1665 VANADIUM-INDUCED ALTERATIONS IN MACROPHAGE RESPONSES TO BIOLOGICAL RESPONSE MODIFIERS IN VITRO. M D Cohen, R B Schlesinger, and I T Zelikoff. NYU Medical Center, Inst. of Environ. Medicine, Tuxedo, NY

Previous *in vivo* studies have demonstrated that vanadium impairs host resistance overall, and the antimicrobial activity and function of several intracellular enzymes of macrophages (Mϕ). To determine if the observed immunomodulation might be a result of altered interactions of Mϕ with biological response modifiers, the release/activity of two major cytokines and the production of reactive oxygen intermediates after stimulation of vanadium-treated cultured mouse WEHI-3 Mϕ with lipopolysaccharide (LPS) or interferon-γ (IFNγ) were assessed. In addition, the binding affinity and numbers of IFNγ surface receptors were quantitated. Results demonstrate that the levels and activities of LPS-induced interleukin-1 and tumor necrosis factor-α were decreased as vanadium concentrations increased. After treatment of cells with IFNγ for 48 hr, hydrogen peroxide (H_2O_2) formation in metal-free Mϕ increased ≈ 40% while vanadium-treated cells had decreased H_2O_2 formation; similar effects upon superoxide anion formation were also observed. Binding studies indicated that the vanadium-treated Mϕ had ≈ 50% fewer IFNγ surface receptors, but the binding affinity of the remaining receptors were 100-400 times greater than those on control Mϕ. This study shows that *in vitro* exposure to vanadium can alter Mϕ-mediated immune responses by modifying their interactions with bioactivating agents. This inability to bind and respond to these external signals could contribute to the overall diminution of host immunocompetence observed *in vivo*.

1666 PRODUCTION OF REACTIVE OXYGEN METABOLITES IN HUMAN LEUCOCYTES BY LINOLEIC AND OLEIC ACID ANILIDES AND THEIR MODIFICATION BY FMLP AND PMA. K Heiskanen, M Tuomala and K Savolainen. Natl Publ Hlth Inst, Dept of Toxicol, P.O.B 95, SF-70701 Kuopio, FINLAND

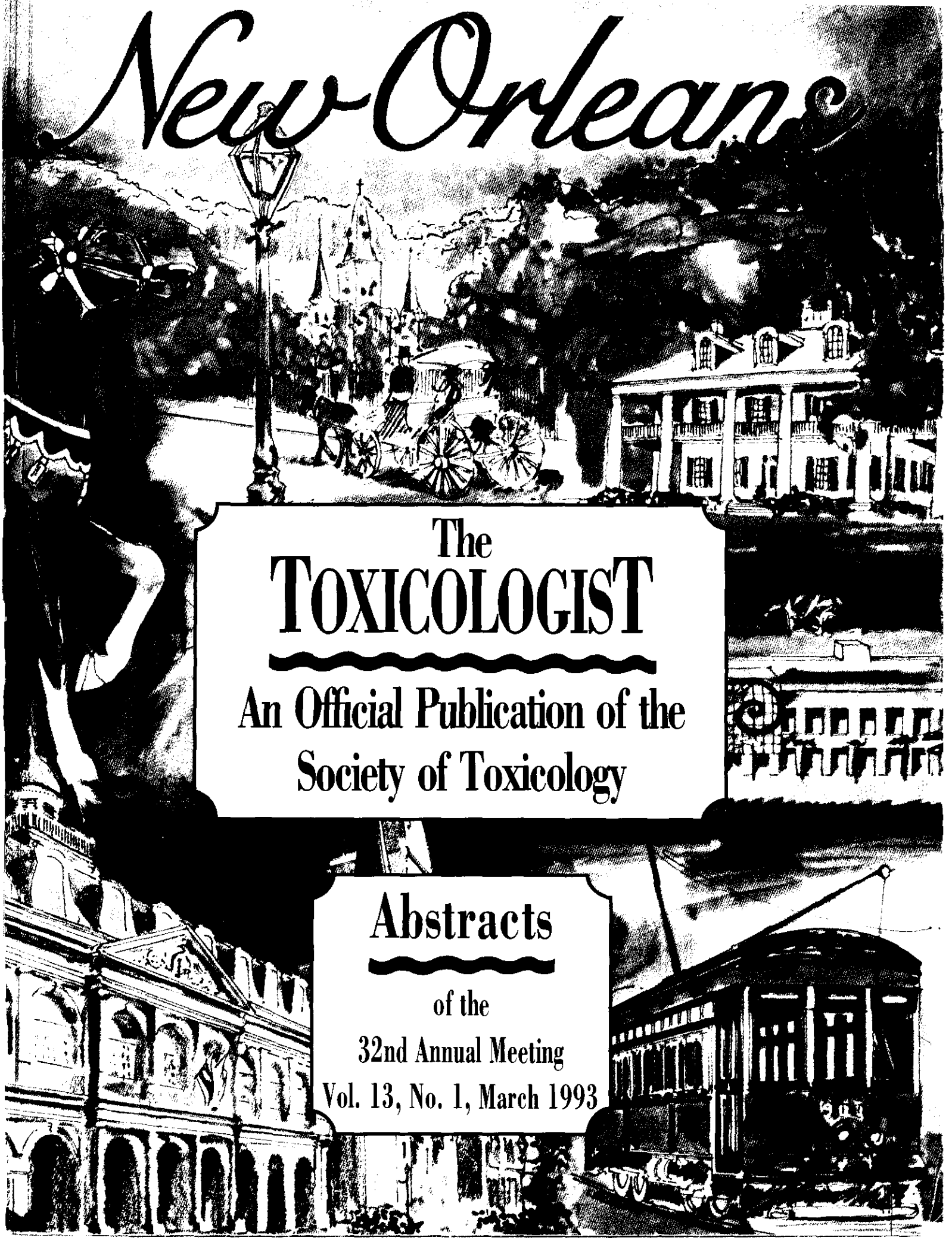
Human polymorphonuclear leucocytes (PMNL) were exposed to linoleic (LAA) or oleic acid anilide (OAA), two major contaminants in food oils that caused the Toxic Oil Syndrome (TOS) epidemic 1981 in Spain. The production of reactive oxygen metabolites (ROM) was measured with a luminometer. Also, interactions of fatty acid anilides (LAA,OAA) with a chemotactic peptide (FMLP) and phorbol myristate acetate (PMA) were studied. Both LAA and OAA induced ROM production in a dose dependent manner. This response was partially inhibited by a specific protein kinase C inhibitor Ro 31-7549. The interaction of LAA and OAA with FMLP was additive. On the contrary both LAA and OAA inhibited the PMA induced ROM production. Moreover, the peak of ROM production by PMNL after PMA exposure was shifted from 11 to 40 min after the maximal dose of either LAA or OAA. These results suggest that fatty acid anilides stimulate ROM production in PMNL. Moreover, modifications of FMLP- and PMA-induced ROM production by LAA and OAA and partial inhibition of LAA- and OAA-induced ROM production by protein kinase C inhibitor, provide evidence that protein kinase C is at least partially involved in alterations in PMNL functions in TOS. Supported by the Fondo Investigacion Sanitaria from Spain and the World Health Organization.

1667 **INTERACTIONS OF SODIUM FLUORIDE (NaF) WITH fMLP-, PMA-, QUARTZ- AND CHRYSOTILE ON THE PRODUCTION OF REACTIVE OXYGEN METABOLITES IN HUMAN LEUKOCYTES. M Tuomala, J Naarala, and K Savolainen. Natl Publ Hlth Inst, Dept Toxicol, P.O.B. 95, SF-70701 Kuopio, FINLAND.**

Quartz, chrysotile, phorbol myristate acetate (PMA) and chemotactic peptide (fMLP) activate phagocytic cells with a consequent production of reactive oxygen metabolites (ROM) in human polymorphonuclear leukocytes (PMNL). NaF activates G-protein, stimulates PI turnover and causes an increase in $[Ca^{2+}]_i$. PMNL (5×10^5 cells/ml) were exposed to graded doses of NaF (1μM -10 mM) and then to 10 mM of NaF and then to combinations of NaF and fMLP (2×10^{-7} M), PMA (5×10^{-9} M), quartz (100μg/ml) or chrysotile (100 μg/ml). Chemiluminescence, induced by ROM production, was measured with a luminometer. NaF alone increased the production of ROM from 5 mV to 60 mV at the highest dose. The same dose of NaF increased fMLP-, quartz- and chrysotile-induced, but not PMA-induced, ROM production additively. The present results suggest that NaF alone increases ROM production, possibly via G-protein activation, and causes additive increases in ROM production in fMLP, PMA and quartz stimulated PMNL. The additivity of NaF-agonist interaction suggests that the increase of ROM production by NaF and different agonist is due to an interaction in the same cell signalling pathway. Supported by The Academy of Finland and The Finnish Work Environment Fund.

1668 **PROPANIL IMMUNOTOXICITY ON BONE MARROW STEM CELLS** G Blyer[a,b], K Landreth[a,b], S Theus[c], L Soderberg[c], J Gandy[c] and J Barnett[a]. [a]West Virginia U Sch. Medicine and [b]Mary Babb Randolph Cancer Ctr, Morgantown, WV, and [c]U. Arkansas for Med Sc, Little Rock, AR.

Propanil, a post-emergent herbicide, has differential immunotoxic effects on various functions and cells of peripheral lymphoid tissues. To determine whether this compound also affected production of lymphoid and myeloid cells, we undertook a study of propanil's effects on lymphoid and myeloid cells in the bone marrow. The ability of exogenous colony-stimulating factors to stimulate myeloid, B lymphoid and erthyroid colony formation (CFU) in bone marrow cells was determined 7 days after i.p. injection of propanil in corn oil. The ability of early stem cell progenitors, i.e., pluripotent and multipotent stem cells, to develop colonies in soft agar culture was significantly depressed in treated animals. Erythroid progenitors (BFU-E) and B cells (CFU-B) were also markedly depressed in treated animals. However, more differentiated macrophage (M-CFU) and granulocyte (G-CFU) progenitors were unaffected by propanil treatment. The effect of propanil on early hematopoietic progenitors indicates an immunotoxic effect on stem cells. The lack of an effect on later stage committed myeloid progenitors may be the result of a differential effect of the propanil or the interval from the time of agent administration to assay. Supported by NIH grant ES04875 and the Marconi Fellowship Program.



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Abstracts

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster/discussion, and poster sessions of the 32nd Annual Meeting of the Society of Toxicology, held at the New Orleans Convention Center, New Orleans, Louisiana, March 14-18, 1993.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 457.

The issue also contains a Keyword Index (by subject or chemical) to the titles of all the presentations, beginning on page 485.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology, and appear in numerical sequence, other than the symposia abstracts, which are collected in the front.

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