P21 was markedly induced in cells treated with BaP, while CDK1 expression was significantly reduced by 50%. In contrast, P53 and cyclin B levels were unaffected by BaP treatment. This pattern of change in G2 proteins is consistent with G2M arrest. Morphologic evaluation of cells using hematoxylin and eosin staining found no increase in the number of apoptotic cells following 10 uM BaP treatment for 2, 3, 4 and 5 day periods in the presence of FBS. DNA fragmentation analysis was performed using agarose gel electrophoresis. No DNA laddering was observed in control or BaP-treated cells grown in the presence of 10% FBS. In comparison, serum deprivation for 4 days induced DNA laddering in control JEG-3cells, and no effect of BaP was observed under this condition. In summary, data indicate that the mechanism of inhibition of proliferation seen in JEG-3 cells treated with BaP involves cell cycle arrest at G2/M, not apoptosis. (Supported by NIEHS Superfund grant 07375)

1815 SELECTIVE ACCUMULATION OF 8-HYDROXY-2'-DEOXYGUANOSINE IN THE LUNG FOLLOWING ACUTE TREATMENT WITH BENZO(A)PYRENE.

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The lung has been shown to be a target organ for the effects of Benzo[a]pyrene (B[a]P). 8-hydroxy-2'-deoxyguanosine (oxo8dG) is a mutagenic oxidized base formed in DNA during the metabolism of B[a]P by the peroxidase and prostaglandin H synthetase systems. The objective of this study was to determine the capacity to cleave oxo8dG in the lung, liver, and kidney by measuring the activity of 8-oxoguanosine DNA glycosylase (Ogg1),and whether exposure to B[a]P had an effect in this DNA repair system. Male Sprague-Dawley rats were administered 20 mg/kg B[a]P i.p., 2 times/day for 5 days. A 26% decrease in the capacity to remove oxo8dG was observed in lung tissue at 72 hours and recovered 20% above control values at 120 hours. The capacity of the liver and kidney remained at baseline for all time points analyzed. A 7-fold increase in oxo8dG was observed in the lung at 72 hours and returned to basal levels by 120 hours. A statistically significant increase of Ogg1 protein levels was observed at 120 hours. Oxo8dG and Ogg1 protein levels were not significantly changed in the liver and kidney. This study demonstrates that organ-specific differences exist in the accumulation of oxo8dG and the capacity to remove this mutagenic base following i.p. treatment with B[a]P. (Supported in part by Veteran's Affairs Merit Review Grant and NIOSH Grant 416005-01)

1816 INTRANASAL INSTILLATION OF BENZO(A)PYRENE IN RATS: LOCALIZATION AND TRANSPORT IN THE OLFACTORY SYSTEM.

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Inhalation of environmental pollutants, such as polycyclic aromatic hydrocarbons (PAHs), may result in high local exposure of the olfactory mucosa. This tissue contains high levels of cytochrome P450-enzymes with a capacity to bioactivate xenobiotics. In addition it has been shown that materials which come into contact with the olfactory mucosa may be translocated to the brain *via* axonal transport in the olfactory neurons. Benzo(a)pyrene (BaP) is a prototypic PAH carcinogen. In the present study tritiated BaP was instilled intranasally in rats and the disposition of labelled material in the olfactory mucosa and olfactory bulbs was examined by autoradiography and beta-spectrometry. The results showed formation of high levels of tissue-bound metabolites in Bowman's glands and a weaker labelling of the olfactory epithelium. Our data also showed uptake of labelled material in the olfactory bulbs. We conclude that application of BaP on the olfactory mucosa results in a cell-specific bioactivation and a translocation of BaP and/or its metabolites to the olfactory bulbs. Several chemicals, including BaP, induce nasal tumours in experimental animals. The toxicological implications of the uptake in the olfactory bulbs are not known.

1817 7H-BENZO(C)FLUORENE:DNA ADDUCT FORMATION IN MCF7 AND HEPG2 CELLS.

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7H-Benzo[c]fluorene (B[c]F) has been recently identified as a major DNA adduct-forming component of coal tar in lungs of mice fed a coal tar containing diet. It appears from these results that B[c]F may have the potential to induce lung tumors in mice. The purpose of this study was to determine if human cells have the ability to form B[c]F:DNA adducts as detected in mouse lung. MCF7 (human breast cancer) and HepG2 (hepatoma) cells were treated with increasing concentrations (0.2 - 10 µg/ml) of B[c]F for 20 hours and adduct formation was evaluated using 32P-post-labeling. Two adducts were detected in both cell lines. One of these adducts corresponded to that observed in the lungs of mice treated with pure B[c]F. The ratio of the two adducts varied between the two cell lines, suggesting that B[c]F metabolism by a different spectrum of enzymes influences the level of certain metabolites. Adduct level increased in a dose-dependent manner. However, total B[c]F adduct levels were considerably lower (~500-fold) than the levels observed with equimolar concentrations of benzo[a]pyrene. These results clearly demonstrate that MCF7 and HepG2 have the capacity to metabolically activate B[c]F to derivatives that covalently modify DNA. The similarities in adduct patterns also suggest that the activation pathway is similar in human cells and in mouse lung. This research was supported by funds from EPRI.

1818 EVALUATION OF SKIN AND LUNG DNA ADDUCTS FOLLOWING THE TOPICAL ADMINSTRATION OF BENZO(C)FLUORENE, BENZO(A)PYRENE OR COAL TAR.

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Recent studies have demonstrated that benzo[c]fluorene (B[c]F) is capable of forming DNA adducts in mouse lung following oral administration. The purpose of this study was to compare the DNA adducting properties of B[c]F, benzo[a]pyrene (B[a]P), and coal tar in mouse skin and lung tissue following topical administration. B[c]F or B[a]P was administered to shaved backs of CD1 mice at doses of 0.5 µmmol, 1.0 µmmol and 4.0 µmmol. Coal tar was administered to mice at levels comparable to 0.5 µmmol and 1.0 µmmol B[a]P. Mice were sacrificed after 24 h and DNA adduct levels were determined using ^{32}P-postlabeling analysis. B[a]P:DNA adduct levels in mouse skin were 450 to 1100 times higher than the adduct levels observed with an equimolar dose of B[c]F. In contrast, adduct formation in lung tissue following B[a]P topical administration was only 8 to 15 times higher than the levels observed with B[c]F. The low level of adducts observed with B[c]F in mouse skin suggests that B[c]F has a much lower rate of metabolic activation when compared with B[a]P. These results are consistent with previous studies that have demonstrate that B[c]F is not a tumor initiator on mouse skin. However, in the case of the topical administration of coal tar, the level of B[a]P DNA adducts in mouse skin was only 1.8 to 2.7 times higher than the adduct formed with B[c]F. In addition, B[c]F adduct levels in lung of mice treated topically with coal tar were 2 times higher than the adduct levels observed with B[a]P. These results clearly demonstrate that both B[c]F and B[a]P exhibit significantly different DNA adducting properties when administered to mice as pure compounds or when contained within a complex mixture such as coal tar. This research was supported by funds from EPRI.

1819 REPRODUCTION TOXICITY STUDIES OF DBA IN DRINKING WATER OF RATS.

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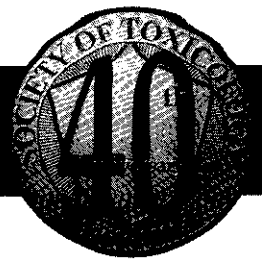
Dibromoacetic Acid (DBA) tested in Crl:CD®(SD)IGS BR VAF/Plus® rats at 8467 - 424,500 X infant dose [PK, range-finding (RF)]. Sponsor: Chlorine Chemistry Council's Research Foundation for Health and Environmental Effects. Continuous drinking water provided at concentrations of 0 (Carrier), 125, 250, 50, 1000 ppm (RF) or 0 (Carrier), 50, 250 and 650 ppm [multigen (MG)]. Mg/kg/day doses calculated ≤ weekly. 10/sex + 6 male (M)/15 female (F) satellite rats/group (RF); 30/sex/group (MG). DBA provided 14 (RF) or 70 days (MG) premating to 70 (M) or 29 days postpartum (PP), F; F2 *in utero* + milk and drinking water (ppm = F1) to 29 days PP, 1 week (W) postweaning (PW) (RF) or after F3 pups at day 21 PP (MG). Viability, signs, weights, feed and water, cycling, gestation, fertility, implants, litter sizes, sex ratios, morphology, weights and sex noted. Culled (8, 4/sex) PP 4 (MG only). PP 29, 2/sex/litter continued (1 W, RF; F3 offspring, MG). Target/reproductive organ weights, landmarks, sex maturity and histopath, [(testes, epididymides (MG)]. Highest mg/kg/day consumed F2 W1 PW. No quantifiable levels of DBA in PK studies. 1000 ppm (RF) too toxic: severe ↓ water, feed and weight gains; pup deaths (after day 15 PP, F1 ↓ weight, 125, 250, 500, 1000 ppm; PW, 250, 500, 1000 ppm M, 500, 100 ppm F). In MG, ↓ water/feed consumption, 50, 250, 650 ppm. Absolute + relative (body weight) weights of adrenals ↓ F,



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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 40th Annual Meeting of the Society of Toxicology, held at the Moscone Convention Center, San Francisco, California, March 25–29, 2001.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 451.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 479.

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