SATURDAY

394 Characteristics of CRS After Burn Pit Exposure in a Cohort of Veterans

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RATIONALE: Military deployment exposures, particularly burn pits (BP), may be associated with development of chronic rhinosinusitis (CRS). We hypothesized that Veterans with CRS with BP exposure may have more severe CRS.

METHODS: We conducted a retrospective cohort survey-based study of patients at the San Diego VA. Inclusion criteria included diagnosis of CRS. Survey questions included deployment history, military inhalation hazards (BP and other) and smoking history. We also obtained information including gender, age, medications, comorbidities and results from prior pulmonary function tests, sinus and chest CT scans, eosinophil and IgE levels and allergy testing. Two cohorts based on self-reported BP exposure were assessed for degree of sinus disease, survey responses and chart characteristics.

RESULTS: Eighteen patients were included (8 with BP exposure, 10 without), and the median BP exposure was 12 months. All patients were male. The median age in the BP group was 41.5 versus 55 in the non-BP-exposed. Three patients in each group had nasal polyps. There was no significant difference in radiographic sinus disease severity by Lund-Mackay score between the two groups (median score 8.5 BP versus 6 non-BP, $p=0.62$). A trend towards decrease in peripheral eosinophilia was present in BP-exposed compared to non-BP-exposed (absolute eosinophil count 210 versus 325, $p=0.09$). Three patients received a biologic (dupilumab), and none had systemic steroids during the study period.

CONCLUSIONS: Our initial cohort analysis suggests a potential decrease in peripheral eosinophilia in BP-exposed Veterans despite no change in CRS severity. Future large-scale and immunophenotyping studies in BP-exposed CRS patients are needed.

395 Transgenerational effects of early environmental estrogen (EE) exposure on asthma development

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RATIONALE: Early exposure to Bisphenol A (BPA) is associated with an increase in asthma prevalence. Bisphenol S (BPS) is the most widely used BPA substitute, but the effects of BPS on immune development have not been examined. To test the hypothesis that early exposure to EEs, including BPS, enhances the allergic sensitization that underlies childhood asthma, we conducted the study.

METHODS: To simulate human exposure, 10 mg/ml BPS in the drinking water to the female BALB/c mice (F0) was given from one week before pregnancy until the weaning of F1 pups. The pups were sensitized with low doses of ovalbumin (OVA) injection or control on a postnatal day (PND) 4 and inhalation of OVA on PND 18-20. On PND 22, serum IgE anti-OVA levels were quantified, and airway inflammation and hyperresponsiveness were assessed. Non-OVA-sensitized female pups were saved and mated with non-exposed male mice at eight weeks of age for the next generation. The resulting pups were sensitized, and the asthma phenotype was examined up to F4.

RESULTS: Pups exposed to BPS displayed an asthma phenotype in response to their "suboptimal" sensitization. OVA-specific IgE and airway hyperresponsiveness were significantly increased in the F1-F4 pups derived from BPS-exposed F0 dams than in the pups derived from non-exposed dams. Eosinophilic airway inflammation is significantly increased in F1-F3 pups derived from BPS-exposed dams.

CONCLUSIONS: Maternal exposure to EE, including BPS, promotes the development of experimental asthma. The immune alterations may be epigenetically perpetuated, causing multigenerational effects.

396 Investigating the Role of Airway Epithelium in Shaping Immune Response to Indoor Fungal Contaminant Exposure

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RATIONALE: The fungal contaminants *Stachybotrys chartarum* and *Aspergillus versicolor* modulate pulmonary immune responses in murine models of repeated exposure. These complex responses exhibit features of Th1 and Th2 immunity and are poorly defined. The respiratory epithelium acts as a barrier to inhaled fungi and modulates innate and adaptive immunity. Understanding how the respiratory epithelium facilitates antifungal immunity will support development of more advanced *in vitro* fungal exposure paradigms mimicking *in vivo* exposures.

METHODS: Murine pulmonary epithelial cells (MLE-12) were stimulated with five doses of live or heat-inactivated (HIC) *S. chartarum* or *A. versicolor* conidia for 48 hours; these were extrapolated from fungal deposition levels that provoked an immune response in prior murine exposures. To evaluate cytotoxicity, lactate dehydrogenase release was measured at four timepoints followed by a tetrazolium-based assay (MTS). Epithelial cell-secreted cytokines will be assessed by a multiplex bead-based immunoassay to define how these relate to responses observed during *in vivo* exposures.

RESULTS: Preliminary data indicate *S. chartarum* and *A. versicolor* impact *in vitro* epithelial cell viability, with *S. chartarum* producing toxicity at significantly ($p<0.05$, $n=3$ independent experiments) lower doses than *A. versicolor*. This occurred independently of conidia viability. In this model, calculated LC50s for live and HIC *S. chartarum* were $4.68*10^3$ and $2.37*10^3$ conidia/mL, respectively. For live and HIC *A. versicolor*, LC50s were $1.87*10^6$ and $6.14*10^5$ conidia/mL, respectively.

CONCLUSIONS: This study illustrates that *S. chartarum* is more acutely toxic to MLE-12 cells than *A. versicolor*. Ongoing cytokine characterization may reveal how immune responses to these fungal contaminants are initiated and sustained.

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