highest doses. With the exception of an increase in reticulocyte numbers, hematological parameters were not affected. The antibody forming cell response to sheep erythrocytes was not altered by Elmiron administration. Evaluation of the functional activity of the mononuclear phagocytic system demonstrated a slight decrease in vascular half-life of sheep erythrocytes and a significant increase in the percent uptake by the liver in the high dose animals. At histolopathology, a slight to moderate presence of vacuolated histiocytes were noted in the spleen and mesenteric lymph nodes. These studies demonstrate that the extensively used vehicle Elmiron when administered at doses of 1000 mg/kg or greater may alter function and histopathology of macrophages in mice, consistent to effects reported in rat (Supported by the NIEHS Contract ES 05454).

879 INTERACTIONS OF MERCURY WITH LIVER-STAGE RESPONSES TO MALARIA INFECTION.

J. F. Nyland[1], A. Lima[1], G. Mouton[2], K. West[3], F. Zavala[1] and E. Silbergeld[1]. *[1]EHS & MMI, Johns Hopkins, Baltimore, MD, [2]Grambling State, Grambling, LA and [3]University Hosp of West Indies, Kingston, Jamaica.*

Malaria, a life-threatening parasitic disease transmitted by mosquitoes, has re-emerged in Amazonia over the past two decades. Among the many factors proposed for this re-emergence are changes in population distribution, failures of vector control and pharmacologic management, as well as local and global environmental changes including the widespread use of mercury (Hg) for gold extraction. Our previous studies with BALB/c mice have shown that pretreatment with Hg impairs host resistance to subsequent infection by sporozoites of the murine-specific Plasmodium yoelii. Hg also decreased production of nitric oxide by splenocytes, and down-regulated expression of both IFN-gamma and nitric oxide synthase. These effects appeared to involve hepatic mechanisms, since Hg did not affect parasitemia following infection with blood stage plasmodia. In addition, we reported that Hg pretreatment failed to prevent parasitemia in animals immunized twice with irradiated sporozoites. In these studies we explored early responses at the liver stage of infection in BALB/c mice pretreated with Hg by studying liver-stage infection and cytokine levels in animals pretreated with Hg and infected with P. yoelii sporozoites. At 40 hours following infection, Hg pretreatment unexpectedly decreased plasmodia in liver, detected by measurement of a plasmodial 18S rRNA sequence in the liver (specific for liver stages of P. yoelii parasites). However, at this time, in Hg treated mice, levels of IFN-gamma and IL-6 protein were reduced in spleen homogenates, and mRNA levels of these cytokines were reduced in liver. We also examined plasmodia in liver after a single immunization with irradiated sporozoites, followed one week later by infection with live sporozoites. In this model, we found no effect of Hg on early liver-stage immunity. These results indicate that Hg can affect early hepatic responses to malaria infection but that these effects may not predict the interactions of Hg with acquisition of immunity (defined by parasitemia).

880 THE EFFECTS OF CIGARETTE SMOKE EXPOSURE AND PREGNANCY ON INNATE AND ADAPTIVE IMMUNE RESPONSES IN B6C3F1 MICE.

E. M. Vancza, S. P. Ng and J. T. Zelikoff. *New York University School of Medicine, Tuxedo, NY.*

It is well-known that cigarette smoke (CS) exposure *in utero* negatively affects the development and viability of the offspring, causing a host of defects including lower birth weight, nicotine-related neurological problems and alterations in immune function. Despite this, 20-30% of women in the United States still smoke. Although adult smokers experience some immunosuppression, the relationship between CS and the immune response has not been extensively examined for pregnant women. This study investigates the role of pregnancy on CS-induced immune modulation by examining innate and adaptive immunity in pregnant and non-pregnant B6C3F1 mice. Following inhalation of mainstream CS for 5d/wk (4hr/d from gestational d5 to parturition for the dams), inflammation was assessed via differential counts of brochoalveolar lavage fluid and blood. Effects on tumor surveillance were evaluated *in vivo* by tumor challenge with cultured lymphoma cells and *ex vivo* by examination of cytotoxic T lymphocyte (CTL) activity. While no significant differences in lung inflammation were observed between the groups (i.e., air and CS or dams and virgins), pregnancy modulated the response to transplanted tumor cells in CS-exposed mice; tumor incidence in the smoke-exposed dams was 53.8%, while 87.5% of the exposed virgins demonstrated tumors. Furthermore, CTL activity measured in the spleens of both groups of females appeared higher in CS-exposed dams than in their virgin counterparts. These findings suggest that pregnancy may actually protect against the immunosuppressive effect of CS. Moreover, results begin to provide insight on the link between the immune response in smoking mothers and some of the adverse health outcomes affecting their offspring. Philip Morris Foundation Inc.

881 SMOKING DURING PREGNANCY REDUCES IMMUNE TUMOR SURVEILLANCE MECHANISMS IN THE OFFSPRING: A TOXICOLOGICAL MODEL.

S. P. Ng[1], A. E. Silverstone[2], Z. Lai[2] and J. T. Zelikoff[1]. *[1]Nelson Institute of Environmental Medicine, New York University School of Medicine, Tuxedo, NY and [2]Department of Microbiology & Immunology, SUNY Upstate Medical University, Syracuse, NY.*

Accumulating epidemiologic evidence suggests that prenatal exposure to intact cigarette smoke increases the incidence of cancer in the offspring. A study was proposed to examine the effects and underlying mechanisms of prenatal exposure to mainstream cigarette smoke (MCS) on offspring resistance to tumor challenge and surveillance mechanisms critical for the recognition and destruction of developing neoplasms. Pregnant $B_6C_3F_1$ mice were exposed by whole body inhalation to MCS for 5 d/wk (4 hr/d from gestational d5 to parturition) and smoke-induced effects on offspring host resistance to transplanted tumors, body/organ weight, natural killer cell and cytotoxic T-lymphocyte (CTL) activity, lymphoproliferation, cytokine levels, immune cell subpopulations and lymphoid organ histology were examined. At a concentration of smoke equivalent to smoking 2-3 packs of cigarettes, prenatally-exposed male offspring challenged at 5-wk of age with EL4 lymphoma cells demonstrated a >2-fold increase in tumor incidence (relative to age-/gender-matched air-exposed offspring). Furthermore, CTL activity in the smoke-exposed 5- and 10-wk-old male pups was significantly lower than the age-/gender-matched controls. Prenatal exposure to cigarette smoke also reduced (compared to age-/gender-matched controls) mitogen-stimulated T-lymphocyte proliferation in the 3-wk-old male offspring; circulating numbers of white blood cells and lymphocytes were increased in the smoke-exposed offspring. No effects were observed on body/organ weight, cytokine levels or immune cell subpopulations. Results demonstrate that exposure of pregnant mice to a relatively low dose of MCS decreases offspring resistance against nascent tumors and persistently reduces immune functions associated with tumor surveillance. This study suggests that children of mothers who smoke during pregnancy have a greater risk of developing tumors in later life. Supported by Philip Morris Foundation Inc.

882 GESTATIONAL EXPOSURE TO PFOS SUPPRESSES IMMUNOLOGICAL FUNCTION IN F1 MICE.

D. E. Keil[1], T. Mehlman[1], L. Butterworth[1] and M. M. Peden-Adams[2]. *[1]Analytical Sciences Branch, NIOSH, Morgantown, WV and [2]Department of Pediatrics, Medical University of South Carolina, Charleston, SC.*

Perfluorinated hydrocarbons have been manufactured for over 40 years and have numerous applications in industry. This group of compounds has recently generated much interest as common metabolites (i.e., perfluorooctane sulfonate (PFOS); perfluoroctanic acid (PFOA)) are found to be persistent in the environment, have been detected in blood samples of both wildlife and humans, and appear to have a common mechanism of action. Studies show that these perfluorinated compounds cause peroxisomal proliferation, hepatomegaly, altered steroidogenesis, and body weight decreases that are associated with a wasting syndrome; however, effects on immune function have not been extensively assessed. This study examined the immunotoxicological effects of PFOS on the developing immune system should exposure occur during pregnancy. Therefore, C57BL/6N pregnant dams (mated with C3H/HeJ males) were orally exposed with 0, 0.1, 1.0 or 5.0 mg/kg of PFOS during each day of gestation. F1 offspring were evaluated for immunological alterations at 4 and 8 weeks of age. In general, there were no treatment effects on body, spleen, or thymus mass, and limited effects on kidney and liver mass. Corresponding flow cytometric analysis of CD4/CD8 lymphocytic subpopulations in the thymus and spleen were not altered in 4- or 8-week F1 mice. However, assessment of functional immunological parameters at 8-weeks of age revealed functional deficits. Natural killer cell activity was dose-responsively suppressed in both male and female F1 adults, whereas IgM plaque forming cell (PFC) responses were only suppressed in male F1 adults. Our data indicate that prenatal exposure to PFOS can suppress functional immunological responses that are evident at adulthood, with increased vulnerability exhibited in the male F1 offspring.

883 CHANGES IN THE OVINE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS DURING PREGNANCY AND LACTATION FOLLOWING CHALLENGE WITH ESCHERICHIA COLI LIPOPOLYSACCHARIDE.

L. C. Kabaroff[1], N. Karrow[1] and H. Boermans[2]. *[1]Animal and Poultry Science, University of Guelph, Guelph, ON, Canada and [2]Toxicology, University of Guelph, Guelph, ON, Canada.*

Lipopolysaccharide (LPS) is a gram-negative bacterial membrane component that is known to induce a systemic inflammatory response through the activation of blood monocytes and hepatic kupffer cells. These cells secrete the pro-inflamma-

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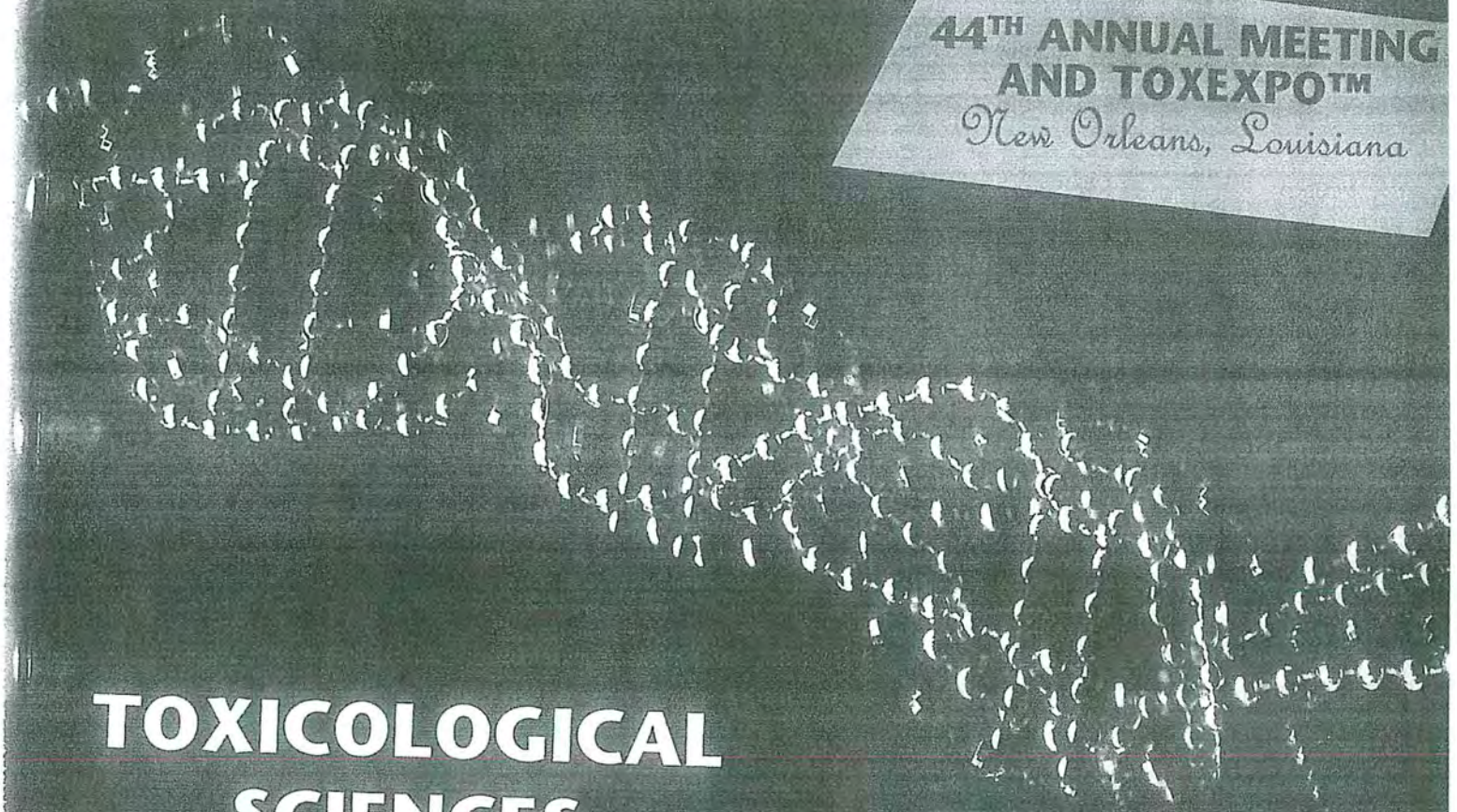

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