ment did not produce any significant change of any of these parameters. However, when co-administered with COC these immunotoxic effects were antagonized. Studying the possible mechanisms of COC-induced immunotoxicity revealed that COC caused a significant increase in serum corticosterone concentration. Co-administration of KET effectively blocked the stimulatory effect of COC on serum corticosterone without any significant change of plasma and tissue concentrations of norcocaine (NC). The results of this study indicate that exposure to COC in early postnatal period can induce immunotoxic reactions which were antagonized by KET most likely through neuroendocrinal mechanisms.

1819 LIFETIME EXPOSURE TO TRICHLOROETHYLENE (TCE) MODULATES IMMUNE FUNCTION.

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Trichloroethylene (TCE) is an industrial solvent used in the cleaning and degreasing of metal components in various machine industries. Not only is it commonly inhaled during occupational situations, but its widespread use has resulted in groundwater contamination leading to human exposure *via* drinking water. It has been reported, in murine studies, that TCE can both exacerbate autoimmune disease and suppress immune function. While these studies have addressed effects in adult rodent models, none have explored immunological effects during developmental stages. To determine the immunological effects of TCE in B6C3F1 mice, exposure to TCE in drinking water (1000 ppb or 10, 000 ppb) began when pairs were mated (female C57 and male C3H mice) and continued through weaning (21-day old) or adulthood (56-days old). The vehicle control group was administered emulphor-treated water. Endpoints assessed included splenic and thymic weights and cellularity, natural killer cell (NK) activity, antibody plaque forming cell (PFC) response, lymphocyte proliferation, and T-cell immunophenotypes. At 21 days of age, alterations were evident. Body weight and length were significantly decreased by the 10, 000 ppb treatment. NK cell activity and T- and B-cell proliferation were not altered. IgM antibody responses to sRBC challenge were suppressed in both male and female pups by 10, 000 ppb TCE and by 1000 ppb TCE in the male pups only. Additionally, there was a distinct decrease in splenic CD4+CD8- T-cells resulting in a concomitant decrease in the CD4+:CD8+ ratio. At 56-days of age, the most striking effect was noted with increased NK cell activity in both treatment groups. Currently studies are being conducted to verify the PFC response and T-cell immunophenotypes in the adult mice. These data suggest that lifetime exposure to TCE modulates both innate and adaptive immune responses and this should be considered when assessing health risks to TCE.

1820 IMMUNOTOXICOLOGICAL ASSESSMENT OF A P38 MAP KINASE INHIBITOR.

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The p38 MAP kinase signaling pathway plays a pivotal role in the initiation and progression of inflammation. Compounds that inhibit this kinase inhibit the production of inflammatory cytokines and are potential therapies for inflammatory diseases. A p38 kinase inhibitor was tested to evaluate its effects on the net health of the immune system using the mouse sheep red blood cell (SRBC) antibody forming cell response and host resistance model to influenza virus. Female B6C3F1 mice were administered the p38 kinase inhibitor by oral gavage for 28 days at doses of 0, 3, 30 and 300 mg/kg/day. Animals were immunized with SRBC and the number of splenic cells producing antibody (AFC) to SRBC was quantitated through the production of hemolytic plaques. Cyclophosphamide was administered as a positive control. In the influenza host resistance model, Balb/c mice were administered the p38 kinase inhibitor at doses of 30 and 150 mg/kg/day or anti-TNFα antibody at 250 µg/week, 7 days prior to a mouse-adapted influenza virus intranasal infection. Administration of the compound continued post-infection for 21 days. Dexamethasone was used as a positive control. Analyses included the measurement of the clearance of infectious influenza virus on Day 2, 6, 8, 10 and 21, and influenza specific IgG in the lung on Day 2, 10 and 21. Results of the studies were as follows: A decrease of 48% and 70% in the antibody forming cell response was observed with the p38 kinase inhibitor at a dose of 30 and 300 mg/kg/day, respectively. The compound did not affect any of the parameters evaluated in the influenza host resistance model. A significant decrease in AFC response was observed with cyclophosphamide and dexamethasone significantly reduced viral clearance and IgG production. A small decrease in influenza specific IgG production was noted with the anti-TNFα antibody on Day 21. In conclusion, although modulation of the immune response was observed with the p38 kinase inhibitor this did not affect the ability of the host to clear or eliminate a viral infection.

1821 EFFECT OF DIESEL EXHAUST PARTICULATE (DEP) ON BACILLUS CALMETTE-GUERIN (BCG) LUNG INFECTION IN MICE.

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The effect of exposure to diesel exhaust particulate (DEP) on Bacillus Calmette-Guerin (BCG) lung infection in mice was studied. C57Bl6 female mice were infected with BCG (2.5x10^4 bacteria/mouse) by tracheal aspiration with or without co-administration of DEP (100 mcg/mouse). Five weeks later, mice exposed to DEP+BCG had about four-fold higher BCG load in lungs than mice exposed only to BCG ($p<0.05$). DEP treatment alone had no effect on the total number of lung lymphocytes or numbers of T, B or NK cells recovered from lungs. In contrast, BCG infection significantly increased recovery of all types of lymphocytes from lungs. Co-exposure to DEP+BCG further increased the recovery of lymphocytes from lungs of BCG infected mice. The pulmonary lymphocyte subpopulation expressing the greatest levels of mRNA for IFN gamma after BCG infection was CD4+ T cells and expression levels were similar in mice exposed to BCG or BCG+DEP. Recovery of IFN gamma secreting T cells was significantly higher ($p<0.05$) from lungs of BCG and BCG + DEP infected mice as compared to control or DEP only exposed mice, but BCG and BCG+DEP groups of mice were not significantly different. These results indicated that co-exposure to DEP+BCG did not significantly affect the level of IFN gamma response of mice to BCG infection. However, *in vitro* studies demonstrated DEP treatment inhibited IFN gamma induced nitric oxide secretion by mouse alveolar macrophages. Thus, DEP exposure did not alter the IFN gamma response to BCG infection, but reduced a key microbiocidal response of macrophages to IFN gamma. Reduced responsiveness of DEP exposed macrophages to IFN gamma may contribute to a less efficient clearance of BCG from the lungs of BCG infected mice.

1822 ROLES OF REACTIVE OXYGEN SPECIES, HEME OXYGENASE-1, AND NITRIC OXIDE IN DIESEL EXHAUST PARTICLE-MEDIATED PULMONARY IMMUNE RESPONSES TO *LISTERIA MONOCYTOGENES* IN RATS.

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This study examines the hypothesis that diesel exhaust particles (DEP) suppress pulmonary immunity to *Listeria monocytogenes (Listeria)* through the induction of reactive oxygen species (ROS), heme oxygenase-1 (HO-1) and altered cytokine production by alveolar macrophages (AM) and lymphocytes. Cells were isolated from Brown Norway rats intratracheally inoculated with saline or 100, 000 *Listeria* at 7 days post-infection. The *Listeria*-infected AM showed increased production of IL-6, IL-10, IL-12, and TNF-α over the saline control in response to lipopolysaccharide (LPS), whereas the *Listeria*-infected lymphocytes showed increased production of IL-2, IL-10, and IFN-γ when challenged with concanavalin A (ConA) or heat killed Listeria (HKLM). DEP or DEP extract, but not the washed DEP, inhibited AM secretion of IL-6, IL-12, and TNF-α and lymphocyte production of IL-2 and IFN-γ, but enhanced AM production of IL-10. The effect of the DEP extract on cytokine production was preceded by a time-dependent induction of ROS and ROS-induced HO-1 protein and activity in AM. α-Naphthoflavone (ANF), a CYP 1A1 inhibitor, partially inhibited DEP-induced ROS and HO-1 expression and reversed the DEP effect on cytokine secretion. L-NAME (N-nitro-L-arginine methyl ester), a NO synthase inhibitor, inhibited the DEP-induced ROS generation and HO-1 induction, but augmented the DEP-induced IL-10 production by *Listeria*-infected AM, suggesting that NO down-regulates IL-10 production. Similar to DEP extract, hemin induced HO-1 expression, an increase in IL-10 and a decrease in TNF-α production by AM. In comparison, DEP extract at a level that induced less HO-1 than hemin, showed greater effect on IL-10 secretion. These results show that both HO-1 and NO play a role in AM production of IL-10, and that due to its organic content, DEP suppress the host immune responses by inhibiting the innate and T cell-mediated immunity and augmenting AM production of IL-10 (NIH HL-62630).

1823 EXACERBATION OF RESPIRATORY SYNCYTIAL VIRUS INFECTION BY ULTRAFINE CARBON BLACK PARTICLE EXPOSURE.

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Exposure to particulate matter (PM) may exacerbate preexisting respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), bronchitis and pneumonia, however few experimental studies have addressed the effects of PM on