433

PARENT-OF-ORIGIN TRANSMISSION OF THROMBOPHILIC ALLELES TO INTRAUTERINE GROWTH RESTRICTED NEWBORNS AND TRANSMISSION-RATIO DISTORSION IN UNAFFECTED NEWBORNS. *C Infante-Rivard, C R Weinberg (McGill University, Montreal, Quebec CANADA)

Study results on the role of thrombophilic polymorphisms with respect to adverse pregnancy outcomes, in particular intrauterine growth restriction (IUGR), are very inconsistent. Such inconsistencies may in part be due to two types of effects, which have not been considered before with thrombophilic genes: parent-of-origin and transmission-ratio distortion effects. We investigated both effects in a case-parent study (newborn, mother and father) including 493 cases (newborns whose birth weight for gestational age and sex was below the 10th percentile according to national standards), and 472 controls (above the 10th percentile). Log-linear models were used to analyze transmission of variant alleles among case- and control-parent trios. A significant distorsion in transmission, which was seen in affected but not in unaffected offspring, suggests that two common polymorphisms, Val34Leu in Factor XIII and 4G/5G in Plasminogen Activator Inhibitor-1 (PAI-1) increase risk of IUGR when the parent of origin is the father. Unaffected but not affected newborns inherited the variant alleles A1298C in the methylene tetrahydrofolate reductase gene and the G1691A variant in Factor V Leiden significantly less often than expected, and both unaffected and affected newborns inherited the G20210A variant in the Prothrombin (or Factor II) gene significantly less often than expected, suggesting these three genes exhibit segregation distrosion or reduce gestational survival. We conclude that paternally-derived variants of the thrombophilic genes Factor XIII and PAI-1 may increase the risk of intrauterine growth restriction possibly by influencing blood flow. Certain other thrombophilic alleles appear to select for gestational survival.

434-S

INFORMATION DISCLOSURE IN POPULATION-BASED RESEARCH INVOLVING GENETICS: A FRAMEWORK FOR THE PRACTICE OF ETHICS IN EPIDEMIOLOGY. *V L Kristman, N Kreiger (University of Toronto and Cancer Care Ontario, Toronto, Ontario, Canada)

The completion of the Human Genome Project has resulted in increased epidemiological research to identify genes and their products as risk factors for adverse health events. Along with the increase in research, a parallel increase in ethical issues associated with genetic research is noted. One such issue is whether or not epidemiologists should disclose individual genetic results to research participants. Existing national and international ethical guidelines are not helpful for determining if disclosure is the moral choice. The purpose of this paper is to provide a framework for epidemiologists illustrating an ethical approach to the dilemma of disclosure of individual genetic information. The core principles of research ethics are introduced and applied to the issues surrounding disclosure of genetic information. A principle-based framework is developed from an analysis of the current ethical arguments for and against disclosure. Finally, an example demonstrating the use of the framework is provided. The proposed framework will not solve all ethical dilemmas related to individual disclosure of genetic information. However, it is a useful starting point to facilitate the consideration process.

435

GENE-ENVIRONMENT INTERACTION IN PARKINSON'S DISEASE. *E McCanlies, G Murphy, D Fekedulegn, G W Ross, C M Burchfiel (NIOSH, Morgantown, WV, 26505)

Cytochrome P450 2D6 (*CYP2D6*) codes for a phase I enzyme that is responsible for the biotransformation of a range of chemicals. Studies investigating the role of *CYP2D6* and the risk of Parkinson's disease (PD), alone and in conjunction with environmental exposures, are contradictory. We used data from the Honolulu Heart Program/Honolulu-Asia Aging Study (HHP/HAAS) to investigate the association between *CYP2D6* HhaI polymorphism in exon 6, various occupational exposures (e.g. metals, pesticides, chemicals) and the risk of PD. HHP/HAAS is a longitudinal cohort study begun in 1965 designed to evaluate heart disease, stroke, and later dementia in 8,006 Japanese-American men aged 45–68. Occupational exposure was independently assessed by three industrial hygienists who determined likelihood of exposures for each participant's usual occupation. Genotyping data was available for 75 incident cases of PD (mean age at baseline 54.4; standard deviation (SD) 5.1) identified through death certificate, medical record review, and medical examination. A total of 127 controls without PD were frequency matched by age (mean age at baseline 54.4; SD = 5.3) to the case group. No association was observed between *CYP2D6* HhaI polymorphism and PD in this population (Odds Ratio (OR) = 0.8; 95% Confidence Interval (CI)= 0.4, 1.4), nor was PD found to be associated with occupational exposures to solvents or pesticides either independently or in the presence of *CYP2D6* ($p>0.05$). However, PD cases were two times more likely to have occupational exposure to metals than the controls (OR= 2.2; 95% CI= 1.2, 4.0). This association did not change in the presence or absence of *CYP2D6*. In conclusion, we found that among the Asian-Americans in the HHP/HAAS study *CYP2D6* HhaI polymorphism in exon 6 was not associated with PD, nor was there evidence of an interaction between this gene and an occupational exposure ($p >0.05$). Our findings did however indicate that occupational exposure to metals may be associated with PD. This finding warrants further follow-up.

436-S

RESPONSE BIAS FROM FAILURE TO PROVIDE A BLOOD SAMPLE AMONG PARTICIPANTS IN THE ONTARIO FAMILY COLORECTAL CANCER REGISTRY. *H Ghadaki, G McKeown-Eyssen (University of Toronto, Toronto, Ontario, M5S 1A8)

Systematic differences between study participants and non-participants may bias results for all study designs. We investigate such response bias associated with failure to provide a blood sample in the Ontario Familial Colorectal Cancer Registry (OFCCR), a registry for genetic and environmental studies of colorectal cancer (CRC). The OFCCR collected information on 1516 incident CRC cases, aged 20–69, diagnosed between 1997–2000 and 1931 population controls. Participants completed self-administered questionnaires on family, medical history, lifestyle, and diet and asked to provide a blood sample for DNA derivation. Descriptive analysis comparing participants with and without a blood sample report the magnitude of response bias. Bias in the strength of association between CRC and risk factors was determined through univariate case-control comparisons using t-tests and chi-square tests conducted separately for participants with and without a blood a sample. Multivariate logistic regression with interaction terms assessed effect modification from failure to give blood. Significant interactions were observed. Among those with a blood sample, cases were younger than controls (62.4 vs 63.2 years), consumed more dietary fat (77.4% vs 73.7% of energy) and less fruit (5.59 vs 5.72 servings per week), and were less likely to report a history of high triglycerides (5.5% vs 9.9%). In contrast, among those without a blood sample, cases were older than controls (63.4 vs 57.0 years), consumed less dietary fat (73.8% vs 78.37% of energy) and more fruit (5.71 vs 5.27 servings per week), and were more likely to report a history of high triglycerides (8.6 vs 6.9%). Willingness to provide a blood sample from which DNA can be derived, modified relationships between the risk of CRC and demographic and lifestyle characteristics, and medical history. These findings have implications for the design and conduct of investigations of gene-environment interactions.

* = Presenter; S = The work was completed while the presenter was a student

T 6-6-05
ISSN 0002-9262
PRINTED IN THE U.S.A.

Supplement to:

American Journal of
EPIDEMIOLOGY

Volume 161 Number 11 June 1, 2005

www.aje.oupjournals.org

Abstracts
2005 Epidemiology without Borders

A Joint Meeting of the Society for Epidemiologic Research and Canadian Society for Epidemiology and Biostatistics

Toronto, Canada, June 27–30, 2005

Published for the Johns Hopkins Bloomberg School of Public Health by Oxford University Press
Sponsored by the Society for Epidemiologic Research

Founded in 1920 by W. H. Welch and W. H. Howell as the *American Journal of Hygiene* at the

OXFORD JOURNALS