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The Influence of Cigarette Smoking on Human Sperm Quality and DNA Fragmentation

The possible noxious effects of cigarette smoking on male fertility and particularly on conventional sperm parameters have become an area of growing interest. In recent years, there has been an increasing body of evidence that several environmental toxicants may impair semen quality and thus male fertility in animals as well as in humans.

Among different air pollutants, cigarette smoke contains toxic chemicals, mutagenic and carcinogenic compounds, which can adversely affect male fertility. Several studies have shown a correlation between the consumption of tobacco and an alteration of sperm quality. Both conventional sperm parameters such as sperm density, motility, viability and morphology, and nuclear integrity seem to be concerned.

Cigarette smoking is linked to significantly increased levels of seminal reactive oxygen species, which are responsible for oxidative stress thereby possibly inducing alterations of the sperm plasma membrane and a high degree of DNA fragmentation.

A study has now been conducted to compare the conventional sperm parameters and the degree of DNA fragmentation in smokers and non-smokers. The subjects for this study were two groups of patients (smokers n=51 and non-smokers n=57) attending an assisted reproductive techniques (ART) department of the University Maternity Hospital, Nancy, France.

Smoking intoxication was assessed by questionnaire and measured with the CO-Tester®. Sperm parameters were measured according to the WHO criteria and the degree of DNA fragmentation in spermatozoa was analyzed using the TUNEL-assay with flow cytometry detection.

The study showed that smokers' spermatozoa have a significantly higher DNA fragmentation than non-smokers (32% versus 25.9%, $p<0.01$). In contrast there is no significant difference in conventional parameters between smokers and non-smokers. The degree of sperm DNA fragmentation is not significantly correlated with any of the conventional parameters. These findings suggest that cigarette smoking may have deleterious effects on sperm nuclear quality and that sperm DNA fragmentation can therefore be considered as an independent parameter with diagnostic, prognostic, and strategic value in the treatment of infertility.

Source: Toxicology, Vol. 223, Issue 1-2, June 2006.

HEALTH EFFECTS OF CHILDHOOD DENTAL RESTORATION USING DENTAL AMALGAM OR RESIN COMPOSITE MATERIALS: A COMPARATIVE STUDY

Dental amalgam consists of approximately 50% elemental mercury. It has been used in dental prosthesis for about 150 years and was thought to be inert once it sets. Increasingly sensitive technology has recently demonstrated, however, that some of the elemental mercury in amalgam is vaporized under pressure from mastication, and positive correlations have been found between urine, blood, and tissue mercury levels and the surface area or number of amalgam fillings. Since high levels of mercury have been demonstrated to be toxic, the fact that dental amalgam induces some level of mercury exposure raised safety concerns. However, there is little or no evidence concerning health effects of low-level mercury exposure from amalgam, especially in children. A comprehensive review of evidence published since 1996 concluded that there still is not "sufficient evidence to support a causal relationship between dental amalgam restorations and human health problems".

The use of dental amalgam for posterior restorations remains part of standard care in the United States and in most other countries. Although alternatives to amalgam have been developed (primarily resin composite material), available evidence suggests that they do not match the strength and durability of amalgam and are associated with more recurrent caries and higher failure rates. In addition, the composite restorations cost more, are more technique sensitive, and have not been assessed with regard to related chemical exposures and their potential health effects. Given the cost-benefit dilemma associated with choosing between materials, it is important to determine any health risks associated with amalgam.

Thus a recent study reports the results of a clinical trial comparing the health effects among children who had dental restoration performed using dental amalgam or resin composite materials.

A total of 507 children in Lisbon, Portugal, aged 8 to 10 years with at least 1 carious lesion on a permanent tooth, no previous exposure to amalgam, urinary mercury level <10 µg/L, blood lead level <15 µg/dL, Comprehensive Test of Nonverbal Intelligence IQ >67, and with no interfering health conditions were selected for the study.

Intervention involved routine, standard-of-care dental treatment, with one group receiving amalgam restorations for posterior lesions (n=253) and the other group receiving resin composite restorations instead of amalgam (n=254).

Neurobehavioral assessments of memory, attention/concentration, and motor/visuomotor domains, as well as nerve conduction velocities comprised the main outcome measures.

During the 7-year trial period, children had a mean of 18.7 tooth surfaces (median, 16) restored in the amalgam group and 21.3 (median, 18) restored in the composite group. Baseline mean creatinine-adjusted urinary mercury levels were 1.8 µg/g in the amalgam group and 1.9 µg/g in the composite group, but during follow-up were 1.0 to 1.5 µg/g higher in the amalgam group than in the composite group (p<0.001). There were no statistically significant differences in measures of memory, attention, visuomotor function, or nerve conduction velocities (average z scores were very similar, near zero) for the amalgam and composite groups over all 7 years of follow-up, with no statistically significant differences observed at any time point (p values from 0.29 to 0.91). Starting at 5 years after initial treatment, the need for additional restorative treatment was approximately 50% higher in the composite group.

In this study, children who received dental restorative treatment with amalgam did not, on average, have statistically significant differences in neurobehavioral assessments or in nerve conduction velocity when compared with children who received resin composite materials without amalgam. These findings, combined with the trend of higher treatment need later among those receiving composite, suggest that amalgam should remain a viable dental restorative option for children.

Source: JAMA, Vol. 295, No. 15, April 2006.

Dental Mercury Exposure and Neurobehavioral Response in Humans

The central nervous system (CNS) is the critical target organ of elemental mercury (Hg^o), and there is little debate regarding the potential for toxicity from high-dose Hg^o exposures consistent with urinary mercury (HgU) levels exceeding 50 µg/L. There is a growing body of evidence from studies of dental professionals suggesting statistically significant exposure-effect associations between CNS-related declines and HgU levels less than 4 µg/g creatinine, approaching concentrations comparable to those observed in the general population.

Previous reports have described a porphyrinogenic response to low-level Hg^o exposure among a majority (~85%) of human subjects, characterized by predictable dose- and time-related increases in the concentrations of coproporphyrin, 5-carboxyl porphyrin and the atypical, ketoisocoproporphyrin (KICP), in the urine, and this response has been proposed as a biomarker of Hg^o exposure and potential toxicity.

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Dental Mercury Exposure and Neurobehavioral Response in Humans

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Notably, the remaining 12-16% of human subjects have been found in several population-based studies to manifest an atypical response to Hg^o exposure, characterized by excretion of highly elevated concentrations of coproporphyrin, 5-carboxyl porphyrin and KICP in the urine, exceeding the population mean (39.37, SD 28.74 µg/g creatinine) by more than 4-fold, well above the 80 µg/g creatinine upper 95% confidence limit (p<0.05).

Researchers have recently described a polymorphism, characterized by an A814C substitution in exon 4 encoding an asparagine-to-histidine change at amino acid 272 (N272H) of the human gene encoding the heme biosynthetic pathway enzyme, coproporphyrinogen oxidase (CPOX), in a population of dental professionals. Within this population, the frequencies of the homozygous common A/A allele genotype, the heterozygous (A/C) genotype, and the homozygous (C/C) genotype were 0.72, 0.25, and 0.03, respectively, and were equally prevalent in males and females.

This polymorphism in exon 4 of the coproporphyrinogen oxidase gene (CPOX4) was found to be predominant (>60% prevalent) among subjects manifesting this atypical response to Hg^o. In the present study, the potential effect of this polymorphism on domains of neurobehavioral performance that are known to be associated with exposure to Hg^o was evaluated. Notably, neuropsychiatric disturbances associated with prolonged Hg^o exposure are similar to those observed in the form of porphyria (hereditary coproporphyria) that is associated with inherited CPOX deficiencies and include increased irritability, depression, and anxiety (or affective disorders) coupled with neurologic declines in central and peripheral nervous system functions manifested in both cognition and sensory function. Of note, these conditions can be more strongly induced in females by endocrine factors where the mechanism of expression remains to be defined. A question of specific interest, therefore, is whether there is evidence of increased risk of neurotoxicity associated with Hg^o exposure among subjects with the CPOX4 polymorphism.

In the present study, it was hypothesized that neurologic health effects associated with Hg^o may be increased in the presence of the CPOX4 polymorphism, and their independent and joint effects were evaluated. This hypothesis was investigated in two independent populations composed of male dentists and female dental assistants.

In 1998, licensed dentists in Washington State (n=3750) were mailed a packet that included a letter of introduction, an informed consent, a screening questionnaire, and a urine collection kit. A total of 2675 urine samples were returned. A total of 1488 male dentists meet eligibility criteria for this study, which included (1) uninterrupted employment for five consecutive years prior to testing; (2) absence of health conditions that could alter performance or alter excretion of HgU including, but not limited to, all CNS system disorders, head trauma, diabetes, other kidney disease (e.g. lithiasis, pyelonephritis, orthostatic proteinuria), endocrine disorders, and cancer; and (3) no history of chelation therapy. Eligibility was further restricted to male dentists due to the very small number of female respondents. Between 1999 and 2001, from this pool a stratified random sample of 194 male dentists were recruited from groups formed by quartiles of HgU levels (to assure a full range of exposure). Finally, 233 female dental assistants meeting the same restrictions were recruited from the offices of participating dentists to provide a female cohort with a full range of exposures (as exposure levels are known to be related to office parameters). Mean (SD) HgU levels among dentists and dental assistants in the final study cohort were 3.32 (4.87) and 1.98 (2.29) µg/L, respectively.

A behavioral test battery was administered on the day of urine and buccal cell collections for 194 male dentists and 233 female dental assistants occupationally exposed to Hg^o for an average of 19 and 10 years, respectively.

In dentists, Hg-related declines were observed in one of three measures of attention, one of two measures of working memory, one of two measures of visual memory, visuomotor processing, as well as all three manual coordination tests. Furthermore, all scores for higher order cognitive flexibility functions remained intact, suggesting that Hg^o exposure may be too low to disrupt performance that is subject to strategy.

In dental assistants, Hg-related declines were also observed in performance in one of three measures of attention, visuomotor processing, and two of three motor coordination tests, but also expand the set of potentially positive findings to include the domains of perception, cognitive flexibility, and sensory function as measured by vibration threshold sensitivity. This pattern in both genders suggests that at least one or more measures within the domain of attention, working memory, visuomotor skill, and motor function were adversely affected at very low levels of Hg^o exposure. However, the results among dental assistants are more dispersed within and across domains, suggesting larger individual differences within dental assistants may increase sensitivity to Hg^o exposure, as reflected in lower levels of training among assistants as compared with dentists.

More objective behavioral testing was supplemented with an assessment of persistent symptom groups previously employed successfully among dentists and affect scales using the Profile on Mood Scales (POMS), Beck's Depression Index, and Symptom Check List-90 (SCL90). Overall, effects of Hg^o exposure on symptomology and affect were more prevalent among women, in part attributable to greater reporting of responses and/or use of medications, particularly, hormones. However, uneven results reported across three separate instruments used to assess mood suggests that the POMS may be slightly more sensitive to Hg^o exposure.

In light of the observed consistency in the expected direction across many measures demonstrating decreased performance associated with either increased HgU or with CPOX4 polymorphism, the statistically significant findings are more convincing. While requiring confirmation through further research, these findings support existing evidence of genetic susceptibility to Hg toxicity in human subjects. Ongoing studies are directed toward replication and further characterization of these associations in adults and children with low-level Hg^o exposure.

Source: Neurotoxicology and Teratology, Vol. 28, Issue 1, January – February 2006.

Health Impacts of Increases in Daily Levels of Particulate Matter in Ambient Air in Mexico City

Cardiovascular diseases are the main cause of death in Mexico City and have shown a rising trend over the past 20 years. In various epidemiological studies, the increase in cardiovascular mortality has been associated with an increase in the daily levels of particulate matter with an aerodynamic diameter of less than 10 µm (PM_{10}) and especially of fine particles [particles of less than 2.5 µm ($PM_{2.5}$)], even at levels under the national ambient air quality standards. Further, an increase in hospital admissions for acute myocardial infarction has been associated with an elevation in particulate matter and carbon monoxide (CO) concentrations.

Several physiological mechanisms have been proposed to explain the effect of these contaminants on cardiac events including alterations in the calcium channels of the myocardial cells and myocardial ischemia. The increase in acid aerosol level may have an irritating effect on the respiratory tract, resulting in acute bronchospasm, pulmonary edema, hypoxemia and an increase in oxygen demand. Another pathway is the inflammatory responses that increase endothelial dysfunction. Studies in animals exposed to diesel emissions have documented significant inflammation of the airways among those exposed to unfiltered fuels. Such inflammation may result in an increase in the coagulability of the blood and instability of the atherosclerotic plaque, resulting in an increase in the probability of development of clot formation and, consequently, of myocardial ischemia. Finally, alterations in the autonomic nervous system may increase the risk for cardiac arrhythmias.

One of the mechanisms that may allow for the functioning of this final process is the stimulation of sensory receptors located along the respiratory tract. This involves an alteration in the vagal response, an effect that can be observed as a decrease in the heart rate variability (HRV). Several HRV indexes have been developed to characterize cardiac autonomic function into parasympathetic (vagal) and sympathetic (adrenergic) responses using time-domain and/or frequency-domain measurements. An initial observation showed that environmental exposure to particulates was associated with changes in cardiac autonomic function in a panel of nursing home residents; further studies found an acute association (a same-day effect) between environmental and occupational exposures to particulates and fluctuations in HRV.

CO has been associated with an increase in hospital admissions due to arrhythmia and congestive cardiac failure. Other studies found an increase in the number of strokes associated with this pollutant. Recently, it has been reported that CO could have an impact on autonomic cardiac regulation.

Most of the studies have not simultaneously used electrocardiography (ECG) Holter monitors with $PM_{2.5}$ and CO personal samplers to assess this short-term relationship. Also, it is not clear if this effect may be stronger in sensitive populations such as patients with ischemic heart disease. These patients have a diminished ventricular ejection fraction (VEF) and a reduced HRV with predominant sympathetic activity over parasympathetic activity. Therefore, a further effect from PM and CO exposures may have significant clinical impact.

The present study sets out to assess the effect of $PM_{2.5}$, also known as respirable or fine particles and CO on HRV in 5-min periods in patients with known ischemic heart disease. Thirty patients were selected from the outpatient clinic of the National Institute of Cardiology of Mexico and followed during 11 h, using ECG ambulatory electrocardiograms and personal monitors for CO and $PM_{2.5}$. Frequency-domain measurements were calculated using power spectral analysis and assessed the association with pollutants using mixed models analysis in 5-min periods. A decrease was found in HRV measured as high frequency (coefficient = -0.008, 95% confidence interval (CI), -0.015, 0.0004) for each 10 µg/m^3 increase of personal $PM_{2.5}$ exposure. A decrease was also found of low (coefficient = -0.024, 95% CI, -0.041, -0.007) and very low frequencies (coefficient = -0.034, 95% CI, -0.061, -0.007) for 1 parts per million (ppm) increase in CO personal exposure after adjustment for potential confounding factors. These results show that for this high-risk population, the alteration of the cardiac autonomic regulation was significantly associated with both $PM_{2.5}$ and CO personal exposures.

Among the study limitations was the lack of information on personal exposures to other pollutants. It would have been of interest to measure ozone concentrations since some studies have found an ozone-particle interaction affecting HRV. Also, a potential additional limitation was the use of the personal data ram (PDR) device to monitor personal $PM_{2.5}$ exposures, given that some studies have found that they overestimated PM concentrations, comparing them with Harvard impactors (HI2.5) measurements with this device. Therefore, the nondifferential measurement error would not affect the associations that have been reported in this study.

For this vulnerable group of patients, a consistent association between increased personal $PM_{2.5}$ and CO exposures and decreases in HRV was found. These results suggest that exposures to these pollutants may alter the balance of cardiac autonomic control, and thus may increase the susceptibility of high-risk patients to adverse cardiac events. Further studies are needed to confirm these findings.

Source: Journal of Exposure Science and Environmental Epidemiology, Vol. 16, No. 2, March 2006.

CARDIOVASCULAR EFFECTS OF PULMONARY ZINC EXPOSURE

Exposure to particulate matter (PM) in ambient air has long been associated with cardiopulmonary health effects. Records show that the majority of deaths associated with increased exposure to PM have been cardiovascular in nature. This has prompted significant interest in investigating the interactions of pulmonary and vascular responses following pulmonary exposure to toxic agents.

In a recent study researchers developed a rat model of pulmonary exposure to zinc in order to demonstrate cardiac, coagulative, and fibrinolytic alterations.

Male Wistar Kyoto rats were instilled intratracheally with saline or zinc sulfate, 131 µg/kg (2 µmol/kg); the alterations were determined at 1, 4, 24, and 48 h postexposure. High-dose zinc enabled changes to be shown in circulating levels of zinc above normal and induce significant pulmonary inflammation/injury such that cardiac impairments were likely. At 1-24 h postexposure, plasma levels of zinc increased to nearly 20% above the base-line. Significant pulmonary inflammation and injury were determined by analysis of bronchoalveolar lavage fluid and histopathology in zinc-exposed rats at all time points. Starting at 4 h postexposure, pulmonary damage was accompanied by persistently increased gene expressions of tissue factor (TF) and plasminogen activator-inhibitor-1 (PAI-1), but not thrombomodulin (TM). Cardiac tissues demonstrated similar temporal increases in expressions of TF, PAI-1, and TM mRNA following pulmonary instillation of zinc. In contrast to extensive pulmonary edema and inflammation, only mild, and focal acute, myocardial lesions developed in a few zinc-exposed rats; no histological evidence showed increased deposition of fibrin or disappearance of troponin. At 24 and 48 h postexposure to zinc, increases occurred in levels of systemic fibrinogen and the activated partial thromboplastin time.

This small effect of zinc on cardiac pathology despite a marked stimulation of coagulation and fibrinolytic pathways may suggest that a longer period of time is needed for discernible histopathological damage to occur following exposure, or blood coagulation changes may not necessarily result in visual pathological lesions in the heart in acute scenarios. One pertinent observation is that this acute exposure resulted in massive pulmonary-cell damage and neutrophilic inflammation, but not infiltration or accumulation of macrophages. The roles that pulmonary neutrophil versus macrophage infiltration may play in inducing procoagulative and degenerative changes in the heart are not clear; however, studies of these functions may provide insight into mechanisms of cardiovascular impairment for a variety of pulmonary ailments.

Despite procoagulative gene expression induced by zinc exposure, no indication of enhanced fibrin deposition in the heart could be found. The staining technique employed, while giving a good indication of large changes in fibrin deposits, was not useful for detecting increases in the deposition of fibrin in capillaries; further analysis is required for this specific detection. Furthermore, although no widespread myocardial injury occurred at the time points studied, it had been previously demonstrated that myocardial lesions do occur following chronic extended exposure to zinc-containing particles, and, thus, a chronic exposure to zinc or a predisposed disease susceptibility may be necessary to detect altered fibrin deposition and myocardial degeneration.

Evidence for a procoagulative status was strengthened in this study by the increased levels of plasma fibrinogen. Plasma fibrinogen in animals and humans has been shown to increase in response to PM. The increase in plasma fibrinogen following intratracheal instillation of zinc was not as remarkable as that seen with intratracheal exposure to metal-rich combustion particles, despite the greater severity of the pulmonary injury; these findings suggest that the mechanism of fibrinogen increase and its role in overall cardiac impairment may differ with different types of pulmonary insults. Although the increase in plasma fibrinogen is indicative of a procoagulative status, the actual clotting time of the blood increased after 24 and 48 h in the zinc-exposed animals. This increase is consistent with an increase in the mRNA expression of the clotting inhibitor TM in the heart. This may suggest an adaptive response in the heart and explain the lack of histologically discernible deposition of fibrin. The lack of TM expression in the lung may be reflective of overt pulmonary injury and the lack of compensatory ability.

The study showed that pulmonary exposure to zinc resulted in a rapid increase in circulating zinc, which persisted for up to several hours. Acute zinc-induced pulmonary injury and inflammation were associated with marked procoagulative effects on the heart with suggestions of mild acute cardiac lesions. The cardiac procoagulative effects could be due either to pulmonary injury and neutrophilic inflammation and/or a direct effect exerted by zinc itself. While pulmonary injury/inflammation were marked and progressive, circulating zinc remained high for several hours following exposure, and the heart would potentially encounter high concentrations of zinc following its first passage through the pulmonary artery and, subsequently, the left ventricle.

Source: Toxicology and Applied Pharmacology, Vol. 211, Issue 1, February 2006.

CHLORPYRIFOS AND NEURONAL DEVELOPMENT

There is mounting evidence that the organophosphate insecticide chlorpyrifos adversely affects mammalion brain development through a variety of mechanisms. This widely used insecticide has both direct and indirect effects on neural cell replication and differentiation resulting in immediate and delayed changes in synaptogenesis, neurotransmitter release, expression of neurotransmitter receptors, and intracellular signaling, over and above the consequences of cholinesterase inhibition.

The disparate nature of chlorpyrifos effects on brain development, combined with potential impact on the maternal-fetal unit or general aspects of fetal or neonatal growth and development, renders it especially difficult to identify specific underlying mechanisms from *in vivo* studies or to discern why specific developmental stages or neurotransmitter systems might be especially targeted by chlorpyrifos. Accordingly, recent attention has focused on *in vitro* models, including neuronotypic and gliotypic cells as well as primary cultures of mixed neurons and glia. PC12, a transformed neuronotypic cell line, provides one of the most useful model systems for evaluations of developmental neurotoxicants.

Thus, in a recent study to determine if chlorpyrifos directly affects neuronal cell replication and phenotypic fate, and to identify the vulnerable stages of differentiation, researchers at Duke University Medical Center, North Carolina, USA, exposed PC12 cells to chlorpyrifos concentrations spanning the threshold for cholinesterase inhibition (5-50 μM) and conducted evaluations during mitosis and in early and mid-differentiation.

In undifferentiated cells, exposure to 5 μM chlorpyrifos for 1-3 days reduced DNA synthesis significantly without eliciting cytotoxicity. At the same time, chlorpyrifos increased the expression of tyrosine hydroxylase (TH), the enzymatic marker for the catecholamine phenotype, without affecting choline acetyltransferase (ChAT), the corresponding marker for the cholinergic phenotype. Upon exposure to nerve growth factor (NGF), PC12 cells developed neuritic projections in association with vastly increased TH and ChAT expression accompanying differentiation into the two phenotypes. Chlorpyrifos exposure begun at the start of differentiation significantly reduced ChAT but not TH activity. In contrast, when chlorpyrifos was added in mid-differentiation (4 days of NGF pretreatment), ChAT was unaffected and TH was increased slightly. Thus, chlorpyrifos exerts stage-specific effects, reducing DNA synthesis in the undifferentiated state, impairing development of the cholinergic phenotype at the start of differentiation, and promoting expression of the catecholaminergic phenotype both in undifferentiated and differentiated cells. Chlorpyrifos administration *in vivo* produces deficits in the number of neurons and cholinergic function, and because the study was able to reproduce these effects *in vitro*, the results suggest that chlorpyrifos directly influences the phenotypic fate of neuronal precursors.

Source: Environmental Health Perspectives, Vol. 114, No. 5, May 2006.

The Effects of Lead on the Avian Auditory Brainstem

Lead is a significant environmental toxin. It has been shown to be a potent toxin to the central nervous system, and low levels of lead have been correlated with decreases in the IQ of children. Lead exposure is also a risk factor for dyslexia, and significantly, dyslexics have deficits in auditory temporal processing, including backward masking. Auditory temporal information is essential for appropriate speech detection, and it is not known where within the auditory axis temporal processing takes place, nor is it understood how lead exposure modifies the cells of the auditory system.

To address these questions, researchers have developed an animal model of auditory temporal processing using chickens and have established that low level exposure to lead during avian development results in decreased immunoreactivity for neurofilament and phosphorylated neurofilament.

This does not appear to be a general response of the avian brainstem to lead as other regions of the brainstem do not appear to show these changes and the alterations in neurofilament is most obvious in the axons of the auditory brainstem. Similar studies performed in mice also confirm that lead exposure does not uniformly alter neurofilament quantity or structure within the entire brainstem, although nuclei and fiber tracts within the auditory brainstem are altered. Neurofilaments are composed of three subunits, NFH (high molecular weight), NFM (medium molecular weight), and NFL (low molecular weight). Axons are not considered completely mature until NFH is formed and are thought to play a role in axonal transport. Lead has been shown to impair slow axonal transport in the rat and also slows the transport of neurofilament proteins. Recent studies have demonstrated that neurofilaments actually move at fast conventional rates but this movement is interrupted by prolonged pauses, with axonal neurofilaments spending up to 97% of their time pausing during transport down the axon. Significantly hypophosphorylated neurofilaments are transported more quickly than extensively phosphorylated ones and it has been hypothesized that phosphorylation results in detachment of neurofilaments from their motors. The present study found a lead-induced decrease in phosphorylation of NFM. Because lead does slow the transport of neurofilament proteins and also decreases slow axonal transport, hypophosphorylation of neurofilament could be a compensatory mechanism by which the neuron is attempting to

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The Effects of Lead on the Avian Auditory Brainstem

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restore neurofilament transport back to normal levels.

Importantly, a recent study has shown that there is a reduction in the conduction velocity within the cochlear nerve of neurofilament deficient quail. The auditory nerve fibers in these quail are smaller in diameter and lack the central cores of neurofilament within their axons and cell bodies. The authors of this study demonstrated that decreased amounts of neurofilament within axons resulted in decreased conduction velocities. This suggests that the decrease in neurofilament that were observed in the present study in the axons surrounding Nucleus Magnocelluris and Nucleus Laminaris following lead exposure may result in decreased conduction velocities of these axons. Future studies will test this hypothesis.

Source: NeuroToxicology, Vol. 27, Issue 1, January 2006.

ARSENIC TOXICITY IN PARP DEFICIENT CELLS

Poly(ADP-ribose) polymerase-1 (PARP-1), the best-characterized member of the PARP family is an abundant nuclear zinc finger protein found in most eukaryotes. PARP-1 primarily functions as a DNA damage sensor by recognizing and binding with high affinity to both single-stranded DNA (ssDNA) and double-stranded DNA (dsDNA) breaks that arise directly or indirectly as byproducts of ongoing DNA repair process. Further PARP-1 also facilitates the access of other DNA repair factors to the sites of DNA damage. PARP-1 is also known for its ability to modulate the cellular responses either to survive or to undergo apoptotic death, depending on the extent of DNA damage.

Arsenite is a significant environmental concern worldwide especially in some parts of the United States as well as in Argentina, Canada, India, Japan, Thailand, Taiwan, and Bangladesh. Chronic exposure to inorganic arsenite is associated with hepatic injury, peripheral neuropathy, and a wide variety of cancers. Many different modes of arsenite-induced genotoxicity have been identified, including oxidative stress, altered DNA repair and methylation mechanisms, altered cell proliferation and abnormal gene amplification. Recently, very low concentrations of arsenite have been shown to inhibit poly(ADP) ribosylation of proteins in mammalian cells.

A previous study showed that the PARP-1-deficient mice had drastically shortened telomeres with high chromosomal instability. In addition, PARP-1 deficiency also induced telomere dysfunction and tumor development in mice with a p53 mutant background. PARP-1 thus seems to function in regulating telomere length as well as telomeric end capping. In view of its importance in both DNA repair and chromosome stability, the present study was undertaken to determine whether PARP-1 is an important genetic factor responsible for arsenic-induced cytotoxicity in mammalian cells.

Identification of genetic factors that contribute to arsenic mutagenicity and carcinogenicity is critical for the treatment and prevention of arsenic exposure in human population. As PARP is critical for genomic DNA stability, the role of PARP-1 was evaluated in arsenic-induced cytotoxic and genotoxic effects. The study revealed that telomere attrition, probably owing to arsenite-induced oxidative stress, was much more pronounced in PARP-$1^{-/-}$ mouse embryonic fibroblasts (MEFs; 40%) compared with PARP-$1^{+/+}$ MEFs (10-20%). Correlation observed between telomere reduction and apoptotic death in PARP-1 null cells strongly indicates that the telomere attrition might be a trigger for enhanced apoptotic death after arsenite treatment. Elevated DNA damage detected by alkaline comet assay points to an impaired repair ability of arsenite-induced DNA lesions in PARP-$1^{-/-}$ MEFs. Consistent with elevated DNA damage, increased micronuclei induction reflecting gross genomic instability was also observed in arsenite-treated PARP-$1^{-/-}$ MEFs. Microarray analysis has revealed that arsenite treatment altered the expression of about 311 genes the majority of which have known functions in cellular responses to stress/external stimulus and cell growth and/or maintenance. The results suggest an important role for *PARP-1* gene product in the maintenance of chromosome-genome stability in response to arsenite-induced DNA damage.

Source: Cancer Research, Vol. 65, No. 23, December 2005.

BIOREMEDATION OF PAH-CONTAMINATED ANOXIC ESTUARINE SEDIMENTS

Estuarine sediments are frequently polluted with hydrocarbons from fuel spills and industrial wastes. Polycyclic aromatic hydrocarbons (PAHs) are components of these contaminants that tend to accumulate in the sediment due to their low aqueous solubility, low volatility, and high affinity for particulate matter.

Documented impacts on critical habitats include contamination of benthic ecosystems, with subsequent harm to the marine food chain.

Researchers have studied the anaerobic biodegradation of PAHs in sediment since the late 1980s. For anaerobic processes, PAH degradation coupled to sulfate reduction is the most relevant to coastal marine sediments, because sulfate is abundant in seawater, whereas nitrate concentrations are typically low and Fe(III) is often only slightly available.

PAHs are generally slowly degraded in the environment, particularly in marine systems. The low degradation rates of PAHs may be due to their stable structures, adsorption onto particulate matter, or nutrient deficits in the environment. The bioremediation of PAH-contaminated anoxic sediments has been restricted to the application of alternative electron acceptors. However, little information is available on the effects of applying surfactants, inorganic or organic nutrients, or growth factors on PAH biodegradation in anoxic sediments.

Now, a new study has been conducted to examine the degradation of PAHs in anaerobic estuarine sediments to investigate the possible role of microbial activity. The effects of adding biostimulating agents (surfactants, nutrients, carbon sources, and growth factors) on the extent and rate of PAH degradation were also evaluated.

In the study, PAH-contaminated sediments were collected as grab samples from an estuary immediately adjacent to a petrochemical factory in the industrial area of Gwangyang Bay, Korea.

In petroleum-contaminated sediments near the petrochemical plant, *in situ* PAH concentrations ranged from 10 to 2,900 μg/kg dry sediment. To enhance the biodegradation rate of PAHs under anaerobic conditions, sediment samples were amended with biostimulating agents alone or in combination: nitrogen and phosphorus in the form of slow-release fertilizer (SRF), lactate, yeast extract (YE), and Tween 80. When added to the sediment individually, all tested agents enhanced the degradation of PAHs, including naphthalene, acenaphthene, anthracene, fluorene, phenanthrene, fluoranthene, pyrene, chrysene, and benzo[a]pyrene. Moreover, the combination of SRF, Tween 80, and lactate increased the PAH degradation rate 1.2-8.2 times above that of untreated sediment (0.01-10 μg PAH/kg dry sediment/day). The results indicated that *in situ* contaminant PAHs in anoxic sediment, including high molecular weight PAHs, were degraded biologically and that the addition of stimulators increased the biodegradation potential of the intrinsic microbial populations. These results will contribute to the development of new strategies for *in situ* treatment of PAH-contaminated anoxic sediments.

Source: The Journal of Microbiology, Vol. 43, No. 4, August 2005.

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