LPS-induced production of NO in a concentration-dependent manner at 48 and 72 hr after exposure. The data suggest that metallic oxides may disrupt NO production in macrophages. This effect may contribute to the pathophysiology of various diseases by compromising host defense mechanisms and cell signaling.

1526 CADMIUM PERTURBS CALCIUM HOMEOSTASIS IN RAT OSTEOSARCOMA (ROS 17/2.8) CELLS

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The mechanism of the toxic effects of Cd^{2+} on normal bone growth and bone cell function is not completely understood at this time. However, Cd^{2+} does perturb the cytosolic free Ca^{2+} concentration and directly activate protein kinase C (PKC) in ROS 17/2.8 cells. PKC is activated by Ca^{2+} and mediates Ca^{2+} metabolism. Therefore, cadmium may cause changes in steady state Ca^{2+} metabolism which is normally precisely controlled. Such changes would have implications for cell functions mediated by the Ca^{2+} messenger system. The purpose of this study was to characterize the effect of Cd^{2+} on Ca^{2+} metabolism in ROS 17/2.8 cells. Cells were labeled with ^{45} Ca (1.87 mM Ca) for 20 hr in the presence of 0.01 μM, 0.1 μM, or 1.0 μM Cd^{2+}. Following an EGTA rinse, kinetic parameters were determined from ^{45}Ca efflux curves. Three kinetic compartments described the intracellular metabolism of ^{45}Ca. Cadmium caused a large (approximately 10X) dose-dependent increase in Ca^{2+} flux across the plasma membrane and an accompanying decrease in the most rapidly exchanging intracellular Ca^{2+} compartment (S_1). This change indicates an increased efflux of calcium from ROS 17/2.8 cells. However, there was no change in total cell Ca^{2+} because flux between S1 and the intermediate Ca^{2+} compartment (S_2) was also increased and S_2 increased significantly. This data suggest that Cd^{2+} is perturbing steady state calcium metabolism by increasing Ca^{2+} efflux from the cell and by causing redistribution of Ca^{2+} within the cell. This work is supported by NIH grant ES06087.

1527 INTERACTIONS OF NICKEL(II) WITH HISTONES. ENHANCEMENT OF 2'-DEOXYGUANOSINE OXIDATION BY Ni(II) COMPLEXES WITH CH_3CO-CYSALA-ILE-HIS-NH_2 (CAIH), A MODEL OF THE BINDING SITE OF HISTONE H3

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The mechanisms of carcinogenesis by nickel, a human carcinogen, may include mediation of promutagenic oxidative damage through Ni(II) binding to chromatin components, including histone H3 [Bal, W. et al., *Chem. Res. Toxicol.* 8: 683-692, 1995]. To further test this hypothesis, studies of 2'-deoxyguanosine (dG) oxidation by H_2O_2 in the presence of CAIH and/or Ni(II) have been carried out in 100 mM phosphate buffer, pH 7.4 at 37°C. The dimeric CAIH oxidation product, CAIH disulfide, and its weak, octahedral Ni(II) complex, rather than the monomeric CAIH and its strong, square planar Ni(II) complex were found to be major catalysts of 8-oxo-dG formation. The complexes were much more active than the ligands alone, especially at submillimolar H_2O_2. The reaction was found not to involve detectable amounts of free radicals or Ni(III). These results support the hypothesis and also indicate that molecular mechanisms of nickel carcinogenesis may involve oxidative damage processes catalyzed by weak Ni(II)-peptide disulfide complexes.

1528 ELIMINATION OF INGESTED ALUMINUM IN THE BILE OF UNANESTHESIZED RATS

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We evaluated the importance of bile as an excretory route for orally-administered aluminum. Bile ducts in 30 male Sprague-Dawley rats were cannulated to allow both bile collection and reinfusion of bile acids. Five days following surgery, rats were given a single oral dose of aluminum (0, 0.2, 0.4, or 0.8 mmol) as aluminum lactate in 1 ml of 16% citrate by gavage. Bile was collected 1–7 hr after dosing from conscious rats. Biliary aluminum excretion was highest 1–2 hr after dosing which probably reflected first pass hepatic elimination of aluminum from the portal circulation. Rats dosed with 0.2, 0.4, or 0.8 mmol aluminum excreted significantly higher total amounts of aluminum in bile (2.73 ± 0.43 μg; 1.99 ± 0.29 μg; and 2.80 ± 0.93 μg, respectively) than did the control rats (0.34 ± 0.03 μg). Biliary aluminum excretion did not differ among animals given aluminum suggesting that this process was saturated at these doses. Rats dosed with 0.8 mmol aluminum retained significantly greater amounts of aluminum in serum, liver, spleen, and kidney than those given 0.2 or 0.4 mmols. This suggests that physiological mechanisms that protect against soft tissue aluminum accumulation and retention of aluminum in plasma were overwhelmed in animals given the 0.8 mmol dose. Supported by Coll. of Agriculture & Life Sci. Project 2623 and NIH DK41116.

1529 OXIDANT-PRODUCING ACTIVITY OF FE(II) IN TISSUE CULTURE MEDIA

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Ferrous iron (Fe^{2+}) is able to produce oxidants and may play an important role in diverse pathologies such as tissue aging and cancer. Using electron spin resonance and spin trapping technique, we investigated the role of cell culture medium compositions, and pH, on the formation of oxidants produced by Fe^{2+} and O_2. We found that oxidant formation in distilled water increased proportional to the concentrations of Fe^{2+} from 50 μM to 5 mM, and then sharply decreased to zero as the concentration of Fe^{2+} reached 50 mM. This phenomena was observed in several tested cell culture media, and oxidant-producing activity for a given concentration of Fe^{2+} was in an increasing order as follows: complete α-MEM < bicarbonate buffer < distilled water < 10 mM of PBS < 50 mM of PBS < 250 mM of PBS. The concentration of Fe^{2+} which gave the maximal oxidant-producing activity was shifted higher in proportion to the concentration of PBS, i.e. from 5 mM of Fe^{2+} to 50 mM when PBS was increased from 10 mM to 250 mM. The disappearance of free radical adducts at higher concentrations of Fe^{2+} is probably due to the low pH and low oxygen diffusion in the tested media, which can significantly slow down the oxidative reactions. Our studies strongly indicate that pH of the cell culture medium plays a determinant role in Fe^{2+}-catalyzed oxidant formation, and should be taken into account when testing Fe^{2+} compounds in biological systems. This work was supported by NIOSH OH03253.

1530 GADOLINIUM CHLORIDE-INDUCED SITE-SPECIFIC MINERALIZATION OF THE STOMACH IN RATS

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Studies have identified interstitial, fundic gastric mineralization in rats exposed intravenously to $GdCl_3$. To determine the relationship of gastric mineralization to changes in circulating calcium and phosphorus levels, groups of 5 male Sprague Dawley rats were injected intravenously with 0.07 mmol/kg $GdCl_3$ or saline and euthanized on Day 3. Ten of the rats exposed to saline or $GdCl_3$ were fasted 16 hr prior to dosing to determine the effects of fasting on ensuing histomorphologic changes. The stomachs were fixed by injection of neutral-buffered formalin into the stomach lumen and the entire stomach of each rat was embedded in paraffin, sagittally sectioned at 5 micrometers and stained with H & E and Von Kossa's stain. This procedure allowed for the examination of the entire contiguous stomach mucosa. H & E stained sections of stomachs from 10/10 rats exposed to $GdCl_3$ were characterized by a linear band of patchy, minimal-to-mild degeneration and minimal necrosis of the cells lining the upper one-third of the neck of the gastric glands. Von Kossa stained sections revealed a narrow, linear band of interstitial mineral deposited in this same region. Mineral deposition was frequently present in areas that lacked clear evidence of cellular degeneration or necrosis and was restricted to the parietal cell-rich, fundic portion of the glandular stomach; the pyloric area, which lacks parietal cells, was devoid of mineralization. Fasting of rats for 16 hr prior to dosing did not alter the incidence or severity of the observed lesions. X-ray microanalysis of the mineralized band in previous studies indicated that such gastric mineral deposits contained mostly Ca, P and some Gd. Total plasma calcium and phosphorus levels in earlier studies were increased but ionized calcium levels in this study were unchanged. The mechanism for Gd-induced mineralization of the gastric interstitium in the vicinity of parietal cells is unknown but it is speculated to be due to local perturbation of Ca-dependent parietal cell function in conjunction with elevated total plasma calcium levels.

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 35th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 10-14, 1996.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 351.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 375.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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