

**10486- Apolipoprotein E Genotype and Lead Exposure in Predicting 24 Month Infant Bayley Scale Score**

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**Background.** Apolipoprotein E (APOE) regulates cholesterol and fatty acid metabolism, two important factors in nerve growth and metabolism. While the E4 allele is associated with Alzheimer's disease, isoform specific effects on infant development have not been studied to our knowledge. **Methods.** This study was nested within a randomized controlled trial of calcium supplementation in breastfeeding mothers in and around Mexico City. Cord blood samples were collected at birth and used to measure lead concentration and for APOE genotyping. A multiple linear regression model was constructed using the 24 month Mental Development Index (MDI) of the Bayley Scale as the dependent variable. APOE genotype, maternal calcium supplementation and sex were entered as indicator terms. Cord lead concentration, maternal IQ, gestational age, and maternal years of education were entered as continuous variables. To explore potential interactions with lead exposure, we stratified by the presence or absence of the E4 allele and repeated the regressions within each strata, using the cord lead level and the same covariates as predictors. **Results:** Among 435 subjects with archived blood available for genotyping, 309 subjects had complete data on APOE genotypes and 24 month MDI scores. Of these, 55/309 (16%) carried at least one copy of APOE4. Mean (STD) MDI scores among APOE4 carriers were 94.1 (14.3) and among E3/E2 carriers were 91.2 (14.0). After adjusting for the covariates, the beta coefficient for APOE4 carriers in predicting 24 month MDI was 4.3 (95% CI 0.03-8.5;  $p=0.049$ ). In the stratified regressions, the beta for cord lead level predicting MDI among subjects without the E4 allele was -0.78 (95% CI: -1.30 to -0.27), among subjects with at least one E4 allele the beta was -0.38 (95% CI -1.6 to 0.85). **Discussion:** In this population of urban Mexican children, subjects with at least one copy of the APOE4 allele had higher 24 month MDI scores. Furthermore, the adverse effect of cord lead levels on MDI scores was attenuated among APOE4 carriers, suggesting a possible gene-environment interaction. Given that the APOE protein functions in neuronal growth and repair, these results suggest that subjects with the E4 isoform may have advantages over the E2 and E3 isoforms with respect to early life neuronal/brain development. Further study in a larger cohort will be needed to validate these results.

**10749- GSTT AND GSTM ASSAYS FOR DNA EXTRACTED FROM NEWBORN AND ADULT BLOOD SPOTS: CASE STUDIES FROM CANCER EPIDEMIOLOGY**

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Newborn bloodspots are collected almost universally for births in the U.S. in order to screen for inborn errors of metabolism. Some states of the U.S. store these samples for many years. The samples provide an opportunity for retrospective and prospective population-based DNA testing amenable to epidemiologic studies of gene-environment interactions. Blood spots can also be useful in certain epidemiological field studies, where the collection of whole blood from subjects may be impractical or proscribed.

We have adapted and demonstrated methods of extracting DNA from stored, dried blood spots from newborns and adults, for use in polymerase chain reaction (PCR)-based assays of important polymorphisms of "phase II" metabolizing enzymes involved in the elimination of genotoxic xenobiotics, specifically glutathione-S-transferase (GST)M1 and T1 loci. Homozygosity and heterozygosity for the null allele at each of these loci decrease the rate of detoxification of DNA-reactive electrophiles and thereby increase the potential for mutagenesis and carcinogenesis. Homozygous null genotypes comprise about 50% and 30% of the U.S. population, respectively. Numerous case-control epidemiologic studies have demonstrated gene-environment interactions of these null alleles, specifically in terms of increasing the risk from teratogenic and carcinogenic exposures.

This poster presents the DNA extraction and PCR methods. In addition, we illustrate the use of this assay in the context of a case-control study of non-Hodgkin's lymphoma in Egypt. We obtained blood spots from 100 randomly selected and anonymous infants born in New Jersey in 1996. From an ongoing case-control study of adults at a large oncology referral center in Cairo, Egypt, we obtained blood spots from 167 cases with non-Hodgkin's lymphoma and 156 hospital controls. Laboratory results are as follows and are within the reported world-wide range of variability of these polymorphisms.

<u>Study population</u>	<u>GSTM1 null</u>	<u>GSTT1null</u>
Population-based infants (New Jersey)	43%	20%
Adult lymphoma cases (Egypt)	39%	20%
Adult lymphoma controls (Egypt)	23%	19%

**Post-flood fungal contamination of indoor in buildings and potential genotoxic hazard.**

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Background: Molds, their germs (spores), mold-contaminated airborne particles and fungal metabolic products (mycotoxins) increase a genotoxic risk and allergic responses leading to hypersensitivity diseases of man (e.g., respiratory allergic symptoms). Experimental data indicate that a long-term exposure to airborne particles contaminated by toxinogenic molds increases the risk of cancer of the respiratory system. The fungal growth observed inside of flooded buildings suggested a potential health hazard to the persons involved in their reconstructions and future occupants. The following presentation includes a summary of original data from our study, which demonstrate that fungal post-flood contamination (observed inside of flooded buildings) represented a real health hazard for inhabitants.

Methods: Investigations were carried out in residential and school buildings in 5 localities of the post-flood area (City of Ostrava, August 1997). Mold samples (133 specimens) were obtained by swabbing walls of residential rooms and basements. The mold isolates were cultivated and extracted into chloroform (for the TLC detection of mycotoxins and genotoxicity tests – Ames test, SOS Chromotest and the detection of embryotoxicity on 40hr old chick embryos).

Results and Conclusions: From 133 swabs from walls, 110 different strains of molds (67 from the genus *Penicillium*, *Aspergillus* and *Fusarium*) were isolated, 30% of them were toxicogenic. The following mycotoxins were identified in the extracts of the samples: Patulin, Tenuazonic acid, Penicillinic acid, Penitrem A, Ochratoxin A, Deoxynivalenol, Zearalenon. The results of the mycotoxin analysis showed a remarkable occurrence of the *Fusarium* strains with T-2 toxin production (from trichothecene group). Some mold extracts were investigated for mutagenic activity in microbial test systems and embryotoxicity. Mutagenicity was observed especially in the assay with metabolic activation *in vitro*. Owing to the measures taken by the hygiene service of the CR directly after the flood in the city of Ostrava (protective respirators, intensive anti-mold decontamination of buildings), the mycological contamination of upper respiratory airways (proved by the throat smears) did not show a direct human risk.

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