotoxic and, if not repaired, may eventually induce base pair substitution, chromosomal aberrations, micronuclei, sister chromatid exchange, and DNA strand breaks observed in lymphocytes of individuals occupationally exposed to VCM.

At least four pathways of DNA repair operate on specific types of damaged DNA, including base excision repair (BER), nucleic acid excision repair, double-strand break repair, and mismatch repair. Previous studies have revealed that the etheno DNA adducts produced by VCM may be repaired by BER, which is responsible for repairing small lesions, such as oxidized or reduced bases and DNA single-strand breaks.

Numerous epidemiological studies showed that several BER gene polymorphisms, including *XRCC1 Arg194Trp* and *Arg399Gln, PARP1 Val762Ala* and *APE1 Ile64Val,* were associated with DNA damage and human cancer risk.

To comprehensively investigate the roles of the polymorphisms in the BER genes in chromosomal damage and identify potential genetic markers in VCM-exposed workers, researchers investigated the relationship between the frequency of micronucleus induced by VCM in peripheral lymphocytes and three amino acid substitution variants in BER genes, namely, *TDG Gly199Ser, PARP1 Val762A1a,* and *APE1 Ile64Val*.

The VC monomer plants and VC polymerization plants involved in this study are in Shanghai.

Through personal interview, the VCM-exposed workers who participated in this study provided information on demographic factors (age, sex, and race), lifestyle factors (smoking habits and alcohol consumption), and occupational exposure. Blood sample was collected for genotyping after written informed consent was obtained from each participant. Workers exposed to VCM for a period of more than 1 year were selected if the following criteria were met: blood samples had been provided; Cytokinesis-blocked micronucleus assay (CBMN) tests and PCR-restriction fragment length polymorphism (RFLP) for all the studied genes were completed successfully. A total of 185 workers (117 men and 68 women; average age = 34 years, range: 20 to 53 years) met these criteria, all of whom were ethnically Han Chinese. The cumulative exposure levels in ppm-years were evaluated based on years worked in these plants. The median cumulative VCM exposure of the 185 workers was 32.17 ppm-year (range: 1.33 to 845.53 ppm-year). The VCM-exposed workers were then divided into high (>32.17 ppm-year) and low exposure (≤ 32.17 ppm-year) groups.

Teachers and graduate students without VCM exposure were selected as a control group, from the School of Public Health, Fudan University, including 20 Han Chinese men and 21 women (average age = 35.3, range: 23 to 57 years). Each control completed a detailed questionnaire and the CBMN test.

BER is the predominant pathway for averting the mutagenic and cytotoxic effects of damaged DNA bases generated by either endogenous or exogenous factors, including lesions that arise spontaneously due to the intrinsic instability of DNA and those that are induced by environmental chemicals, such as VCM. This study shows that among Chinese VCM-exposed workers, genetic polymorphism *TDG Gly199Ser* was associated with increased micronucleus frequency. Furthermore, researchers observed a combined effect of *TDG* and *APE1* polymorphisms on micronucleus frequency, in agreement with the notion that APE1 coordinated with TDG in the repair of DNA base damage.

Although each step in BER pathway can be performed in isolation, numerous studies have shown that physical or functional protein-protein interactions in the BER process display a cooperative manner to repair the target bases. In this study, individuals carrying at least one copy of the *TDG 199Ser* allele and *APE1 64Val* allele were associated with increased micronucleus frequency compared with those carrying wild-type genotypes for both genes. The base-excision activity of TDG is enhanced by the subsequent repair enzyme APE1, which exhibits a better affinity for the AP lesion and results in the displacement of TDG. Moreover, because TDG physically contacts APE1 to form a stable complex, these two polymorphisms in *APE1* and *TDG* resulting in amino acid substitution may impact the protein-protein interaction, leading to a global change in repair efficiency. It is possible that APE1 coded by the *64Val* variant cannot repair efficiently the AP lesion, generated by TDG coded by the *199Ser* allele, because of the imbalance of the action of the proteins in processing DNA damages.

The results of the present study indicated that *TDG Gly199Ser* polymorphism was related to micronucleus frequency in VCM-exposed workers and APE1 and TDG functioned in a coordinated manner. The strengths of this study include a homogeneous ethnic background of VCM-exposed workers, reduction in information bias by performing direct interviews in collecting demographic and lifestyle information, and well-documented exposure history in the workplace. Although no association between *APE1 Ile64Val* and *PARP1 Val762Ala* polymorphisms and micronucleus frequency was found in the present study, researchers have not yet evaluated other polymorphisms in these genes, which may also affect the risk of chromosomal damage. Thus, additional studies are required to validate these findings and to further investigate the specific polymorphisms of other genes involved in the base-excision repair pathway and the gene-gene interactions associated with VCM induced chromosomal damage.

Source: Journal of Occupational and Environmental Medicine, Vol. 51, No. 5, May 2009.

OCCUPATIONAL STYRENE EXPOSURE AND HEARING LOSS

After about 20 years of epidemiological research on hearing functions in workers exposed to solvents, numerous reviews are available. They focus not only on the solvent effects alone but also on interactions with noise impacts. In the following study, the assessment of possible styrene effects have been examined.

Two open issues in this field have been addressed in the current study. On the one hand, further data are necessary in order to establish a reasonable dose-response relationship among the existing research studies. On the other hand, data are also necessary in order to establish the lowest observed adverse effect level of styrene on hearing function. Independent of these issues, a third question can be raised from the studies available. Several studies differentiate between acute and chronic exposure data, but apparently, only in one study additional examinations were carried out after a rest period. In this respect, no other results than in the first examination were found. This approach is instrumental for the evaluation of chronic effects since the impact of acute work and exposure can be excluded.

Despite the inconsistent epidemiological results, there are consistent findings on the toxicological mechanisms that induce changes on the outer and inner hair cells in the cochlea as well as at the cell membranes due to high styrene exposure alone and combined with noise, as shown in animal studies.

This current study extends an initial investigation in a boat building factory which covered only a few workers and a smaller range in the frequency band examined during pure tone audiometry. Taking into account the pre-exposure of the study sample and the above remarks on the open issues in this domain of research, the following three questions are addressed:

1. Are there additional findings on hearing loss using high frequency audiometry (9,000-16,000 Hz) besides standard audiometry (125-8,000 Hz) to investigate various exposure levels of styrene which reach currently up to 50 parts per million (ppm) styrene and higher concentrations at workplaces in the past?
2. Can dose-response relationships as well as thresholds of effects be established considering different exposure measures?
3. Are there indications for reversibility of possible effects if the workers are examined at times of improvement during work holidays?

A group of workers from a boat building plant, some of whom were laminators, were examined in subgroups of current low (n = 99, mean mandelic acid MA + phenylglyoxylic acid PGA = 51 mg/g creatinine), medium (n = 118, mean 229 mg/g creatinine) and high (n = 31, mean 970 mg/g creatinine) exposure to styrene. In addition, subgroups chronically exposed to high-long (n = 17) and low-short (n = 34) styrene levels were analysed. The examinations were carried out during normal work days and during the company holidays. Hearing thresholds and transient evoked otoacoustic emissions (TEOAE) were measured. Statistics included multiple co-variance analyses with repeated measures, linear regressions, and logistic regressions.

The analyses of all participants demonstrated no clear exposure effects. Particularly no sufficient proof of dose-response relationship measured against parameters of current exposure (MA + PGA, styrene/blood) and of chronic exposure (cumulative and average life time exposure response) was found. The analyses of groups exposed to high levels show elevated thresholds at frequencies up to 1,500 Hz among the subgroup exposed to high styrene levels (e.g. 40-50 ppm as average) for a longer period of time (e.g. more than 10 years). These participants also demonstrated signs of "improvement" at frequencies above 2,000 Hz during work holidays, when they were not exposed to styrene. A significantly elevated odds ratio for cases of hearing loss (more than 25 dB in one ear, 3,000-6,000 Hz) was found among the group exposed to high levels (above 30 ppm as average) for a longer period of time (more than 10-26 years). The measurements of TEOAE did not exhibit significant results related to exposure.

In view of the results which were classified as possible styrene-related effects (1) the cases with higher risks of hearing threshold of more than 25 dB at 3,000-6,000 Hz, (2) the significant group differences at 125-1,500 Hz and selectively at 8,000-12,500 Hz as well as (3) the "improvement" effects at frequencies above 8,000 Hz all of which predominantly related to the high-long exposed subgroup, it remains unclear why no corresponding results could be found in linear regressions (with the exception of 1,000 and 1,500 Hz). Thus, the findings can be seen as results that are both reproduced and newly discovered of styrene effects on hearing functions, with the shortcoming of lacking consistency between all investigative approaches used. But the results of this investigation put emphasis on effects of high exposure levels prevailing at the workplace more than one decade before. On this note, this study presents additional findings to the existing studies with differing results published on styrene-related hearing impairments.

With respect to the three questions, that guided this study, the following conclusions can be derived:

1. The findings in this study showed worse hearing thresholds, for frequencies 1,000-1,500 and 8,000-12,500 Hz, in long-term exposed workers with high styrene levels of 30-50 ppm as an average and higher concentrations above 50 ppm in the past. The results found in the literature of ototoxic effects below 20 ppm styrene could not be confirmed.
2. A dose-response relationship could not be proven, with an exception of 1,000 and 1,500 Hz in relation to chronic exposure. However, this single result should be interpreted with caution taking into account the great number of missing dose-response relationships.
3. Improvements of hearing function could be observed among all participants due to the repeated measurement concept during holidays. However, in the high-long exposed sub-group compared to the short-low exposed sub-group, this improvement had an exposure-related enhancement.

Source: International Archives of Occupational and Environmental Health, Vol. 82, No. 4, March 2009.

Possible Nonfood Exposures to Bisphenol A: Implications for Risk Assessment Studies

Bisphenol A (BPA), an industrial chemical used in a variety of consumer products, is ubiquitous in the modern environment, with residues found in the urine of an estimated 93% of Americans over 6 years of age, according to data from the 2003-2004 National Health and Nutrition Examination Survey (NHANES). Recent research indicates that BPA acts as an endocrine disruptor and may increase the risk of heart disease, diabetes, and liver problems in adults. Until now, most exposure was thought to occur through diet, and the chemical was thought to be eliminated from the body quickly and completely. But a new study shows that urine BPA levels of subjects who had fasted for several hours were not as low as expected, suggesting either nondietary exposures or accumulation in fatty tissue, or both.

Although BPA is fat-soluble and thus can accumulate in fatty tissues, animal and human data suggest it tends to be rapidly metabolized, with elimination thought to be virtually complete within 24 hours of acute exposure. To gain a better understanding of how BPA is eliminated from the body, investigators in the current study used data from 1,469 adult participants in the 2003-2004 NHANES. Study participants (excluding children and insulin-dependent diabetics) had been asked to fast for at least 6-9 hours. Using the urine drawn from each study participant, the investigators modeled log BPA concentration against fasting time, adjusting for urine creatinine and other confounders, to estimate what they termed the population-based half-life of BPA for a 0- to 24-hour fasting period.

In these NHANES data, the population-based half-life is much longer than expected based on published acute exposure studies. Regressions demonstrate a strong BPA decline in the 4.5-8.5 hr interval, possibly representing an initial elimination phase subsequent to oral intake. However, from 8.5 to 24 hr, the slope is essentially flat, so population-based half life is very long.

The relationship between fasting time and the highest BPA levels (12-80 ng/mL) was weak, and high levels were seen in some long-fasting subjects. Even when restricted to participants fasting 8.5-24 hr, and excluding at risk subjects as previously described, 7.5% of participants had a BPA level > 12 ng/mL. These results are substantially greater than the national median (2.7 ng/mL), and suggest the possibility of important nonfood exposure.

Risk assessments for BPA have been based in part on evidence that food is the primary, and almost exclusive, exposure source, and that rapid and complete BPA elimination occurs after exposure. The persistence of population BPA levels despite extended fasting appears to contradict this evidence. Research to resolve this contradiction could include experimental pharmacokinetic studies of chronic BPA exposure, continued search for important nonfood sources, and further investigation of BPA in human adipose tissue and its effects on adipokine production. If such studies confirm that either or both of the base assumptions are flawed, risk assessments for BPA will require reevaluation.

Source: Environmental Health Perspectives, Vol. 117, No. 5, May 2009.

Toxicological Evaluation of the Effect of Water Contaminated with Lead, Phenol and Benzene on Liver, Kidney and Colon of Albino Rats

Wastes in open dump sites and unlined-landfills are potential threats to water bodies. Run-offs from open dump sites and leachate from landfills may contain bacteria, virus and parasites that can contaminate water. They can be highly toxic, containing high concentration of heavy metals e.g. lead, and organic compounds such as pesticides, phenols, benzene and polychlorinated biphenyl (PCB) which are hazardous to man. These chemicals are liver and kidney toxicants, known or suspected carcinogens, and capable of damaging the reproductive and central nervous system.

In Nigeria, for instance, there are indiscriminate open dumps and unlined-landfills which pose great threat to water bodies. Analyses of groundwater and surface water around landfill sites and open dump sites showed gross contamination of water by both inorganic and organic chemicals. Water related diseases have been reported among the people living close to open dump and landfill sites.

Water pollution is a very serious hazard to which the human population is exposed. Polluted water has been shown to be unfit for drinking. The impacts of contamination are even more persistent in groundwater due to lack of biological degradation. Lead is a natural contaminant which affects both adults and children, resulting in mental retardation, delayed development, and impaired psychological and neurobehavioural functions. Ingestion of phenol-contaminated water can lead to liver damage, gastrointestinal irritation, and weight loss. Benzene enters water from burning coal and oil, petroleum stations, motor vehicle exhaust, which can result in disorders in blood, reduced numbers of red blood cells and aplastic anaemia. The presence of lead, phenol and benzene has been reported in most contaminated water bodies in Nigeria, where the concentration in leachate was as high as 100 times the recommended permissible limit. Clinical cases associated with these chemicals have also been reported to be on the increase among people living close to landfills.

The level of contaminants in drinking water are seldom high enough

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CUMULATIVE LEAD EXPOSURE AND COGNITION IN OLDER WOMEN

Many older people in the U.S. population were chronically exposed to lead from paint and gasoline prior to the 1980s. To date, most of the research on lead and cognitive functioning in older age has focused on men, despite the fact that women live longer on average and therefore may be more likely to develop dementia over the course of their life span. Now, in a prospective look at a subset of data from the Nurses' Health Study – which began in 1976 and included 121,700 registered nurses aged 30-55 years – researchers report that even low-level cumulative lead exposure may exacerbate cognitive decline in older women.

The study looked at 587 women (now aged 47-74 years) who had undergone bone lead evaluations as part of two studies during the 1990s; to assess long-term exposures, bone lead concentrations were determined at each woman's mid-tibial shaft and patella. All but 6 of those individuals had also provided blood samples for assessment of more recent lead exposure.

The study found that cumulative community-level exposure to lead, measured by concentration of lead in tibia bone, was associated with significantly worse overall performance on cognitive function tests. Specifically, the average decrement in cognitive test scores observed for each SD increase in tibia lead corresponded to the decrement in scores observed for each 3-year increase in age among women in the study.

Levels of two other lead biomarkers – patella lead and blood lead – were also associated with worse cognitive function, but these associations were not significant. This pattern of association suggests that lead exposures in the distant past may be more important than relatively recent exposures in influencing cognitive function in these women, because tibia lead levels measure cumulative exposures over the past decades, in contrast to the more recent exposures measured by patella and blood lead levels. Although tibia lead assessments cannot distinguish between chronic low-dose exposures and high exposures during a critical period in the past, chronic low-dose exposures likely prevailed among the women in this study, who probably incurred most of their exposures to lead from gasoline emissions and consumer products beginning in childhood and lasting at least through the 1980s, when these products were phased out in the United States.

Few large-scale studies of cumulative lead exposure and cognition in older adults have included women, and none has reported results that are specific to women. The present study indicates that cumulative lead exposure may adversely affect cognitive aging even among women, whose exposure to lead is typically lower than that of men. This association has important consequences for public health, because impaired cognitive function is a strong risk factor for dementia and because women have a higher lifetime risk than men of developing dementia.

More generally, although lead levels in the environment have fallen dramatically in the past two decades, many older adults have endured protracted exposures to lead in the preceding decades and have accumulated lead in their skeletons. Together with previous findings, the results of this study have important implications for the cognitive functioning of this growing population of older adults. In the United States, the population of persons ≥ 65 years of age is projected to double between 2000 and 2030, leading to a rapid rise in the number of individuals afflicted with age-related dementia. This phenomenon will likely be echoed throughout the globe. One model has forecasted that a broadly applied intervention, such as a regulatory intervention that delays the onset of Alzheimer disease by 2 years, could reduce the number of prevalent cases in the United States by about 2 million over a 40-year interval. Thus, even if lead has a subtle effect in accelerating cognitive aging, given the pervasiveness of lead exposure in the United States and globally, widespread reductions in this exposure could have a substantial impact on the burden of cognitive impairment in the population.

Source: Environmental Health Perspectives, Vol. 117, No. 4, April 2009.

ARSENIC EXPOSURE AS A RISK FACTOR IN GESTATIONAL DIABETES

In countries around the world, chronic exposure to arsenic has been associated with an increased risk of type 2 diabetes mellitus, and new research indicates that it may also be a risk factor for gestational diabetes (GD).

Arsenic may promote type 2 diabetes by increasing insulin resistance (inability to utilize insulin at the cellular level) and impairing insulin production. Insulin resistance is also a central feature of GD, a potential complication during pregnancy that can lead to a 30-60% increased risk for the mother of developing lifelong diabetes, as well as impaired glucose tolerance, adverse birth outcomes, and obesity in her child.

However, there is evidence that early intervention and treatment, such as dietary counseling, blood glucose monitoring, and insulin or other drugs (if appropriate), may lead to improved outcomes for mother and child. Therefore, it is an important public heath priority to identify risk factors for GD.

Thus, a new study has examined maternal arsenic exposure and risk of impaired glucose tolerance during

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Toxicological Evaluation of the Effect of Water Contaminated with Lead, Phenol and Benzene on Liver, Kidney and Colon of Albino Rats

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to cause serious health effects such as cancer, kidney damage, liver damage, immune system and neurological system damage. Humans, aquatic life and other living organisms are exposed to these contaminants from factories, refineries, waste treatment plants, fertilizers and pesticides washed into the body of river or urban water supplies. It has become necessary to assess the effect of the contaminated water on the liver, kidney and colon of rats for possible prediction of effects on human.

Thus a recent study has investigated the effect of water contaminated with phenol, benzene and lead on the cellular system of rats.

Selected enzyme activity of the kidney and colon of rats was carried out. Standard enzyme assays were also conducted for selected liver enzymes such as alkaline and acid phosphatases, alanine and aspartate transaminases, and gamma glutamyl transpeptidase. Serum indices of liver and kidney function were also determined. The direct bilirubin of test rats was observed to be 3.2 ± 0.2 U/mol/l while that of control rats was 1.2 ± 0.003 U/mol/l. The total bilirubin of test rats was found to be 8.4 ± 0.8 U/mol/l while that of the control rats was 5.6 ± 0.5 U/mol/l. Generally, enzyme activity in the tissues of test rats was found to be significantly lower relative to control, while the enzyme activity of the serum of test rats was significantly higher than control. It could be inferred that experimental data suggest possible damage to the tissues and that consumption of polluted water may account for increasing cases of renal and hepatic failure among people in developing countries.

Source: Food and Chemical Toxicology, Vol. 47, Issue 4, April 2009.

ARSENIC EXPOSURE AS A RISK FACTOR IN GESTATIONAL DIABETES

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pregnancy, which is an important determinant of GD, in a population of pregnant women living in an area surrounding the Tar Creek Superfund site in Ottawa County, Oklahoma.

The area, once active in lead and zinc mining, has an above-average poverty rate compared with the rest of Oklahoma and the nation. Mine waste contaminated with assorted metals is still present and has been used to build roads, playgrounds, driveways, and house foundations. Moreover, 25% of drinking water samples tested in the area have naturally occuring arsenic levels exceeding the Environmental Protection Agency maximum contaminant level of 10 µg/L.

Total arsenic concentrations were measured in blood and hair samples collected at delivery from 532 women; blood was available from all women and hair from a subset of 179. Routine prenatal glucose tolerance tests conducted between weeks 24 and 28 of pregnancy yielded plasma glucose measurements, and questionnaires and medical record review provided data on sociodemographic characteristics, potential sources of arsenic exposure, and pregnancy history.

Blood arsenic concentrations, a measure of biologically active arsenic, were between 0.2 and 24.1 µg/L, whereas hair arsenic concentrations, an indicator of cumulative exposure, were 1.1-724.4 ng/g. Blood glucose levels ranged from 40 to 284 mg/dL. At a cut-off value of > 140 mg/dL, 12% of the women were identified as having impaired glucose tolerance; a cut-off value of 130 mg/dL yielded a prevalence of more than 20%. A statistically significant relationship existed between each increasing quartile of blood arsenic exposure and impaired glucose tolerance after controlling for health and demographic factors. Depending on the glucose test cut-off value, women in the highest quartile of arsenic exposure were 2.4-2.8 times more likely to have impaired glucose tolerance than women in the lowest quartile of exposure.

Understanding the effects of environmental exposures on impaired glucose tolerance during pregnancy may have substantial public health importance beyond the direct effects on GD. Studies are needed to investigate environmental or behavioral factors that may contribute to risk for development and progression of diabetes, obesity, and its complications. Such studies should incorporate culturally specific lifestyle factors into treatment and prevention strategies to reduce risk across racial, ethnic, and socioeconomic groups. Future research in this area will be important for understanding whether different pathophysiologic mechanisms or risk factors are responsible for increased obesity and diabetes risk, especially in children. In addition, better understanding of modifiable risk factors for GD such as diet and activity patterns related to environmental exposures may lead to efforts at primary prevention.

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