634 IMMUNE FUNCTION STUDIES IN RATS FED THE COLOR ADDITIVE AMMONIA CARAMEL COLOR. G F Houben, A H Penninks, W Seinen, J G Vos, and H Van Loveren. Research Institute of Toxicology, University of Utrecht; TNO-Toxicology and Nutrition Institute, Zeist; National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

Ammonia Caramel Color (AC) is used as a color additive in a variety of products for human consumption. Administration of AC has been associated with decreased numbers of lymphocytes in blood, spleen and lymph nodes, decreased cortex over medulla ratio in the thymus, and decreased IgA levels in serum, especially of rats fed a diet with a relatively low content of vitamin B6. These effects are caused by 2-acetyl-4(5)-tetrahydroxybutyl-imidazole (THI). In the present studies, immune function assays were conducted with young male Wistar rats fed a diet low (2-3 ppm) in vitamin B6 and exposed to 0.4 or 4% AC in drinking water or to a solution of 5.72 ppm THI for 28 days. Natural killer cell activity in the spleen was decreased. Also the mitogen responsiveness of spleen cells (tested after 14 days of exposure) to ConA, PHA, and LPS was reduced. The IgG but not IgM response to Sheep Red Blood Cells, measured by ELISA, was decreased. Enhanced clearance of Listeria monocytogenses was observed, possibly indicating enhanced macropghage activity. Resisitance to Trichinella spiralis was reduced, as evidenced by the increased numbers of muscle larvae found after infection. In contrast to IgM, IgG, and IgA responses, the IgE response to the parasite was decreased. These results indicate that AC and THI affect the functionality of the immune system of rats.

635 EFFECTS OF BENZO(A)PYRENE ON HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS IN VITRO. S P Mudzinski. Depts. of Pathology/Laboratory Medicine and Microbiology/Immunology, Albany Medical College, Albany, NY. Sponsor: M Aschner.

Human peripheral blood mononuclear cells from different individuals were exposed in vitro to the environmental carcinogen benzo(a)pyrene (BaP;10^{-9}M to 10^{-6}M) and stimulated by the T-cell mitogen Con A. After three days, percentages of cells with detectable cell-cycle related antigens were quantified by flow cytometry and correlated with cellular DNA content or light scatter. Viability, ^{3}H-TdR incorporation, and cell recoveries were also measured. Compared to vehicle controls, cell recoveries and ^{3}H-TdR incorporation were diminished in a dose-related manner by 10^{-9}M to 10^{-6}M BaP. Viability, blastogenesis (increased forward/side light scatter) and percentages of non-blasts expressing activation antigens CD25 (interleukin-2 receptor) or CD71 (transferrin receptor) were significantly decreased by 10^{-7}M to 10^{-6}M BaP. Percentages of blasts expressing CD71 or CD25, or of S- and G_2/M-phase cells expressing intracellular proliferation-associated antigens Ki-67 or PCNA were only slightly decreased by 10^{-6}M BaP. However, the percentages of G_0/G_1 cells expressing Ki-67 or PCNA were significantly decreased by BaP at 10^{-8}M to 10^{-6}M. Cell cycle analysis demonstrated decreased ratios of G_0/G_1 to S- phase cells at 10^{-7} to 10^{-6}M BaP. Among individuals, susceptibility to the inhibitory effects of BaP varied over a 10-fold range. These data suggest that BaP directly or indirectly inhibits human T-cell cycle progression by partially blocking the G_1 to S transition. Supported by NIEHS 04020.

636 LEVELS OF 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN (TCDD) IN SPLENIC TISSUE OF C57Bl/6 MICE ASSOCIATED WITH AN IMMUNOSUPPRESSIVE DOSE OF TCDD. N I Kerkvliet, L B Steppan and C M Neumann. College of Veterinary Medicine, Oregon State University, Corvallis, OR.

Studies were designed using ^{3}H-TCDD to measure total levels of TCDD in splenic tissue, the distribution of TCDD within the splenic compartments, and possible changes which occur following antigen challenge. Female C57Bl/6 mice were dosed po with 5 µg/kg (625 µCi/kg) [1,6-^{3}H]-TCDD. Two days after dosing, one group of mice was injected ip with SRBC while a second group served as non-sensitized controls. Distribution of TCDD was determined in intact spleen, splenocytes, splenic capsule and media associated with processing, as well as liver, fat, thymus and adrenals. The dose on day 2 was distributed 16% to liver, 5% to fat, 2.4% to adrenals and <1% to spleen and thymus. Of TCDD distributed to the spleen, 50% was associated with capsule and media wash. The amount of TCDD in whole spleen was 32.8 pg two days after dosing; the level associated with isolated splenocytes was 0.6 pg per 1×10^7 cells. On day 7, TCDD levels were 28.3 pg per spleen and 0.2 pg per 1×10^7 cells. TCDD levels in SRBC sensitized mice were similar to naive mice. Supported by NIEHS grants ES00040 and ES03966.

637 EVALUATION OF ACUTE IMMUNOTOXICITY OF ALACHLOR IN MALE F344/N RATS. GM Henningsen, RE Biagini, BA MacKenzie, WT Sanderson, SK Robertson and ES Baumgardner. NIOSH, DBBS/ABB and DSHEFS/IWSB, Cincinnati, OH.

Alachlor (2-chloro-2',6'-diethyl-N-[methoxymethyl] acetanilide) is one of the most commonly used herbicides in the United States for pre-emergence control of broadleaf weeds and grass. The EPA classifies alachlor as a suspected human carcinogen due to sufficient evidence of cancer in exposed laboratory animals. Epidemiological evidence of carcinogenicity and data on potential immunotoxic effects of alachlor in animal models do not exist. Since chemical-induced immune dysfunction has been associated with increased cancers and/or infectious diseases in laboratory animals, the potential immunotoxicity of alachlor was studied with a multiple immunoassay model in 9-week old male F344/N rats. Evaluations were made of humoral immunity, cell-mediated immunity, natural killer cell activity, and hematologic and immunopathologic effects. Groups of rats (9-12 per group) were injected (ip) on days -1, 6 and 13 of the 14-day multiple-assay study. Group 1 (*vehicle control*) received 10 ml/kg propylene glycol; groups 2-4 (*test treatments*) received alachlor in 10 ml/kg propylene glycol at 1.25, 2.5 or 3.75 mg/kg; group 5 (*positive control*) received dexamethazone in 10ml/kg physiological saline (PS) at 1 mg/kg; and group 6 (*PS control*) received 10ml/kg PS. The results showed that alachlor had no statistically significant toxic effects (compared to the vehicle controls) for any of the immunologic, hematologic, or pathologic endpoints evaluated. Minor vehicle-related effects occurred. Doses used in this study were 25%, 50% and 75% of the acute (4-hr) LD100 dose of 5 mg/kg reported for Wistar rats receiving single ip injections (in propylene glycol). These findings suggest that alachlor has minimal potential to cause immunotoxicologic effects which could contribute to alachlor's carcinogenic effects in F344 rats.

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