1661 INORGANIC MERCURY SUPPRESSES CHEMOTACTIC ACTIVITY OF HUMAN POLYMORPHONUCLEAR LEUKOCYTES (PMNs). H-M Han, S H Kim, H J Kim and Y Sunwoo. Div. of Immunotoxicology, Dept. of Toxicology, National Institute of Safety Research, Seoul, Korea.

Upon invasive stimuli, PMNs adhere to capillary endothelial cells, migrate to the site of inflammation and phagocytize bacteria, thereby act as a first-line defense mechanism against foreign microorganisms. Mercury is one of wide-spread environmental pollutants and has been shown to alter host susceptibility to bacterial and viral challenges (Koller, Int. J. Immunopharmacol., **2:** 269-279, 1980). Based on these background informations, in the present study, the effect of $HgCl_2$ on the chemotactic activity of human peripheral PMNs was measured using the agarose plate method. A significant difference in chemotactic activity was noted between control and $HgCl_2$-treated cells. The moving distance in control cells was 1.04 $\pm$ 0.20 mm, which was significantly decreased after $HgCl_2$ treatment (1 uM $HgCl_2$: 0.77 $\pm$ 0.16 mm, $P<0.01$; 3 uM $HgCl_2$: 0.61 $\pm$ 0.06 mm, $P<0.01$; 5 uM $HgCl_2$: 0.15 $\pm$ 0.03 mm, $P<0.01$). Cell viability was not altered after $HgCl_2$ treatment (83 $\pm$ 5 % viability in control PMNs versus 81 $\pm$ 8 % viability in 5 uM $HgCl_2$-treated PMNs), suggesting that the reduced chemotactic activity after $HgCl_2$ treatment is not due to nonspecific cytotoxicity induced by $HgCl_2$. Our data suggest that $HgCl_2$-induced decrease in the chemotactic activity of PMNs may have some implications in depressed host susceptibility upon bacterial challenge after mercury exposure.

1662 EFFECT OF CADMIUM ON THE FUNCTION OF HUMAN POLYMORPHONUCLEAR LEUKOCYTES (PMNs). E Y Yoon, O Y Kim, Y Sunwoo, H J Kim and H-M Han. Div. of Immunotoxicology, Dept. of Toxicology, National Institute of Safety Research, Seoul, Korea.

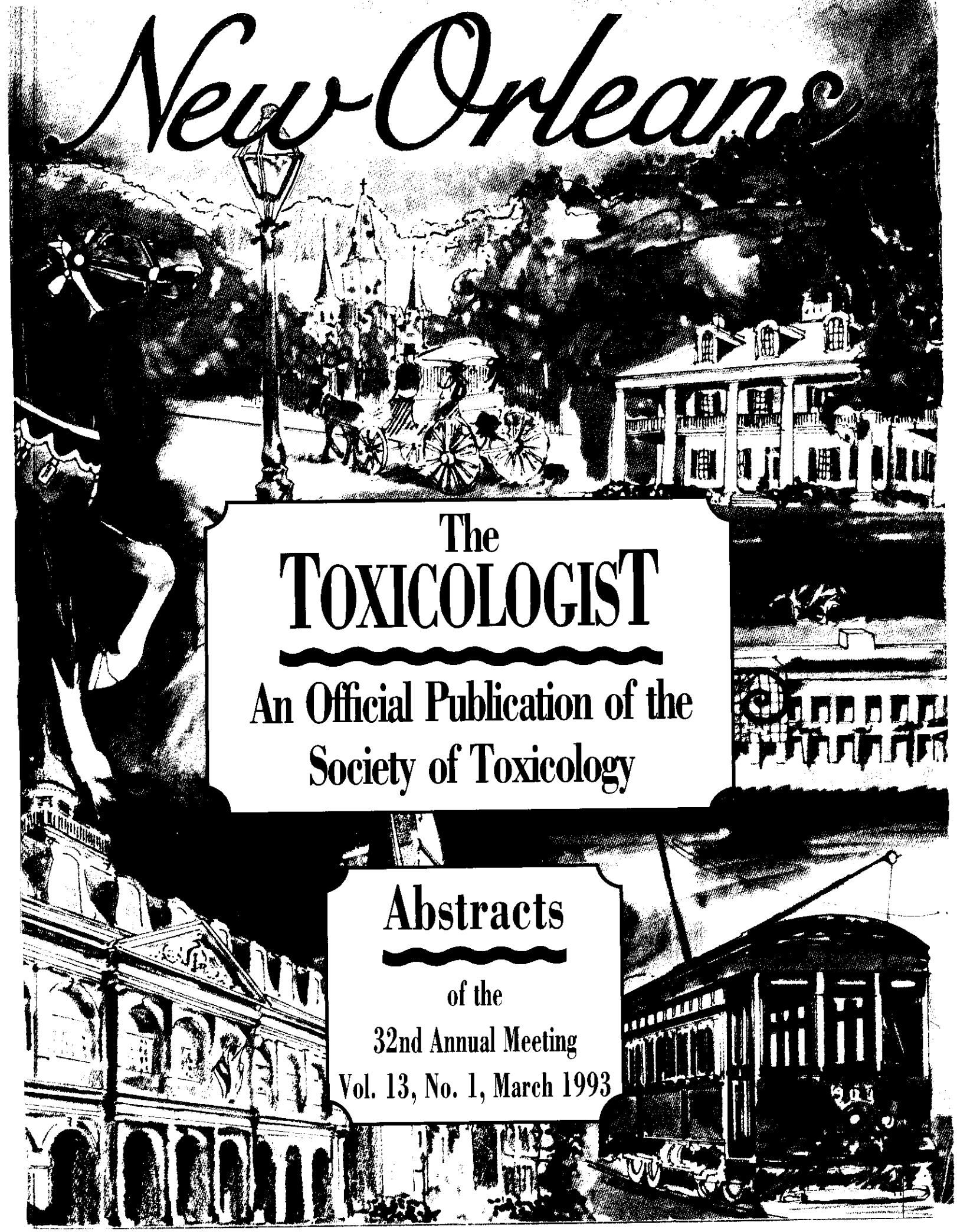
The effect of $CdCl_2$ on the function of human PMNs was investigated. PMNs were isolated from human peripheral blood with density centrifugation in Ficoll-hypaque. To measure the degree of adherence of PMNs to endothelial cells, PMNs (1 X 10^6 cells/ml) were incubated on a ring slide with various concentrations (10 uM - 100 uM) of $CdCl_2$ in a CO_2 incubator at 37°C. After 45 minutes, cells were washed with media two times and fixed with 3 % glutaraldehyde. The numbers of PMNs remaining on the ring slides of the control and $CdCl_2$-treated cells were counted. To measure the chemotactic activity of PMNs, the agarose plate method using formylmethylleucyl phenylalanine as a chemotactic agent was used. $CdCl_2$ significantly decreased glass adherence at all concentrations tested (10 uM $CdCl_2$: 67 $\pm$ 9 % ; 50 uM $CdCl_2$: 57 $\pm$ 5 % ; 100 uM $CdCl_2$: 39 $\pm$ 3 %, $P<0.01$ at all concentrations.) Similarly, a significant difference was also observed in chemotactic activity after $CdCl_2$ treatment (control: 0.82 $\pm$ 0.10 mm ; 10 uM $CdCl_2$: 0.68 $\pm$ 0.14 mm, $P<0.05$; 50 uM $CdCl_2$: 0.41 $\pm$ 0.14 mm, $P<0.01$; 100 uM $CdCl_2$: 0.29 $\pm$ 0.03 mm, $P<0.01$). These changes in the function of PMNs after $CdCl_2$ treatment were not associated with any changes in cell viability (control: 89 $\pm$ 5 % ; 100 uM $CdCl_2$: 85 $\pm$ 6 %). These observations suggest that cadmium-induced suppression of PMN functions may contribute to depressed host resistance upon bacterial challenge after cadmium exposure.

1663 OZONE-INDUCED ALTERATIONS IN MACROPHAGE INTERACTIONS WITH INTERFERON-γ. T McManus, M D Cohen, I T Zelikoff and R B Schlesinger. NYU Medical Center, Inst. of Environ. Medicine, Tuxedo, NY.

Exposure to ozone is known to induce alterations in host resistance to bacterial pathogens and in the general function of lung macrophages. The priming of macrophages (Mϕ) by immune system cytokines such as interferon-γ (IFNγ), IFNα, and tumor necrosis factor-α (TNFα) at the earliest stages of the immune response is crucial to both Mϕ antimicrobial activity and to the subsequent activation of other cells such as lymphocytes and neutrophils. Cultured mouse macrophage-like WEHI-3 cells were exposed *in vitro* to atmospheres of 1.0 or 0.4 ppm ozone (O_3), or air, for periods of 4-6 hr. The Mϕ were then assessed for their IFNγ binding capacity and for the levels of IFNγ-induced responses, i.e. reactive oxygen metabolite formation and enhanced phagocytic activity. The Mϕ exposed to 1 ppm O_3 had 60-65% decreases in radiolabelled-IFNγ binding as compared with air-treated cells; 0.4 ppm O_3 treatment had no significant effect on binding. When the 1 ppm O_3-treated cells were incubated with IFNγ (100 U/ml) for 48 hr, cells produced 79% less superoxide anion radical as compared with IFNγ-stimulated control cells; similar changes in hydrogen peroxide formation were also observed. While control WEHI-3 cells treated with IFNγ displayed increases in their phagocytic activity (increased 35-40% compared with non-stimulated controls), no increases in activity in IFN-stimulated 1 ppm- and 0.4 ppm O_3-treated Mϕ were observed; phagocytic activity actually decreased by 23 and 3%, respectively. These results demonstrate that *in vitro* exposure to ozone can modulate Mϕ functions by affecting their interactions with a major early stage immunopotentiating agent, interferon-γ.

1664 Suppression of Hepatic and Splenic Phagocytosis in Female B6C3F1 Mice Implanted with Morphine Sulfate Pellets. David G. LeVier, Ronnetta D. Brown, J. Ann McCay, Bruce Fuchs, Louis Harris and Albert E. Munson, Pharmacology and Toxicology. Medical College of Virginia/VCU. Richmond, VA.

Morphine sulfate has previously been shown to produce a dose dependent decrease in hepatic phagocytosis. This study was undertaken to determine the time course of suppression of hepatic and splenic phagocytosis following subcutaneous implantation of morphine sulfate pellets. Mice were implanted with either 75 mg morphine sulfate or placebo pellets. The uptake of ^{51}Cr-sRBC by the liver and spleen was taken as an index of phagocytosis. The results indicate that maximum suppression of hepatic phagocytosis by 67% occurred 18 hr following implantation of 75 mg morphine sulfate. Hepatic phagocytic suppression returned to control levels within 48 hours of implantation. The initial suppression of splenic phagocytosis (by 30%) was similar to that of the liver (max. at 12 hr). However, splenic phagocytosis returned towards placebo levels over a longer period of time reaching control following 4 days of implantation. The opiate receptor antagonist, naltrexone (30 mg pellet), completely blocked the ability of morphine to suppress either hepatic or splenic phagocytosis. Corticosterone is known to increase in parallel with plasma morphine levels presumably through a hypothalamic-pituitary-adrenal axis. The glucocorticoid receptor antagonist RU 486 was used to block corticosterone and to investigate its possible role in morphine sulfate induced suppression of phagocytosis. RU 486 (200 mg/Kg) completely blocked morphine sulfate's ability to suppress splenic phagocytosis. In contrast, RU 486 partially blocked the morophine induced suppression of hepatic phagocytosis. This initial study suggests that morphine sulfate suppresses hepatic phagocytosis pimarily through an opiate receptor mediated mechanism, while splenic phagocytosis is suppressed secondarily through a glucocorticoid receptor mechanism. Supported in part by NIEHS Contract ES 05288, NIEHS Toxicology Training Grant ES 07087, NIDA Contract 271-90-7200 and NIMH MH45931 and DAO7292.



The TOXICOLOGIST

An Official Publication of the Society of Toxicology

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of the

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Vol. 13, No. 1, March 1993

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