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PHTHALATES AND MALE REPRODUCTIVE HEALTH: NEW RESEARCH DIRECTIONS. *R Hauser (Environmental and Occupational Medicine and Epidemiology, Department of Environmental Health, Harvard School of Public Health, Boston, MA 02115)

Phthalates, diesters of phthalic acid, are multifunctional chemicals widely used in personal care products, in food packaging and processing materials, and to soften a wide range of plastics, including medical products such as polyvinyl chloride blood and intravenous bags. Their ubiquitous use has resulted in widespread general population exposure via dietary ingestion, dermal absorption, inhalation, and parenteral exposure from medical devices containing phthalates. Although toxicological studies have consistently shown that some phthalates are reproductive and developmental toxicants, there is limited epidemiologic data on the potential effects of phthalate exposure on male reproductive function. Two recent human studies explored associations of urinary concentrations of phthalates with semen quality and sperm DNA damage. In a U.S. study, associations were found between monobutyl and monobenzyl phthalate and lower sperm concentration and motility. In addition, monoethyl and monethylhexyl phthalate were associated with increased sperm DNA damage. However, a Swedish study did not find relationships between these phthalates and semen quality or sperm DNA damage. In the presentation, data from these two primary studies will be discussed and potential explanations will be offered for the inconsistent results. In the field of reproductive environmental health there remain many unanswered questions regarding the impact of the environment on male reproductive health. Suggested needs include studies that target populations with high exposure to chemicals, including phthalates. We also need to identify susceptibility factors and critical exposure windows (life stages) that may increase a man's risk of infertility. Finally, we need to develop methods to better study mixtures of chemicals and develop methods to assess clinical reproductive outcomes of human exposure to the ever-growing list of chemicals.

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EFFECTS OF METALS ON MALE REPRODUCTIVE OUTCOMES. *S Benoff (Fertility Research Laboratories, The Feinstein Institute for Medical Research, Manhasset, NY 11030)

Lead and cadmium are among the top 10 on the CERCLA priority list of hazardous substances. Although linked to production of male subfertility after acute, high level occupational exposures, investigations into the male anti-fertility effects of these metals at levels consistent with chronic, low environmental exposures have produced conflicting findings. Therefore, we studied lead and cadmium in seminal plasma and testis biopsies from men not occupationally exposed to these metals and who did not smoke cigarettes. We observed negative relationships between metal levels and IVF fertilization rates and pregnancy after ICSI, IUI or coitus. To identify mechanisms underlying the production of male subfertility, the relationships between metal levels and serum hormone levels, oxidative stress, testicular gene expression, semen parameters, sperm-egg binding, calcium flux and acrosome exocytosis were assessed.

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URINARY ENDOCRINE ANALYSES AND THEIR APPLICATION TO ASSESS MENSTRUAL CYCLE FUNCTION IN POPULATIONS EXPOSED TO POTENTIAL HAZARDS. *J S Kesner, J W Meadows (RHAT, BHAB, NIOSH, CDC, DHHS, Cincinnati, OH 45226)

The challenge of assessing the relationship between toxic exposures and reproductive well-being of women is heightened by two factors: the ever-expanding number and variety of potentially hazardous agents (chemical and otherwise) in the workplace and environment; and evaluating the inaccessible female reproductive system with its complex menstrual cycle. Advances in sensitive and specific immunoassays to measure the primary female reproductive hormones or their metabolites in urine have greatly facilitated the capabilities to assess the hypothalamo-hypophysial-ovarian axis as it relates to menstrual cycle function in populations of women who may not be highly motivated. However, various immunoassays draw on different analytical strategies to quantify their analytes; these differences and what is being measured are issues to be considered when applying these tools to field studies. These analytical methods, the measurements they yield, and their attendant algorithms for deriving endpoints for statistical analyses are being applied to a variety of population studies to better understand the characteristics of the menstrual cycle, and how its function is affected by external factors including potentially hazardous exposures. The discussion will include an overview of the toxicity of selected pesticides and polyhalogenated biphenyls on female reproductive potential, insights into the effects of these exposures on menstrual cycle function derived from population studies employing urinary endocrine biological measurements, and descriptions of ongoing studies designed to further understand these relationships.

The findings and conclusions in this abstract have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

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ENDOCRINE DISRUPTING CHEMICALS AND ENDOMETRIOSIS. *G M Buck Louis, M A Cooney (Epidemiology Branch, NICHD, Rockville, MD 20852)

Endometriosis remains an elusive disease given its inherent diagnostic challenges, which impact decision making about choice of study design and sampling framework for etiologic research. An evolving body of experimental and observational data suggests a relation between endocrine disrupting chemicals (EDCS) and endometriosis. Specifically, five observational studies involving geographically diverse women with laparoscopically-confirmed endometriosis report significant increases in risk of endometriosis associated with dioxin and polychlorinated biphenyl exposure while three studies have failed to observe an association. Timing of EDC exposure relative to the onset of endometriosis remains a critical data gap as evident by recent experimental data suggesting the importance of in utero exposures and, possibly, generational effects. To date, the mechanisms underlying the purported relation between EDCs and endometriosis are unknown. While much work has focused on the aryl hydrocarbon receptor (AhR) pathway, more recently, other mechanisms are being considered. The growing body of evidence supports systematic epidemiologic research focusing on the etiologic relation between environmental factors including chemicals and the development and progression of endometriosis. This talk will present an overview of the available evidence, purported mechanisms and strategies for overcoming methodological challenges. In so doing, this talk will hopefully spark debate regarding the role of environmental exposures and ovarian dysgenesis.

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