Program

49th Annual Meeting and ToxExpo™

Salt Lake City, Utah
March 7-11, 2010

www.toxicology.org
Abstract #

9:15 AM to 12:00 NOON
Room 150

Symposium Session: Neurological Responses to Inhalable Metal Particles


Sponsor: Inhalation and Respiratory Specialty Section

Endorsed by: Immunotoxicology Specialty Section

Most studies examining the toxicology of inhalable metal particles have focused on responses in the target organ, the respiratory system. Less information exists regarding the effects associated with the inhalation of metals in extrapulmonary organs, specifically the central nervous system. There is increasing interest in the effects of airborne metallic and manufactured metal nanoparticles (particles with one dimension < 100 nm) in the environment and workplace. These smaller particles may translocate more easily from deposited sites in the respiratory tract to brain structures after inhalation. Mechanisms of particle translocation include uptake and transport along olfactory and sensory neurons, transcellular transport across respiratory epithelium to the circulation, and lymphatic clearance. Chemical composition, oxidation state, and solubility all may affect metal transport and biological response to inhalable metals. Both animal and human studies have demonstrated that inhalable metals can translocate to the central nervous system, as well as induce neurobehavioral changes. Alterations in markers of neuroinflammation and cellular toxicity have been observed in specific brain regions using animal models after exposure to a variety of occupational and ambient air pollution. Cognitive deficits, brain abnormalities, and neurodevelopmental effects have been associated with exposure to metals in healthy children in Europe and North America. Our panel of experts from the fields of inhalation, neurological, metal, and occupational toxicology will highlight neurological findings of animal and human studies after occupational and environmental lung exposures. All aspects of the topic, such as metal chemistry, inhalation exposure of metal particles, metals translocation from the respiratory system to the central nervous system, and neurological responses, will be examined. An increase in the understanding of metal particle inhalation and neurotoxicity may allow for the development of prevention strategies to better protect susceptible populations in the workplace and environment.
Abstract #23 10:56

NEUROBEHAVIORAL EFFECTS IN ADOLESCENTS EXPOSED TO METALS. R. Lucchini1, N. J. Zimmermann2, E. Albin1, S. Michelelli1, S. Zoni1, F. Tagliani1, C. Ardini3, G. Parmentier4, F. Donna1, R. Ferri1, Z. Annaletta1, B. Laura1 and E. Bottigelli1. Occupational Health, University of Brescia, Italy; Brescia, Italy; 1Chemistry Laboratory for Technologies, University of Brescia, Brescia, Italy; 2School of Health Sciences, Purdue University, West Lafayette, IN and 3Statistics and Biometry, University of Brescia, Brescia, Italy.

Abstract #24 11:28

NEUROINFLAMMATION, SEVERE AIR POLLUTION AND CHILDREN. L. CalderonGarciduenas1, L. Gonzalez-Gonzalez1, A. D’Angiulli1 and H. Medina-Concha.1 The University of Montana, Missoula, MT; 1Psychology Carleton University, Ottawa, ON, Canada and 1Instituto Nacional de Pediatría, Mexico City, Mexico. Sponsor: J. Antonini.

Monday Morning, March 8 9:15 AM to 12:00 NOON Ballroom B

Symposium Session: Ovarian Toxicity: Current Concepts in Toxicology, Pathology, and Mechanisms

Chairperson(s): William J. Brock, Brock Scientific Consulting, LLC, Montgomery Village, MD, and Ali Faqi, MPI Research, Mattawan, MI

Sponsor: Reproductive and Developmental Toxicology Specialty Section

Endorsed by: Regulatory and Safety Evaluation Specialty Section

Reproductive and Developmental Toxicology Section

Women in Toxicology Special Interest Group

The ovary is responsible for the differentiation and release of a mature oocyte for fertilization and for synthesizing and secreting hormones that are essential for follicle development, estrous cyclicity, and maintenance of the reproductive tract and its function. Reproductive toxicity studies are important components of the regulatory approval of drugs and chemicals. The identification of ovarian toxicity and determination of its cause requires familiarity with ovarian anatomy, physiology, relationships with other components of the female reproductive tract, and the neuroendocrine regulation of the estrous cycle. A mechanistic approach at the morphologic, biochemical, and molecular level demonstrate that various factors are involved in ovarian toxicity. Therefore, our focus will be on the basic concepts of ovarian anatomy, histopathology, and potential mechanisms of toxicity. We will begin by discussing the importance of assessing fertility that utilizes a combination of methods including evaluation of estrous cycle length, fertility endpoints, and ovarian weights. Recent collaborative work suggests a 2-week rodent study may be sufficient to elucidate the effects of pharmaceuticals on ovarian function and its impact on the revised ICH M3 will be presented. Better interpretation of drug induced ovarian toxicity will be highlighted as fertility effects in rodents, especially when both sexes are treated does not often distinguish between male or female mediated effects. A mechanistic model of ovarian toxicity of 4-vinylcyclohexene diepoxide provides an understanding of the potential risk of human exposure to environmental ovarian toxicants and greater insight of toxicants on reproductive health in women will also be discussed.

Abstract #25 9:15

OVARIAN TOXICITY: CURRENT CONCEPTS IN TOXICOLGY, PATHOLOGY, AND MECHANISMS. W. J. Brock1, A. Faqi2, M. Mirsky1, P. Hooper2 and A. Szabo-Askanas.1 Brock Scientific Consulting, Montgomery Village, MD; 1MPi Research, Mattawan, MI; 2Fizer, Groton, CT; 1University of Arizona, Tucson, AZ and 2Daichi-Sankyo, Fukuroi Shizuoka, Japan.

Abstract #26 9:20

OVARIAN TOXICITY—ANATOMY, PATHOPHYSIOLOGY, AND THE ILLUSION OF SIMPLICITY. M. Mirsky. Pfizer, Groton, CT.

Abstract #27 10:00

OVARIAN TOXICITY INDUCED BY PHARMACEUTICALS AND CHEMICALS. A. S. Faqi. Toxicology, MPI Research, Mattawan, MI.

Abstract #29 11:20

COLLABORATIVE WORK ON EVALUATION OF OVARIAN TOXICITY BY REPEATED-DOSE AND FERTILITY STUDES IN FEMALE RATS. A. Sambusigh SANKYO CO., LTD., Fukuori, Shizuoka, Japan. Sponsor: W. Brock.
Abstract

TITLE: NEUROBEHAVIORAL EFFECTS IN ADOLESCENTS EXPOSED TO METALS

AUTHORS (LAST NAME, FIRST NAME): Lucchini, Roberto; Zimmerman, Neil J.; Albini, Elisa; Micheletti, Serena; Zoni, Silvia; Tagliani, Fiorella; Nardoni, Chiara; Parinello, Giovanni; Donna, Filippo; Ferri, Roberta; Annalisia, Zacco; Laura, Borgese; Bontempi, Elza

SPONSOR NAME: James Antonini

INSTITUTIONS (ALL): 1. Occupational Health, University of Brescia, Italy, Brescia, Italy.
2. Chemistry Laboratory for Technologies, University of Brescia, Brescia, Italy.
3. School of Health Sciences, Purdue University, West Lafayette, IN, USA.
4. Statistics and Biometry, University of Brescia, Brescia, Italy.

ABSTRACT BODY: Background: Increased parkinsonism was observed in Valcamonica, a valley in the Italian Alps. Prevalence was higher in the vicinity of ferroalloy plants and associated to the manganese level in deposited dust. The aim of this study was to assess motor and cognitive functions in adolescents in the exposed area.

Methods: Metals were measured in PM10 airborne particles collected with 24-hours personal samplers. Samples were analyzed with Total Reflection X-Ray Fluorescence. Soil was analyzed at surface and 10 cm depth. Adolescents of 11-13 years old were recruited through the local school system for neurobehavioral examination. Various biomarkers were collected for metal analysis.

Results: A total of 303 children residing in the exposed area and a reference area participated in the study. Average airborne manganese was 57.79 ng/m3 (n=86, range 1.24-516.70) in Valcamonica and 22.45 ng/m3 (n=11, range 5.30-36.59) in the reference area. Lead, iron, zinc and chromium also showed significantly higher levels. Manganese results were significantly higher also at the surface and at 10 cm depth of soil and in salad. Children in the exposed area showed impairment of motor coordination and odour identification associated with airborne manganese at multivariate analysis. Blood lead was inversely associated with IQ, but only in the metal exposed area of Valcamonica.

Conclusion: Environmental exposure to manganese in adolescents is related to deficit in motor and olfactory functions whereas concomitant lead exposure is related to decrease of IQ.

Acknowledgement: This work was partially supported by the EU through its Sixth Framework Programme for RTD (contract no FOOD-CT-2006-016253). It reflects only the authors' views. The European Community is not liable for any use that may be made of the information contained therein.

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CONTACT (NAME ONLY): Roberto Lucchini

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PRESENTATION TYPE: Invited Presentation
KEYWORDS: children, neurobehavioral changes, manganese and lead.

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