be causative mediators of defective sperm activation (SDD) in vivo, which is associated with male infertility.

Supported by: Repromedix.

ENVIRONMENT AND TOXICOLOGY

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EFFECT OF ENVIRONMENTAL EXPOSURES ON FERTILITY-RELATED OUTCOMES. L. Brantley, L. M. Frazier, D. A. Grainger, B. Tjaden, V. A. Miller, R. Zackula. Obstetrics and Gynecology, University of Kansas School of Medicine-Wichita, Wichita, KS; Office of Research, University of Kansas School of Medicine-Wichita, Wichita, KS.

OBJECTIVE: Compare environmental exposures with fertility-related outcomes among IVF patients.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Environmental and occupational exposures were assessed by questionnaire, and serum was analyzed for environmental chemicals that may be endocrine disruptors. Assays performed by gas chromatography-high resolution mass spectrometry were adjusted for lipid concentration. Levels were compared to published values for the US adult population during 2001–02 (NCEH Pub. No. 05–0570). Semen analyses employed WHO 4th ed. (1999) strict criteria. Exact Mann-Whitney tests and Spearman's correlations were performed using StatXact (Cambridge, MA).

RESULTS: The most common self-reported exposures among the 26 women and 18 men were insecticides (65.4% and 50.0%, respectively), herbicides (38.5% and 55.6%, respectively), fertilizer (26.9% and 33.3%, respectively) and secondhand tobacco smoke (23.1% and 27.9%, respectively). Persistent pollutant levels were below the national average, but certain individuals had elevated levels. For the chlordane insecticide compound, *trans*-nonachlor, means for women, men and US adults were 19.0, 17.6, and 20.0 ng/g lipid, respectively; the US upper 95% CI of 22.3 ng/g lipid was exceeded by 26.9% of women and 31.2% of men in the study. For the DDT metabolite, *p,p*-DDE, means for women, men and US adults were 109.1, 116.7, and 338 ng/g lipid, respectively, with no values exceeding the US 95% CI of 376 ng/g lipid. For polychlorinated biphenyl (PCB) congener 153, means for women, men and US adults were 13.6, 14.7, and 32.6 ng/g lipid, respectively, and one woman's value exceeded the US 95% CI of 36.1 ng/g lipid. No associations of self-reported exposures to clinical outcomes were statistically significant. Hexachlorobenzene (HCB) was the sole analyte that was statistically related to clinical intrauterine gestation (CIG). Women's median HCB levels were higher when CIG was not achieved (10 ng/g lipid, range 6.8–19.7 ng/g lipid, n = 17) than when CIG occurred (8 ng/g lipid, range 5.6–10.7, n = 9, P=0.041). Men with higher levels of the flame retardant, polybrominated diphenyl ether (PBDE) congener 100, had a higher % normal sperm (Spearman's rho, 0.782, n = 12, P=0.004).

CONCLUSIONS: Numerous persistent environmental contaminants were found in the serum of couples seeking IVF. HCB pollution may have an adverse effect on pregnancy outcome, although the findings need to be confirmed in a larger study.

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ENVIRONMENTAL EXPOSURE TO MERCURY AND EARLY DEVELOPMENTAL ENDPOINTS AMONG WOMEN UNDERGOING IVF. J. O. Doyle, D. L. Wright, L. Godfrey-Bailey, K. Pearson, C. Amarasiriwardena, R. B. Hauser. Obstetrics and Gynecology, Division of Reproductive Medicine, Massachusetts General Hospital, Boston, MA; Department of Environmental Health, Harvard School of Public Health, Boston, MA; Department of Biostatistics, Harvard School of Public Health, Boston, MA.

OBJECTIVE: Despite widespread general population exposure to mercury (Hg), there is limited human data on potential reproductive health effects at environmental background levels. The objective was to determine the relation between hair Hg levels and early developmental endpoints in couples undergoing IVF.

DESIGN: Prospective cohort study of couples presenting for infertility treatment at an academic hospital.

MATERIALS AND METHODS: In women undergoing IVF, the proximal 3-cm length of a hair sample was analyzed for total Hg content. The following endpoints for embryo quality and early developmental outcomes were collected: number oocytes retrieved, total number of mature oocytes, fertilization rate, and embryo grades (1–5, 1 being the best) on days 2, 3 and 5. Linear mixed effects regression models were used to explore the associations between these outcomes and hair Hg, accounting within-woman correlation of outcomes and controlling for maternal age.

RESULTS: 22 women provided a hair sample with a mean (SD) hair Hg concentration of 2.1 parts per million (1.7), with a range 0.038 to 5.7 ppm. The median (25th, 75th %ile) was 1.6 ppm (0.5, 3.3). EPA reference dose is 1 ppm. Increased Hg levels were associated with decreased oocyte quantity, increased fertilization rate and decreased embryo quality, though none of the associations were statistically significant at the 0.05 level. Hg above 1 ppm was associated with a −3.025 (95% CI: −7.00, +0.95; P=0.16) change in number of oocytes retrieved and a −2.989 (95% CI: −6.45, +0.47; P=0.11) change in number of mature oocytes. Each 1 ppm increase in Hg was associated with an estimated 0.037 (95% CI: −0.02, 0.10; P=0.25) increase in fertilization rate. Each 1 ppm increase in Hg was associated with an estimated 0.070 (95% CI: −0.10, 0.24; P=0.43) increase in day 2 score, a 0.105 (−0.09, 0.30; P=0.29) increase in day 3 score, and a 0.215 (−0.06, 0.49; P=0.13) increase in day 5 score.

CONCLUSIONS: In this small patient sample, some women undergoing IVF had elevated hair Hg levels. We found some evidence of a relationship between hair Hg concentrations and oocyte quantity, and a trend of an association between hair Hg levels and poorer embryo quality. As this is an ongoing study, additional patients and IVF data will be included in future analyses.

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SMOKING DISRUPTS TELOMERES THROUGH REACTIVE OXYGEN SPECIES IN EARLY MOUSE EMBRYOS. M. M. Okuka, M. M. McLean, D. L. Keefe, L. L. Liu. Obstetrics and Gynecology, University of South Florida School of Medicine, Tampa, FL.

OBJECTIVE: Reactive oxygen species (ROS) in cigarette smoke contribute to its toxicity. We have shown that oxidative stress damages telomeres, leading to chromosomal instability and apoptosis, so we wondered whether smoking could disrupt embryos through ROS. Cigarette smoke condensate (CSC) simulates smoking, and cigarette smoke also contains cadmium (Cd). We tested the hypothesis that smoking has direct effects on telomere function during early embryo development by evaluating the effects of CSC and Cd on apoptosis, telomere length and genomic instability in embryos, and determining whether a potent antioxidant could abrogate these effects.

DESIGN: In vitro study of effects of CSC and Cd on preimplantation embryos, including telomere shortening, chromosome instability, and apoptosis, and whether the ROS scavenger, N-acetyl-L-cysteine (NAC), could prevent smoking-induced telomere dysfunction and apoptosis.

MATERIALS AND METHODS: Zygotes were treated by incubation in the following media; a) control–KSOM for 120 h at 37°C in 7% CO_2 and 95% air, b) 0.1 mg/ml CSC for 12 h, c) 0.02 mg/ml CSC continuously for 120 h, d) 100 μM Cd based on previous experiments for 12 h, e) 20 μM Cd continuously for 120 h. After treatment, embryos were washed and cultured in normal KSOM. For antioxidant experiments, zygotes were co-treated with CSC or Cd and 25 mM NAC, developed for 120 hr. After treatment, embryos were assayed for telomere length by quantitative FISH, chromosomal instability by spreads and staining with DAPI and apoptosis by TUNEL staining.

RESULTS: Mouse zygotes exposed to CSC and Cd exhibited significantly reduced cleavage and compromised development in a time and dose dependent manner. Untreated zygotes developed to hatching or expanded blastocysts, whereas most zygotes exposed to 0.1 mg/ml CSC for 12 hr or 0.02 mg/ml continuously arrested before blastocyst stage. Zygotes exposed to 100 μM Cd for 12 hr arrested at the one cell stage with no cleavage, followed by cell death, and exposure to 20 μM Cd continuously lead to embryo arrest before blastocyst. Compromised embryos showed telomere shortening and loss, and increased rates of chromosome fusion and instability as well as apoptosis. NAC prevented the detrimental effects of CSC and Cd in the majority of embryos.

CONCLUSIONS: Oxidative stress contributes to smoking induced telomere dysfunction, chromosomal instability and apoptosis in early mouse embryos.

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