

ronmental exposures. Multivariate statistical methods can be effective in quantitating these relationships, however, the limitations of such methods must be considered. These considerations were explored using data from B6C3F1 female mice administered dexamethasone (0.3-30.0 mg/kg/ day) subcutaneously for 16 days. A host resistance model using B16F10 melanoma cells was used and immune parameters were measured including spleen and thymus weight, macrophage function, CD4/8 subpopulations in thymus and spleen, B220/1a subpopulations in peritoneum, NK cell activity, and peripheral blood differentials. For multivariate analysis, two independent experiments of 40 mice with 8 mice per group were used. Additionally, two other experiments each of 40 mice measured resistance to B16F10 tumors. A large number of observations is required for multivariate methods. Thus, by combining the two experiments, one data set of 80 observations was produced. To demonstrate that incorporation of unique experiments into one data set was a viable method, values obtained within one treatment were randomized. This simulates the merger of experiments where the matching of immune parameter values from mice within a single treatment is unknown. Using multivariate methods, this set was compared to the original data set with the correctly matched observations for each mouse. Principal components analysis (PCA) was performed on the immune parameters. Subsequent multiple regression analysis was done using the factor (PCA) as the independent variables with tumors resistance as the dependent variable. Reproducible models between the original and the randomized data set were obtained when certain criteria were met. Variation within a treatment of an experiment will be limited. This can be determined by the coefficient of variation which generally must be less than 30%. Thus, experiments must be done using standard conditions to achieve low variability within treatments. Developing criteria for incorporation of several experiments into a large data set appropriate for analysis by multivariate methods can provide more insight into the relationships between immune parameters and host resistance.

1755 CLINICAL IMMUNOLOGIC EFFECTS OF LEAD EXPOSURE IN WORKERS EMPLOYED AT A SECONDARY SMELTER

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NIOSH, in collaboration with NIEHS, studied a comprehensive panel of clinical immunological outcomes in workers employed at a secondary lead smelter and in workers at a hardware manufacturing company without occupational lead exposure (unexposed). This study is by far the largest to date investigating the immunologic effects of lead among workers for workplaces that operate within the OSHA lead standard. All study participants were male. 145 exposed and 84 unexposed workers participated. Endpoints evaluated included: hematology, lymphocyte immunophenotyping, clinical chemistries including sera immunoglobulin levels, lymphocyte proliferation and natural killer cell cytotoxicity. The median blood lead level (exposed) was 39 µg/dl (range: 15-55 µg/dl) and <2 µg/dl (range: <2-12 µg/dl) among the unexposed group. The median zinc protoporphyrin (ZPP) was 48 µg/dl (range: 2-424 µg/dl) among the exposed and 17.5 µg/dl (range: 1-59 µg/dl) among the unexposed group. Analyses of raw data indicated statistically significant changes in selected parameters (when compared to the unexposed group) including changes in serum IgG and IgA levels, salivary IgA, percent of CD3+ cells and CD19+ cells. Analyses of covariates (age, race, smoking, alcohol use, etc.) is ongoing; however, the relationship between the number of CD3+/CD4+ T-cells and exposure varied by age. Among workers under 30 years of age, there was no difference in the number of CD3+/CD4+ T-cells between the unexposed and exposed group. But among workers 30 years of age or older, exposed workers, on average, had fewer CD3+/CD4+ T-cells. These results emphasize the importance of covariate analyses in human clinical immunological studies.

1756 ORAL EXPOSURE TO 2-BUTOXYETHANOL ALTERS IMMUNE RESPONSES IN BALB/c MICE

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Several members of the glycol ether family have been reported to induce immunotoxic effects in rodent models. We report here the effects of oral exposure to 2-butoxyethanol (BE) on immune function in BALB/c mice. Female mice were dosed by oral gavage at 50, 150 or 400 mg/kg body weight for 10 consecutive days followed by a 3-day rest. No effects were observed at any of the BE concentrations on body weight, spleen and thymus cellularity

or spleen:body weight ratio and thymus:body weight ratio. There was a 3-fold increase in concanavalin A mitogenic stimulation of splenocytes from mice at all BE concentrations tested compared to control. Lipopolysaccharide stimulation was significantly elevated only in splenocytes from mice at the 400 mg/kg BE dose. The mixed lymphocyte reaction was increased over control by 2 fold at all BE concentrations. Cytotoxic T lymphocyte activity was significantly increased in both the 150 and 400 mg/kg dose groups compared to vehicle-exposed mice. This study demonstrates that BE is an immunomodulating agent and that the mouse model responds differently than previously reported results in the rat. This research was supported in part by NIH AREA grant # ESO6782-01A1.

1757 MORPHOLOGIC LESIONS AND ACUTE IMMUNOTOXIC EFFECTS IN TILAPIA (*Oreochromis niloticus*) EXPOSED TO BENZO[a]PYRENE

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Tilapia were exposed by intraperitoneal injection to the polycyclic aromatic hydrocarbon (PAH), benzo[a]pyrene (B[a]P). Histopathologic evaluation of the fish primary hematopoietic compartment, the pronephros, demonstrated increased vacuolation of both stromal and parenchymal cells, as well as dramatic reduction of lymphoid elements. Total pronephros cell counts were also diminished in a dose-dependent manner by the chemical exposure. The oxidative metabolic burst in phorbol myristate acetate (PMA)-stimulated macrophages isolated from the pronephros was significantly inhibited by B[a]P, but only at the highest dose level employed. The phagocytic capacity of pronephros macrophages was not altered by the chemical treatment. In contrast, the proliferative response of splenic T and B lymphocytes to mitogens Con A and LPS, respectively, was significantly decreased by B[a]P. These data correspond well with similar immune alterations in laboratory rodents exposed to B[a]P, indicating fish may respond similarly to mammals following PAH contamination. Further, tilapia exposed to B[a]P at doses not producing overt toxicity showed immune alterations consistent with impaired immunity in mammals, and thus may be in a state of clinically-significant immunosuppression.

1758 MODULATION OF NK1.1 SPLENOCYTES AFTER EXPOSURE TO OCTAMETHYLCYCLOTETRA-SILOXANE (D4)

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Octamethylcyclotetrasiloxane (D4) is a low molecular weight, cyclic polydimethylsiloxane which is present in many consumer goods including over-the-counter medications, personal care and household products. It has previously been shown that natural killer (NK) cell activity is augmented in B6C3F1 mice following exposure to D4. When mice were gavaged daily with 1000 mg/kg for 35 days, significant enhancement was apparent by day 5, peaked on day 7, then returned towards baseline by day 10. Spleen weight and cell counts tended to increase whereas splenic cellularity decreased following exposure for 7 days. Histopathology of the spleen revealed increased hematopoiesis characterized by confluent red pulp foci consisting primarily of erythroid precursor-like cells. Cell population analysis by flow cytometric methods indicated that the percentage of NK1.1⁺/CD3⁻ NK cells and NK1.1⁺/CD3⁺ T cells were not significantly altered after D4 exposure although the total number of NK cells per spleen tended to increase. NK1.1⁺/CD3⁺ T cells have been shown to exhibit NK like cytolytic activity against YAC cells. Results of T cell depletion studies in conjunction with population studies suggest that the increased cytolytic activity is a function of enhanced activity of NK 1.1⁺/CD3⁻ NK cell on a per cell basis. This augmentation may be due to increased binding of the NK cell to its target, increased killing capabilities or increased recycling. The effect may be mediated via direct or indirect mechanisms. Supported by NIEHS-T32-ES07087.

1759 EFFECTS OF CAPSAICIN ON THE IN VITRO ANTIBODY RESPONSE OF HUMAN AND RODENT LYMPHOCYTES

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Capsaicin (CAP: 8-methyl-N-vanillyl-6-nonenamide) is a major pungent



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Preface

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An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 351.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 375.

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