Results: Chronic respiratory effects identified in this review included obstructive and restrictive lung disease, RADS, bronchiolitis, bronchitis, and bronchiectasis. Such effects were not consistently observed among individuals with apparently similar exposures. All of the exposures with reported chronic respiratory effects were of sufficient severity to require extended hospitalization and were associated with severe upper respiratory effects.
Conclusion: A specific acute exposure level that may result in chronic respiratory effects could not be defined from the reviewed studies. However, it is clear that such exposures result in objective clinical signs of upper and lower airway injury, and require extensive hospitalization. This case study provides "real-world" support for the protective nature of the upper respiratory tract in water soluble irritant gas exposures.

1087 LUNG RESPONSE TO COARSE PM: BIOASSAY IN MICE.

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It has been hypothesized that particulate matter (PM) elicits inflammatory and toxic responses in the lung specific to its constituents, which can vary by region, time, and particle size. To identify the mechanism of toxicity in PM collected from a rural area in the San Joaquin Valley of Central California, we studied coarse particles of 2.5 μm - 10 μm diameter (PM2.5-PM10). Potential pro-inflammatory and toxic effects of PM2.5-PM10 in the lung were investigated using intratracheally instilled mice. We determined total and differential cell profiles and inflammatory chemokines in lung lavage fluid, and biomarkers of toxicity resulting from coarse PM exposure. Responses of the mice were readily observed with doses of 25-50 μg of PM. Changes in pro-inflammatory cellular profiles and chemokines showed both dose and time response; peak responses were observed 24 hours after PM instillation, with recovery as early as 48 hours. Furthermore, birefringent particle constituents were found within macrophages and neutrophils recovered from lung lavage fluid of PM treated animals. The presence of birefringent particles was increased with exposure to the insoluble fraction of PM. Our data suggest that pro-inflammatory effects observed from coarse PM collected during the summer months from California's hot and dry Central Valley are driven largely by the insoluble components of the PM mixture, and are not caused by endotoxin.

1088 OZONE EXPOSURE EXACERBATES EOSINOPHILIC AND EPITHELIAL CELL RESPONSES IN SINUS AND NASOLACRIMAL DUCT AIRWAYS IN ALLERGIC RATS.

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Exposure to ozone, the primary oxidant in photochemical smog, enhances mucous and inflammatory cell responses during allergic airways disease in humans and in laboratory animals. We developed a rodent model of allergic sinusitis to test the hypothesis that ozone would exacerbate allergen-induced inflammatory responses in sinus airways. Ovalbumin (OVA) -sensitized rats were first exposed to 0 or 1 ppm ozone (8h/day) and then immediately challenged intranasally with 0 or 0.5% OVA (in saline) for two consecutive days (Days 1 & 2; ozone coexposure), and sacrificed on Day 3. A second group of rats were also challenged on Days 1 & 2, but then exposed to ozone on Days 4 & 5 (ozone exposure post-challenge) and sacrificed on Day 6. Nasal airways were collected and processed for histological and morphometric analysis of intraepithelial mucosubstances (IM) and eosinophil cell density. In co-exposed animals, OVA challenge caused dramatic (30-fold) increase in mucosal eosinophil numbers in the nasal septum, maxillary sinus and the nasolacrimal duct that was not affected by ozone coexposure. In post-challenge studies, OVA caused eosinophilic infiltration in sinus and septum, but not the nasolacrimal duct. Ozone exposure post-challenge enhanced eosinophil recruitment into the mucosa of the sinus (1.3-fold) nasolacrimal duct (3.5-fold) and septum (2.3-fold). Furthermore exposure to ozone post OVA challenge caused increased IM in sinus airways (6-12 fold) and septum (1.2-fold) compared to OVA challenged animals exposed to filtered air. These results demonstrate unique effects of ozone to enhance pre-existing allergic inflammation and mucous responses in disparate nasal airways, as well as suggest a role for ozone in the development and progression of clinical rhinitis, sinusitis and rhinoconjuctivitis. NIH:NCCAM PO1-AT002620

1089 EFFECTS OF *IN VITRO* EXPOSURE OF HUMAN RESPIRATORY EPITHELIAL CELLS TO FORMALDEHYDE.

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Formaldehyde is the most abundant carbonyl in ambient air. Formaldehyde is ubiquitous in the environment because it is a by-product of combustion and is produced as an atmospheric oxidation product of nearly all VOCs. It is commonly used in the medical and health fields, in the manufacturing of building materials, and is present in substantial quantities in occupational and home environments. People are likely exposed to low levels of formaldehyde on a daily basis, it has therefore been suggested that formaldehyde exposure may be linked to increased hospital admissions and increased prevalence of inflammatory diseases. However, the effects of formaldehyde on specific inflammatory mediator production is largely unknown. To evaluate the potential inflammatory effects of formaldehyde, cultured human alveolar lung cells (A549) were exposed to realistic ambient and industrial concentrations of formaldehyde in a series of increasing doses of gaseous formaldehyde, using permeation tube, or large chamber, air mixtures.
Formaldehyde concentrations were measured continuously using a permeable membrane sampler, and detected with fluorometry using an automated Hantzsch derivative reaction (Dasgupta technique). The concentrations in the 3-hr exposures were approximately 55 ppb, 140 ppb, 220 ppb, 390 ppb, and 980 ppb. Inflammation was assessed by measuring IL-6 and IL-8 and cytotoxicity was determined via detection of lactate dehydrogenase (LDH) in cell culture supernatants.
At the 55 to 220 ppb formaldehyde exposure level, there were virtually no differences between exposed cells and control cells for all endpoints. Cells exposed to 390 and 980 ppb, however, showed increases in LDH, IL-6 and IL-8 over controls. The initial data analysis shows that a step-wise response from 220 to 390 to 980 ppb was observed, indicative of a dose-response. Taken together, our preliminary results indicate that formaldehyde induces cytotoxicity and inflammatory mediator production in a dose-dependent manner.

1090 NASAL UPTAKE OF DIACETYL AND BUTYRIC ACID VAPORS.

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Occupational exposure to high levels of butter flavoring vapors (BFV) has been associated with the development of bronchiolitis obliterans. BFV contain a variety of compounds, the most prevalent being diacetyl (2,3 butanedione). Inhalation exposure of rats to diacetyl or BFV results in nasal and/or lower airway necrosis and inflammation. Diacetyl is detoxified by dicarbonyl reductase, an enzyme inhibited by butyric acid. Butyric acid is also a component of BFV raising the possibility of an inhalation dosimetric interaction. The current study was aimed at examining this possibility. Towards this end, upper respiratory tract (URT) uptake of diacetyl alone and in combination with butyric acid vapor was measured in the surgically isolated URT of the male Sprague-Dawley rat at constant velocity inspiratory flow rates of 100, 200 or 400 ml/min and exposure concentrations of 100 or 300 ppm. In vitro metabolism kinetics of diacetyl in nasal mucosal homogenates were also assessed. Diacetyl was metabolized in an NADPH-dependent manner in nasal respiratory and olfactory mucosal homogenates. The total activity in olfactory (1.8 μmol/min) exceeded that in respiratory mucosa (0.3 μmol/min). Both high and low affinity pathways were observed in both tissues. Diacetyl was scrubbed with moderately high efficiency in the URT, with uptake efficiencies of 30-75% being observed depending upon the inspiratory flow rate. Although butyric acid was without effect on URT uptake of a nonmetabolized vapor, diacetyl uptake efficiencies were significantly lower in animals exposed to both 100 ppm diacetyl and 30 ppm butyric acid (36% vs 31%, p=0.02). The selective inhibition of diacetyl uptake provides evidence that diacetyl uptake was dependent on a butyric acid sensitive metabolic pathway, e.g. dicarbonyl reductase. These results suggest that the detoxication enzyme dicarbonyl reductase may be inhibited by the butyric acid vapor present in BFV leading to altered inhalation dosimetry and, perhaps, to an enhancement of diacetyl airway toxicity due to the inhibition of detoxication.
This research supported by NIH R03ES014041

1091 COMPARING THE TOXICITY OF FRESH AND AGED DIESEL EXHAUST USING SEPARATE PARTICLE AND GASEOUS EXPOSURE SYSTEMS.

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Our previous studies have shown that atmospheric aging of gaseous pollutants modifies the chemical composition of air pollution mixtures, ultimately affecting its toxicological potential. The goal of this current project is to determine whether aging of complex gaseous and particulate mixtures, such as diesel exhaust (DE), in the presence or absence of photochemistry, alters the toxicological potential of that mixture. A second goal was to examine the differences between multiple diesel emission sources, specifically those emitted from a 1980 Mercedes and a 2006 Volkswagen. Each freshly emitted DE sample was injected into a 120 m^3 outdoor smog chamber and aged utilizing natural sunlight and humidity. Two separate exposure systems, electrostatic aerosol *in vitro* exposure system (EAVES) and gas *in*

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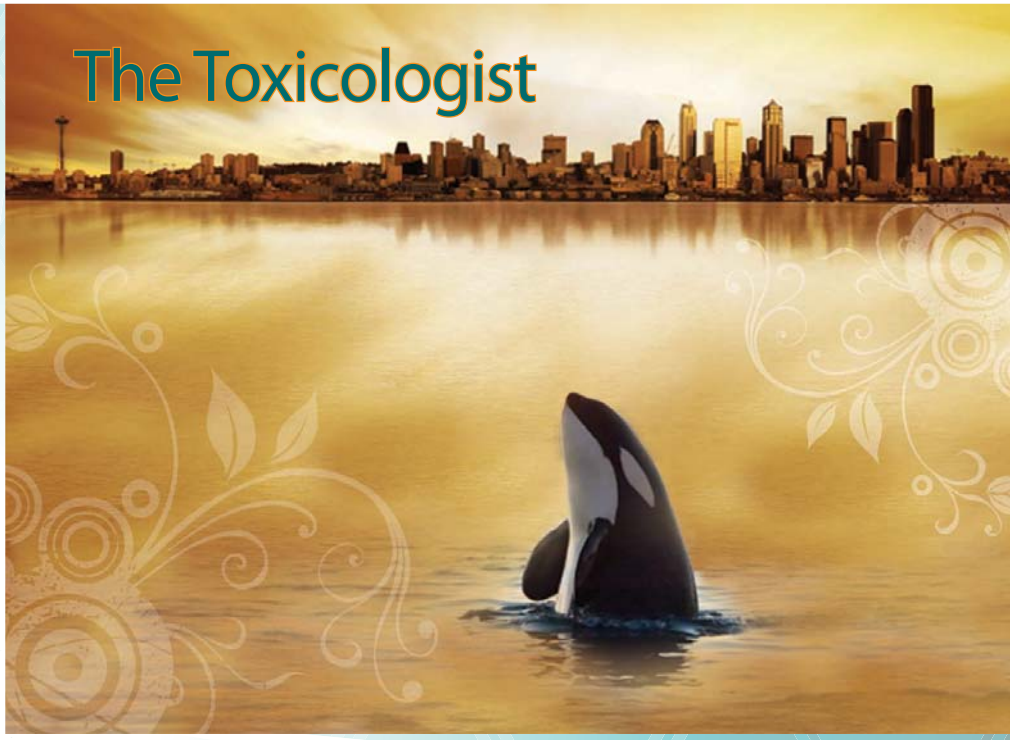

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