PS 667 EVALUATION OF THE IMMUNOMODULATORY POTENTIAL OF DIETHYL PHTHALATE FOLLOWING DERMAL EXPOSURE IN A MURINE MODEL.

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Over the past 50 years the prevalence of asthma and allergy has increased throughout the US and other industrialized nations. During the same period there has been an increase in the production and use of phthalate compounds. Previous studies have suggested that certain phthalate compounds, including diethy-hexyl phthalate and butyl benzyl phthalate, have contributed to allergic disease by functioning as adjuvants, augmenting immunologic responses to other chemical and protein antigens without being allergenic themselves. Diethyl phthalate (DEP), another phthalate ester, used as a plasticizer in a variety of consumer products, has the potential for widespread exposure, both occupationally and in the general population. Although DEP is not an immune sensitizer, little is known about other immunological effects that may be associated with DEP exposure. The current study evaluated the immunotoxic potential of DEP. Dermal exposure to DEP concentrations as low as 50% were shown to be immunosuppressive, resulting in a modest reduction in thymus weights (%) and numbers of CD4+ and CD8+ thymocytes (30.7 and 37.6% respectively) in BALB/c mice. A dose responsive decrease in the primary IgM response to sheep red blood cells was observed following dermal exposure to DEP reaching 54% reduction at the highest concentration. Conversely, prior dermal exposure to 75% DEP enhanced airway hyperreactivity responses to aerosolized methacholine in mice sensitized to increasing concentrations of OVA, suggesting that despite its immunosuppressive properties, DEP may enhance airway responsiveness to environmental and occupationally relevant antigens and thereby contributing to the increased prevalence of allergic disease. These results warrant the need for additional investigation into the mechanisms underlying the immunotoxic effects associated with DEP exposure.

PS 668 AFRICAN DUST ENDOTOXINS AND THEIR PRO-INFLAMMATORY ROLE IN HUMAN BRONCHIAL EPITHELIAL CELLS.

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African dust reaching the island of Puerto Rico is associated with increments in ambient particulate matter (PM). Among the PM components associated with adverse health effects are particle-bound endotoxins (ENX). Therefore, aqueous and organic extracts of PM_{10} samples collected from specific African Dust Events (ADE) reaching Puerto Rico in March 2004 were characterized for their ENX content and evaluated for its cytotoxic and pro-inflammatory responses in the human bronchial epithelial cell line BEAS-2B. To accomplish these aims, we analyzed PM_{10} extracts from samples collected at the Atlantic Ocean and two sites in Puerto Rico (e.g. rural vs. urban). The ENX content in the extracts, as determined by the LAL assay, was higher in the organic fraction of PM_{10} and increased during ADE for all sites. Organic extracts of the ADE samples were highly cytotoxic even at low doses. The levels of IL-6 and IL-8 in cell culture supernatants were significantly higher in cells exposed for 24 hrs to ADE PM_{10} aqueous extracts versus those exposed with non-ADE extracts. However, only IL-8 was induced with the ADE organic extracts. To evaluate the role of ENX in the induced cellular responses, the extracts were pretreated with the ENX inhibitor polymyxin B prior cell exposure and the induction of pro-inflammatory mediators in human lung cells was inhibited. Since inhibition of ENX reduced the pro-inflammatory responses of ADE PM_{10} extracts current experiments are being performed to determine the expression of Toll-like receptor 4, which recognizes ENX, after exposure to PM extracts. The results obtained so far suggest that African dust reaching Puerto Rico increases the ENX content in ambient PM, which can induce inflammatory responses in the lung.
Supported by MBRS-RISE Grant R25GM061838.

PS 669 AFRICAN DUST $PM_{2.5}$ REACHING PUERTO RICO INDUCES OXIDATIVE STRESS AND PRO-INFLAMMATORY MEDIATORS IN HUMAN LUNG CELLS.

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African dust reaching the island of Puerto Rico is known to sporadically increase ambient particulate matter (PM). Particle-bound metals have been associated with adverse health effects. Organic extracts from $PM_{2.5}$ samples collected during African dust events (ADE) reaching Puerto Rico were characterized for its metal content and oxidant capacity. Extracts were also evaluated for its role in inducing oxidative stress and pro-inflammatory responses in the human bronchial epithelial cells (BEAS-2B). ADE and non-ADE $PM_{2.5}$ organic extracts exhibited similar oxidative capacity, using the DTT assay. However, metal compositions of organic extracts, determined by ICP-MS analysis revealed an increase in Cu and V concentrations in ADE vs. non-ADE extracts. This supports the hypothesis that differences in metal concentrations might be responsible for the immune responses observed between extracts. In-vitro experiments showed a reduction in the total antioxidant capacity and glutathione concentrations in lysates of organic extracts (50μg/ml). This reduction was greater in ADE organic extracts. Secretions of IL-6 and IL-8 were significantly higher in cells exposed (24hrs) to ADE vs. non-ADE extracts. However, the levels of MCP-1 were significantly reduced after exposure to either type of extract. The addition of metal chelators (deferoxamine and tetraethylenepentamine) increased antioxidant capacity and decreased the secretion of pro-inflammatory mediators in human lung cells exposed to organic extracts. These results demonstrate that the effects of organic extracts are produced by trace elements. This study suggests that African dust reaching Puerto Rico increases the concentrations of trace elements in ambient $PM_{2.5}$, inducing oxidative stress and inflammatory responses in the lung. Supported by MBRS-RISE Grant R25GM061838

PS 670 HEALTH EFFECTS DUE TO ACUTE EXPOSURE OF DUST SAMPLES COLLECTED FROM NELLIS DUNES RECREATIONAL AREA.

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The Nellis Dunes Recreational Area (NDRA; Las Vegas, NV) is a popular natural site for recreational vehicle operators with over 300,000 visitors per year. Potential health effects caused by PM10 generation from ORV activity were examined. B6C3F1 mice were exposed to dust collected from 3 NDRA map unit sites (2.2, 3.1, or 3.2). Exposure was administered via oropharyngeal aspiration at doses of 0.1, 1, 100, and 1000 mg/kg/day for 3 days. The lowest adverse effect level (LOAEL) for map unit 2.2 was 0.1 mg/kg/day while the LOAEL was 1.0 mg/kg/day for map units 3.1 and 3.2. Each LOAEL was based on significant and dose-responsive decreases in specific IgM B-cell responses and CD4/CD8 splenic lymphocytic subpopulations. Pulmonary histopathology was evident in the 100 and 1000 mg/kg/day dose groups. Observations were primarily multifocal, centriacinar bronchiolitis with accumulation of dust-filled macrophages and interstitial fibrosis. Alveolar bronchiolarization and bronchiolitis obliterans were also common, characteristic of pneumoconiosis. Median particle diameter for map units 2.2, 3.1, and 3.2 was 4.3, 2.4, and 3.1 um, respectively. The predominant mineral was smectite while palygorskite was also common. ICP-MS measured >20 naturally-occurring metals to include: 23-143 ppm total As, 18-24 ppm Pb, 9-18 ppm Cr, 6600-9800 ppm Al, 106-183 ppm Sr, and 274-428 ppm Mn. Research is needed to determine the impact of dust exposure on respiratory health and disease resistance because of the likelihood of human exposure.

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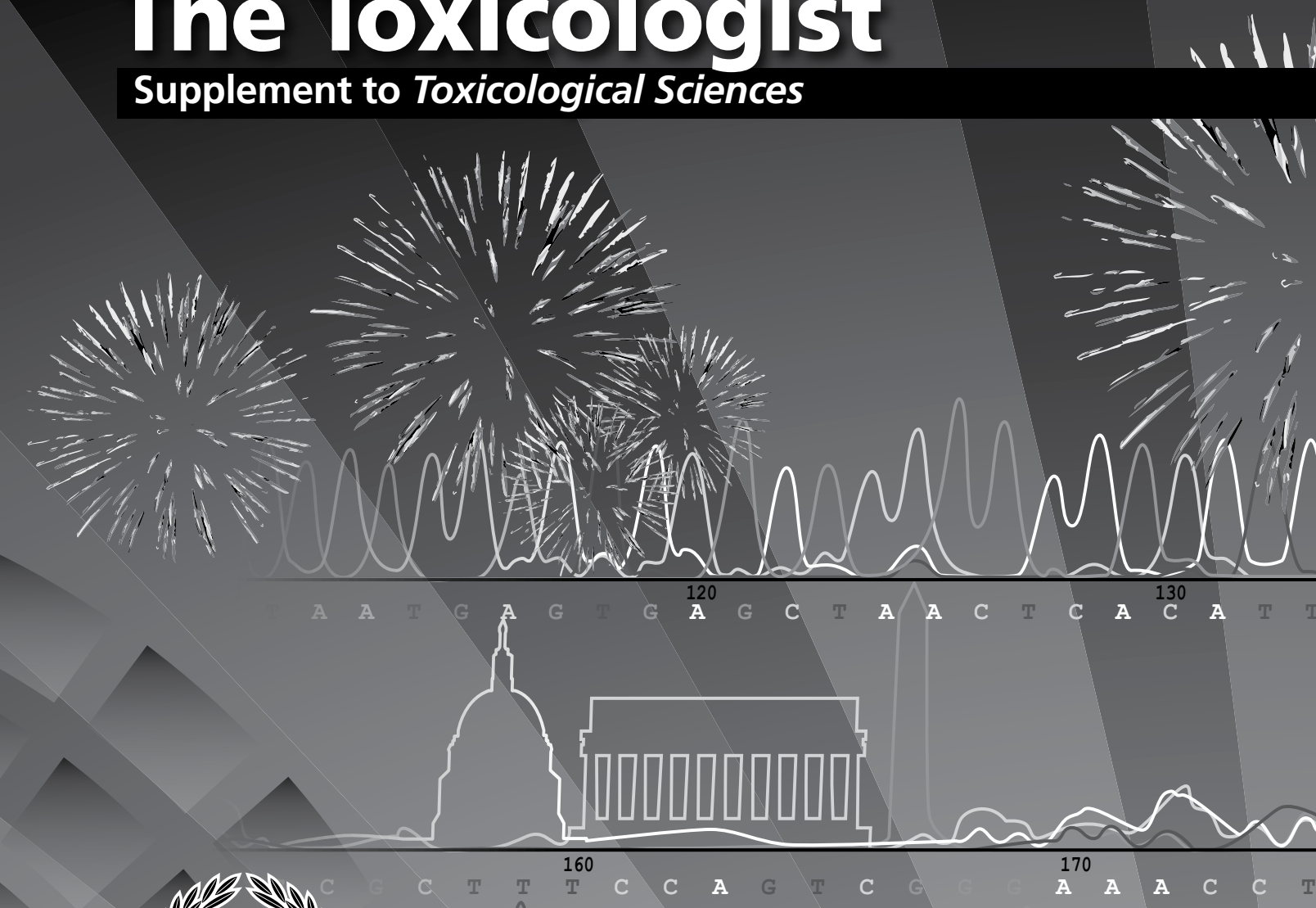

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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