ISEE-316

CHLORINATION DISINFECTION BY-PRODUCTS AND ADVERSE BIRTH OUTCOMES IN GREAT BRITAIN: BIRTHWEIGHT AND STILL BIRTH

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Recent epidemiological studies of the relationship between disinfection by-products, from chlorination, in public drinking water supply and adversa birth outcomes, have reported inconsistent and inconclusive findings. We report here on the largest study to date to examine the relationship of total trihalomethanes (TTHMs) to birth weight and still birth prevalence, between 1993 and 1998, for regions covered by three water companies in England. Modelled estimates of mean annual TTHM concentrations in water zones were linked to routine birth and stillbirth records based on location of maternal residence at the time of birth. Three exposure categories were used: low (<30 mg/l), medium (30-60 mg/l) and high (>60 mg/l). After exclusion of multiple births and births from water zones without valid TTHM data, we studied a total of 934,843 live and stillbirths. In one region (North West), where there was a social class gradient across exposure categories (greater deprivation in the higher exposure categories), we found a graded, inverse association between level of exposure and mean birth weight, and a direct association with prevalence of low and very low birth weight (and more weakly with risk of still birth). However, there was evidence of confounding by social deprivation, and findings were essentially negative in both of the other two regions. For low birth weight, there was an interaction between social deprivation and TTHM exposure, such that in the North West region, the risk in the high compared with the low exposure category was highest in the most deprived areas. We suggest that our findings in one region would appear to merit further investigation in other areas with differing water supply patterns and socio-economic profile.

ISEE-317

THE DEVELOPMENT OF THE AEROBIOLOGICAL NETWORK IN THE CEE COUNTRIES AND THE RELEVANCE OF THE DATA TO THE PARTICULATE DEBATE

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Aerobiology investigates aerial transport of biological materials important to human health. Allergen particles are monitored by volumetric trap, values are given daily in grains/m3. WHO/EURO have organized collaborative studies on the health effects on the respiratory system of SO2 and dust in several countries since 1970s. The evaluation failed in intercomparisons. Later a palynologist was invited for a workshop in 1989 to elucidate the possible role of aeroallergens as a particle component. There were Aerobiological Networks in most of the Western countries but none in the CEECs. Due to the initiative the first 'Eastern European Workshop on Airborne particles morphology by recording volumetric trap' was organized by the first author in Budapest in 1992 with the financial support of the Regional Environmental Center (Budapest). From that time on pollen stations were established, now several stations exist in the CEECs, pollen and spore count databases are available for several years. The first presentation of the light microscopic morphology of suspended particulates collected by a Burkard trap was at the Aerobiological Conference (Farkas et al. 1990). Evaluation of the association between pollen and respiratory symptons was discussed at the 'Health Effects of Particulate Matter in Ambient Air' Symposium (Farkas 1997). Recently the study of the effect of daily variation of pollen count was introduced into the Hungarian APHEA2 project. The increase of total daily pollen count had an impact on the daily cardiovascular mortality. (Páldy et al. ISEE 2000). When health effects of suspended particulates are evaluated, the role of the allergen particles should be considered.

ISEE-318

ON THE EXPOSURE-TIME-RESPONSE-RELATIONSHIP BETWEEN OCCUPATIONAL ASBESTOS EXPOSURE AND LUNG CANCER IN TWO GERMAN CASE-CONTROL STUDIES

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Objectives: Numerous studies have baen carried out to evaluate the association between lung cancer and occupational asbestos exposure. However, the effects of timing of exposure have not been analyzed thoroughly.
Methods: Two German case-control studies with data on occupational asbestos exposure histories have been pooled. Duration of work in potentially asbestos exposed jobs and two derived weighted exposure measures are analysed together with time since last exposure. A spline function is used to model the effect of time since exposure.
Results: The odds ratios (OR) and correeponding 95% confidence intervals were 1.8 (1.2,2.7) and 2.4 (1.7,3.4) for subjects having worked for 3 to 7 years and 8 or more years, respectively, in a job with potential asbestos exposure compared to never-exposed. Based on an evaluation of time since last exposure, the OR decreased significantly to about one-half after more than 20 years since exposure ceased. Using a spline function, applied to workers' complete exposure histories, the effect of an increment of exposure is greatest 10 to 15 years after that exposure was received, then declines. Whether this decline continues and risk returns to baseline after more than 25 years remains unclear.
Conclusions: Risk of lung cancer decreased significantly with time since last exposure. The estimated latency curve suggested a maximum effect 10 to 15 years after the exposure was received. However, this pattern was not statistically significant. It is important to evaluate whether this pattern is consistent with other data sets.

ISEE-319

RISK FACTORS FOR LUNG CANCER IN LIFETIME NONSMOKING WOMEN

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Introduction: To evaluate risk factors for lung cancer in nonsmoking women we used data of a case-control study conducted between 1990 and 1996 in Germany.
Methods: A total of 234 female histologically confirmed lung cancer patients and 535 population controls who had never smoked more than 400 cigarettes in their lifetime were personally interviewed with respect to occupational history, exposure to environmental tobacco smoke (ETS), family history of cancer, previous non-malignant lung diseases (diagnosed by a physician at least 2 years befora interview) and dietary habits (10 food items). Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI).
Results: After controlling for age and region elevated effects of exposure to ETS by spouse (OR=1.7, CI:0.9-3.3) and at work (OR=2.7, CI:1.4-5.2) were observed among highly compared to not or low exposed women. Occupational exposure to lung carcinogens was rare (about 10%), but associated with an increased risk among women who had worked more than 10 yeers in such jobs (OR=2.0; CI:0.99-4.0). An increased risk due to previous lung diseases such as asthma, tuberculosis, emphysema, chronic bronchitis or pneumonia was present for pneumonia (OR=1.6; CI:1.1-2.4) only. A positive family history of cancer or lung cancer showed no elevation in risk. Protective effects were observed for high vs. low consumption of fresh vegetables (OR=0.5; CI:0.3-0.8) and cheese (OR=0.3, CI:0.2-0.6). Results are not confounded by socioeconomic status.
Conclusions: We conclude that ETS particular at work, occupational exposure to lung carcinogens and previous pneumonia are risk factors for lung cancer in nonsmoking women, while a dietary rich in fresh vegetables and cheese seems to be protective.

ISEE-320

NUTRIENT INTAKE PATTERNS IN GASTRIC AND COLORECTAL CANCERS

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The purpose of the study was to present the dietary risk pattern in gastric and colorectal cancer using the same methodological approach in a parallel hospital-based case-control study. In total 180 cases of colorectal cancer and 80 cases of stomach cancer confirmed by histopathology were enrolled from the University Hospital in Krakow. The equal number of controls was chosen from amongst patients with no history of cancer from the same hospital matched to cases by age (+/-5 years) and gender. An interviewer-administered food questionnaire was used to assess the usual dietary pattern. The high carbohydrates intake was associated with increased risk of colorectal cancer (OR=2.45). For stomach cancer, the moderate consumption of carbohydrates increased relative risk markedly (OR=4.2), in the high intake of carbohydrate the risk increased by 8.73. Patterns of dietary risk factors related to intake of fats were definitively different in both cancer sites. Higher fat consumption was not associated with the higher risk of stomach cancer. Medium intake of fats increased the risk of colorectal cancer by 1.96 and that above 83 g/day increased the risk by 2.20. In colorectal cancer the significant protective effect of retinol, carotene and vitamin C intakes has been evident, however, only carotene and vitamin E were inversely correlated with stomach cancer. The study has indicated that retinol intake is inversely correlated with colorectal cancer. Although the considerable changes in the dietary habits taken place over the last ten years, they are insufficient to expect a faster decline in stomach cancer or positive change in colorectal cancer rates.

ISEE-321

ANALYSIS OF NON MELANOMA SKIN, LUNG AND BLADDER CANCER INCIDENCE IN ARSENIC EXPOSED POPULATION

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Our analysis is based on a population of the Prievidza, Central Slovakia district. The subject of our analysis was a database of skin basalioma (800), spinocellular (224), lung cancer (845) and bladder cancer (162) cases collected within 15 years (3 five year intervals) in a region polluted by emissions from burning of coal with high arsenic content ranging between 900 to 1,500 g per metric ton of dry coal. Study base in non-occupational exposed settings are 988,283 man-year and 991,290 woman-year. Study base in occupational settings (power plant male workers) is 21,360 man-year during a period of 15 years Exposure assessment was based on biological monitoring. Determination of arsenic was done in groups of 10 year old boys (in non - occupational settings) by analysing of hair and urine samples at different localities situated up to the distances of 30 km from the local power plant. The standardised incidence of lung and bladder cancer, skin basalioma and spinocellular cancer was done in a district with population ~125,000 in non-occupational exposed settings, while relevant data for occupational exposed settings were registered in male workers of power plant burning arsenic reach coal. Smoking habit was carefully registered in all cancer patients including lung cancer cases and potential contribution of the both factors is subject of a current analysis. The results of our database analysis confirmed expected increased incidence of non-melanoma skin cancer during the period of the high environmental pollution by arsenic emissions. As to lung cancer incidence at our exposure pattern smoking was more important then arsenic exposure itself. The results obtained seemed to suggest that arsenic is probably a promotor rather than a true carcinogen.

statistics for linkage based on preferential transmission: when are they tests of association? *J. Wicks[1,2].* 1) Inst. for Molecular Bioscience, Univ sland, St Lucia, Australia; 2) Department of Mathematics, Univ of Queensland, ia, Australia.

s for linkage based on the preferential transmission of a particular marker allele cted children can have considerably more power to detect linkage for complex ses than traditional sib-pair or LOD-score methods. If such tests are also valid of association, then they have the additional property that positive results are sug- e of tight linkage between the disease gene and the marker, and can therefore be in localising disease genes.

e statistics based on preferential transmission for a bi-allelic marker have the al form

$$N_2)^2/\mathrm{var}(N_1-N_2) \qquad (1)$$

N_i is a function of the data counts corresponding to preferential transmission of er allele A_i, and $\mathrm{var}(N_1-N_2)$ is the variance, or an estimate thereof. The first statistic is kind to be devised was the TDT. Various statistics of the form of (1) have since n devised for different types of nuclear families, and recently, for general pedigrees (Martin et al, 2000).

deriving a statistic of the form (1) to test for linkage, there are often a number of natives for $\mathrm{Var}(N_1 - N_2)$ which may be used. What we show is that this choice is the ding feature in determining whether or not statistics of this form are valid tests of ociation as well as linkage. The TDT is a valid test of association as well as linkage r nuclear families with one affected child only. However, our results show that if the iance used in the TDT is replaced by a different variance estimate, then the resulting sta- ic is a valid test of both linkage and association when used with nuclear families with any mber of affected children and with affected members of larger pedigrees also.

1398

Regional microsatellite variation in Finland. *E.T. Salmela[1,2], P. Lahermo[1], M-L. Savontaus[3], P. Sistonen[4], J. Kere[1].* 1) Finnish Genome Center, University of Helsinki; 2) Department of Genetics, University of Turku; 3) Department of Medical Genetics, University of Turku; 4) Finnish Red Cross Blood Transfusion Center.

Even though the relationships between the Finns and other European populations have been subject to study and numerous disease gene studies have been successfully conducted among the Finns, the population structure of Finland has received little attention. We measured variation in the allele frequencies of 31 microsatellite markers from 15 different chromosomes among the Finnish population. The selection of the markers was based on the occurrence of rare alleles in the Finnish population observed during the routine genome wide scans performed at the Finnish Genome Center. Blood samples of 465 males were collected from different parts of Finland and grouped into nine subpopulations based on the birthplaces of their grandparents. The purpose of the study was to measure the quality and quantity of genetic variation within and between different regions of Finland. The earlier observations based on blood group markers have suggested substantial differences in the allele frequencies of individual markers on the community level but more subtle ones on the county level, and they were supported in this analysis. The total amount of variation was not conspicuously different between the regions of late and early settlement, although differences in the amount of variation between the individual counties within these two groups could be seen. No clear East-West cline was observable in the initial analysis. North Carelians in the east and Swedish-speaking Ostrobothnians in the west had the largest amount of deviations from the average allele frequencies of the Finns. These observed trends are expectable with regard to the Finnish population history.

1399

he origins of the Negroid Makrani population from Pakistan: maternal and pa- ernal perspectives. *L. Quintana-Murci[1], R. Qamar[2], S.Q. Mehdi[2], Q. Ayub[2], A. Mohyuddin[2], T. Zerjal[4], H.J. Bandelt[3], K. McElreavey[1], C. Tyler-Smith[4].* 1) Dept Human mmunogenetics, Pasteur Inst, Paris, France; 2) Biomedical & Genetic Engineering Di- sion, Islamabad, Pakistan; 3) University of Hamburg, Germany; 4) Department of Bi- chemistry, University of Oxford, UK.

The Negroid Makrani population live near the Makran Coastal range in south-western Pakistan and are considered to have strong African roots based on anthropological and cultural evidence. The origins and affinities of this population have been investigated through a detailed genealogical study of mitochondrial DNA (mtDNA) and Y chromosome variation. RFLP and control region (CR) sequence analysis revealed that more than 40% of the Makrani mtDNA lineages belong to sub-Saharan African lineages, including L1a, L2, L3b and L3d. These lineages were not observed in more than 300 individuals belonging to other Pakistani ethnic groups, including Hazara, Hunza, Brahui, Parsi, Pathans, Balouchi, Sindhi and Kalash Kafirs. The Eurasian haplogroup U is the second most represented lineage (25%) in this population, the most dominant subcluster being the ancient U2 lineage. Haplogroup M, which has been proposed to trace an ancient migratory coastal pathway from East-Africa to India, was found at only 6% in the Negroid Makrani, but at more than 30% in the other coastal populations. The proportion of typical western-Eurasian lineages (H, I, J, T, X) in this population is notably lower than in the other Pakistani groups. In sharp contrast, the Y chromosome haplogroup distribution in the Negroid Makrani population is similar to the other Pakistani populations and distinct from African populations. The most represented lineages are haplogroups 3 (30%), 9 (18%) and 1 (18%). In conclusion, the study of the maternal and paternal gene pool of the present-day Negroid Makrani reflects that the sub-Saharan African contribution is mainly of matrilineal origin and that the African male-mediated gene flow has been very limited. Together, these results are consistent with significant directional mating between local males and females related to Bantu-speaking populations from sub-Saharan Africa.

1400

Genetical diversity of two isolated African-Brazilian populations. *K.A. Sandes[1], W.A. Silva Jr[2,3], S.M.B. Sousa[1,4], A.A.L. Barbosa[1], P.L. Santos[1], M.O.Q. Santos[1], P.R.V. Bastos[1], E.S. Souza[1], M.A. Zago[2,4].* 1) Universidade Estadual do Sudoeste da Bahia-Jequie-UESB; 2) Centro de Terapia Celular - Hemocentro de Ribeirao Preto; 3) Universidade Federal do Para - Nucleo Santarem; 4) Faculdade de Medicina de Ribeirao Preto - Universidade de Sao Paulo, Brazil.

Barra and Sao Goncalo are two comunities located in Bahia, a State in the northeast region of Brazil. Both of them are constituted by black individuals who are descendent of ancient slaves brought from Africa. These comunities are considered isolated in reproductive and cultural aspects, since they show high levels of endogamy and low migration levels. With the purpose of studying the genetical diversity of these isolated comunities, we have analyzed the mitochondrial DNA hypervariable segment (HVS I) and have compared the sequences with the reported data from Caucasian, African and Amerindian populations. This segment from 220 individuals was amplified by PCR and sequenced in an ABI377™ automated sequencer. Thus far, 127 sequences have been analyzed and 56 different haplotypes have been identified. On the basis of the "Cambridge reference sequence" (Andrews et al., 1999), 93 variable sites were observed, 67 (72%) of them being polymorphic. The 16,223 (C→T) polymorphic site was the most frequent both in Barra and in Sao Goncalo (96%), a polymorphism reported to be found in 91% of typical African lineages. In average, 7% of the studied lineages were classified as being Amerindian. The FST values show that only 13.25% of the total genetic variation are attributed to differentiation between the two comunities, which means that 86.75% correspond to the variability within each population. Although the two comunities have similar origins and history, they do not share any common sequence.

Poster Presentations

1401

Founder effect in North-Eastern Quebec and the extent of the genetic signature associated with the myotonic dystrophy mutation. *V. Yotova[1], E. Zietkiewicz[1], E. Lemieux-Blanchard[1], M. Labuda[1], S. Bourgeois[1], D. Labuda[1], J. Fortin[2], P. Lepage[2], T.J. Hudson[2], A. Lescault[3], C. Laberge[3].* 1) Research Center, Hopital Sainte-Justine, Montreal, Quebec, Canada; 2) MGH Research Center, McGill University, Montreal Genome Center, Montreal, Quebec, Canada; 3) Centre hospitalier, Universit Laval, Ste-Foy, Quebec, Canada.

Myotonic dystrophy is frequent in French-Canadian population of North-Eastern Quebec (1:650). This dominant disorder is due to a CTG-triplet expansion in the DMPK gene on chromosome 19q13 (OMIM160900). Rather than directly analyzing the expansion, we wanted to define a unique haplotype composed of single-nucleotide polymorphisms, a SNP signature, eventually amenable to automatic screening. By the same token, we investigated the extent of the ancestral carrier-haplotype conservation in a young population issued from a founder effect and addressed the hypothesis of a single introduction of the DM-mutation in North-Eastern Quebec. SNPs were found *in silico* as well as experimentally in a population panel by DHPLC and subsequent sequencing. Twenty of these SNPs were typed in 51 DM-families by allele-specific oligonucleotide hybridization. The resulting haplotype extends over 2.3 Mb according to the recent UCSC map. There are two groups of DM haplotypes. The first, presumably young, is represented by a haplotype seen in 34 copies and a minor recombinant (2 copies). The second is represented by four variants (5, 5, 3 and 2 copies) that can be mutually related through single recombinations. These two groups could therefore represent two separate entries of the DM-chromosomes. On the other hand, they share a shorter core haplotype, suggesting a relatively recent common origin for both groups; genealogical data will help to trace it back in time. In conclusion, the DM-mutation appears to be associated with a limited number of unique SNP-signatures that are not shared with non-affected chromosomes; shorter segments of these haplotypes are relatively common in the population; our data demonstrate an important increase in the extent of linkage disequilibrium that can be related to the young age of the population of Quebec. (Supported by RMGA FRSQ).

1402

Effect of the Her2 V655I polymorphism on breast cancer risk in BRCA1/2 mutation positive and negative families. *J.L. Rutter, N. Chatterjee, S. Wacholder, J. Struewing.* Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD.

Overexpression of the Her2 proto-oncogene has been implicated in carcinogenesis of breast cancer, and is associated with poor prognosis. A polymorphism at codon 655 results in a valine to isoleucine change, and the valine allele has been associated with an elevated risk of breast cancer. We asked whether this Her2 V655I polymorphism could be an important susceptibility biomarker for breast cancer risk in women with and without BRCA1/2 mutations. We have a community-based collection of DNA samples and personal and family cancer history data on 5,318 Ashkenazim volunteers from the Washington, DC area. We extended the kin-cohort method to estimate age-specific breast cancer penetrance by Her2 variant status and also by the joint status of Her2 and BRCA1/2 mutations. Kin-cohort analysis uses the disease history of the relatives of the genotyped volunteers to estimate risk, and the volunteer's genotype information to infer a probabilistic distribution of the possible genotypes among the individual relatives. A subset of 769 subjects was identified that maximizes the information content with the fewest number of assays: 116 were BRCA1/2 mutation carriers, 454 were breast or ovarian cancer survivors or had two first degree relatives with breast cancer or a single relative with breast cancer before the age of 50, and 199 subjects were randomly selected. Her2 genotype frequencies for these 769 volunteers were 74% I/I, 23% I/V, and 2% V/V. Cumulative risks of breast cancer up to age 50, 60, and 70 were calculated. Breast cancer risk was significantly elevated for the BRCA negative/Her2 valine positive subjects, with relative risks (RRs) of 1.71, (95% CI 1.21, 5.76), RR = 1.40 (CI = 1.15, 4.19), and RR = 1.40 (CI = 1.18, 3.32) in the three age groups, respectively. Age-specific relative risks were similar among BRCA1/2 positive subjects, although these did not reach statistical significance due to low numbers. These results suggest that the risk of breast cancer is increased in carriers of the Her2 valine allele, and that the risk may be greater in younger women.

ISEE-448

WHO IS SENSITIVE TO THE EFFECTS OF PARTICLES ON MORTALITY? A CASE-CROSSOVER ANALYSIS.

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We used a symmetric bi-directional case-crossover study design to identify characteristics that make an individual susceptible to sudden death in response to particulate air pollution exposures (PM10). We identified elderly subjects in Chicago with a history of Medicare reimbursed hospital admissions recorded between 1984 and 1991. These subjects were followed to identify deaths. We analyzed those deaths that occurred between 1988 and 1991. We measured the average PM10 exposure on the day of death and the day before death for each individual and compared it to their PM10 exposure on the days 6-14 days prior to death and 6-14 days following death. We controlled for weather covariates using natural splines with 4 degrees of freedom each.

The baseline effect of PM10 was an 11% increased risk of death per 100ug increase in PM10 (95% CI: 4-18). We found that the effect of PM10 was modified among those with a history of diabetes or myocardial infarction (MI) but not among those with a history of conduction disorders or heart failure. The effect of PM10 exposure on those with a prior diagnosis of diabetes was an increased risk of 25% (95%CI: 8%,44%) compared to 9% (95%CI: 1%,16%) in those without a diabetes diagnosis. The effect on those with a prior diagnosis of MI was an increased risk of 20% (95%CI: 0%,43%) compared to 10% (95%CI: 3%,18%) in those without an MI diagnosis.

We used individuals' zip codes to obtain information on socioeconomic factors from the 1990 census. We found no evidence that the effect of PM10 on mortality was modified by living in a zip code that was in the lowest quartile of median household income or the highest quartile of percentage of residents living in poverty.

ISEE-449

CASE-CONTROL STUDIES OF GENE-ENVIRONMENT INTERACTIONS: SAMPLE SIZE, POWER, MISCLASSIFICATION AND THE CASE-ONLY DESIGN ALTERNATIVE

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Studies of disease outcomes and the effects of genotype and of gene-environment interactions play an increasingly important role in epidemiology. Standard case-control and cohort designs are often used to evaluate risk with common genetic polymorphisms, and the variation of risk of exposure by genotype status. Methodological investigations of sample size and power indicate that epidemiological studies require large numbers of subjects to detect even moderate departures of a gene-environment interaction from the assumed null relationship. In addition, misclassification of either exposure status or genotype can further and markedly increase the required sample size. One option for increasing design efficient is to include more than two categories of exposure or include exposure as a continuous variable. An alternative design has been proposed (the case-only design), in which an odds ratio for exposure and genotype is calculated among cases only. Assuming exposure and genotype are statistically independent and the joint odds ratio for exposure and genotype in the target population is multiplicative, the odds ratio computed among cases only is an unbiased estimate of the multiplicative odds ratio for interaction. Due to the strong assumptions, the case-only design often requires far fewer subjects. However, caution is recommended since validity of sample size calculations in achieving nominal power is compromised when assumptions are violated. An evaluation of the impact of misclassification and the modeling of multiple exposure categories on design of studies of gene-environment interactions, and the strength and limitations of the case-only design will help to identify feasibility of proposed studies.

ISEE-450

STUDY GENETIC POLYMORPHISM AND ASSOCIATION TO SOME PATHOLOGIES IN CENTRAL MOLDOVA POPULATION.

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Genetic investigations among farmers occupationally and residentially contacted to pesticide were performed in Central Moldova to evaluate possible genetic risk to some pathologies revealed during the clinical and epidemiological studies in 1991-1995. Polymorphism of ABO, Rhesus, MN, P, and Lewis antigen system, G1m, serum proteins Hp, Tf, Gc, erythrocytic isoenzymes AcP and EsD were studied in 1000 indigenous Moldovans. Allele frequencies, expected and observed distributions of genotypes and heterozygosity were estimated in total population and in groups of farmers with and without similar pathologies. Results were compared with Western Europe Romanic (WER) populations and with Russian of the FSU. Examined population was genetically closed to WER populations. At the same time high level of heterogeneity was found for the Hp, AcP, Gc, P, G1m and Lewis polymorphic loci. Significant decreasing of expected AcPa allele frequency and observed geterozygosity for AcP loci (deficit of ac and cc phenotypes) were established. It was shown that farmers with Tfc allele had approximately 6,5 and 2.6 times higher rate of chronic hepatitis, gastritis and cholecystitis respectively to those with Tf bc allele. It was also established association of AcPa allele with chronic hepatitis, holecystitis and gastritis. Carriers of this allele suffered by these diseases approximately 3.4, 2.5 and 2 times more often than heterozygous phenotypes (ac, bc). Decreasing of Hp1 gene frequency and increasing Hp 1-1 phenotype were determined in farmers with chronic gastritis. The results showed the existence of relative genetic risk to some diseases in studied population. Thus, genetic factor may be one of competing risk together with environmental pollution and other confounders in this area.

ISEE-451

FALLOUT EXPOSURE IN KAZAKHSTAN AND THYROID DISEASE PREVALENCE

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Purpose: Villages near the Semipalatinsk Test Site (STS) in Kazakhstan were exposed to fallout from atomic bomb tests at the STS. Childhood radiation exposure is a risk factor for thyroid cancer, and presence of thyroid nodules is a marker for such exposure. We evaluated thyroid disease prevalence among the persons exposed at young ages and estimated the risk of radiation-related thyroid disease in a population with chronic exposure to mixed gamma and beta radiation from fallout.

Methods: The study population included 2998 current residents of 8 villages near the STS, <20 years of age at the time of exposure (in 1949, 1951, 1953), who had been present then or had migrated from relatively unaffected areas. Villages were selected based on accessibility and on published dose estimates. Screening included residential history and diet interview, thyroid ultrasound, and FNA biopsy of suspicious nodules with consequent cytopathology. Finger-stick blood samples were assayed for level of thyroid stimulating hormone.

Results: Thyroid nodules were detected in 920 participants, of whom 491 were recommended for biopsy; 27 patients had malignant thyroid tumors. Prevalence of nodules was positively and significantly related to exposure. Gamma-ray dose was used as an index of total dose from all sources, which has not yet been determined. Among exposed subjects, published estimates of gamma dose, adjusted on individual basis for a presumed inverse relationship between radiation sensitivity and age at exposure, were positively and significantly associated with disease prevalence.

Conclusions: Thyroid disease prevalence is positively associated with radiation exposure from fallout and inversely associated with age at exposure. Biodosimetry results will be used for dose validation.

ISEE-452

ENVIRONMENTAL POLLUTANTS AND MENSTRUAL CYCLE LENGTH IN A PROSPECTIVE PREGNANCY COHORT

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This study examined factors that relate to the duration of menstrual cycles. The study sample comprised 102 women aged 18-35 years who participated in a prospective pregnancy study of the New York State Angler Cohort Study (NYSACS). Reproductive histories were taken from women upon enrollment and information on sexual intercourse, menses, sport fish consumption, and other behavioral factors was collected. Recovery corrected values for blood samples taken at baseline are reported without adjustment for the LOD because of low level environmental concentrations.

Prospective menstrual information was gathered from the daily diary cards and was compared with the menstrual cycle information reported at baseline. To account for intra-individual variation in cycle length, the median cycle length was computed. Women were considered to have a normal cycle length if their median value was between 25-35 days (n=61) and a long cycle length if >35 days (n=22). Stepwise discriminant analysis revealed two variables that were significant ($p<0.05$) when examining cycle length differences between those with normal cycles and those with long cycles: PCB 25 and aldrin. Aldrin showed the stronger statistically significant interaction with cycle length (R2=.3156). Further, we employed a multiple stepwise linear regression looking at median cycle length and the environmental toxicants studied. Aldrin (R2=0.077), PCB 94 (R2=.122), PCB 194 (R2=.072), PCB 206 (R2=.055) and PCB 134 (R2=.037) contributed significantly to the total R2=.363. These findings suggest that the data from GLC-electron data capture laboratory methods on persistent low-level toxicants should be interpreted cautiously. We suggest prompt laboratory studies to clarify the reproductive effects of these chemicals.

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REFORMULATED GASOLINE CONTAINING 11% MTBE AND SYMPTOMS AMONG COMMUTERS

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Methyl Tertiary-Butyl Ether (MTBE) is added to gasoline to raise oxygen content and reduce tailpipe carbon monoxide emissions. In New Jersey, wintertime oxygenated fuel with a minimum of 2.7% oxygen by weight (15% MTBE by volume) was introduced in 1992, and later in 1995, reformulated fuel was introduced year-round with 2.0% oxygen (11% MTBE). Because many communities reported health complaints during the use of wintertime oxygenated fuel, this study was undertaken to look at symptom reporting and MTBE levels in the cars of commuters using reformulated fuel. Random samples of commuters participated at two different service stations (one in New Jersey where reformulated fuel was in use and one in Pennsylvania where it was not required). A total of 552 people completed questionnaires with demographic information and current health symptoms; of those, 321 allowed cabin MTBE levels to be measured: 18% nondetectable, 28% 1-45ppb, 27% 46-89ppb, and 26% >90ppb (range 0-931 ppb). Participants were asked to rate symptom discomfort from 0-4 for MTBE symptoms (headache, burning sensation of the nose or throat, dizziness or lightheadedness, gastrointestinal upset, sleepiness, cough and difficulty concentrating) and nonMTBE symptoms (fever, diarrhea, sweats or chills and muscle aches). Using multiple regression techniques, only complaints of muscle aches were statistically associated with MTBE levels ($p=0.03$), but were better correlated with the number of hours spent in the car prior to refueling ($p=0.006$). Overall symptom reporting was low. We conclude that those symptoms historically attributed to MTBE exposure in fuels were not correlated to automobile cabin MTBE levels.

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