and lethality associated with these types of exposures, the use of mathematical tools not ordinarily utilized in conventional toxicology are necessary. These tools are based, not on the simplistic Haber's Rule of dose calculation, but on the more rigorous Toxic Load concept of exposure. Haber's Rule: Dose = C x t; Toxic Load: Dose = Cn x t; where C is the concentration of the toxic gas or aerosol, n is the experimentally determined toxic load exponent, and t is the exposure time. Using Haber's Rule, median lethal dose (LCt50) is defined as the product of C and t at which 50% of the exposed population suffers death. This definition assumes that LCt50 is constant as exposures times decrease and concentration increases, but this assumption is usually found to be fallacious for most volatile compound and it is experimentally observed that as concentration increases LCt50 tend to decrease, i.e. as the concentration increases the toxicity appears to increase. This is illustrated in the Table below: Data in the last column assumes that n is equal to 1.5, and since the resulting values in this data set are essentially identical validates that assumption. Actual reported data will be used to illustrate how to calculate the Toxic Load constants. Modeling will be used to calculate the overestimation of casualties that will occur if Haber's Rule is applied when n is not equal to one. Models for both outdoor and indoor chemical releases will be shown and compared. Actual reported accidental releases will be used as examples. The thermodynamics of large releases will be discussed to show that simple assumption of flash evaporation leads to very significant errors in dispersion calculations. The effect of experimental errors, both random and systematic, will be determined.

PS 573 PRELIMINARY ASSESSMENT OF PULMONARY TOXICITY OF MIDDLE EASTERN SOIL EXTRACT IN A RAT MODEL.

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Soldiers deployed to the Middle East are exposed to potentially high concentrations of airborne particulate matter (PM) from local soils. In this study, we characterized the respiratory toxicity of the soluble components of Middle Eastern Dust [MED]. MED was irradiated, mixed with PBS, and incubated overnight. The soluble extracts were screened for cytotoxicity using the MTT metabolism assay in a rat lung epithelial cell culture [RLE-6TN]. The in vivo study examined the effects of MED extract after a single intra-tracheal dose. Adult male CD rats were randomly assigned to PBS Control [CN], Camp Victory [CV], Afghanistan [AF], and Taji [TJ] groups. Rats were anesthetized and dosed with 500 µl of MED extract intratracheally. Rats were killed at 8, 24, 72 h, 2 or 4 wk after dosing. Broncho-alveolar lavage fluid [BALF] was collected from the left lung and total cell count, differential cell count, lactate dehydrogenase [LDH] activity, and total protein concentration were determined. TJ and AF were significantly more cytotoxic in vitro than CV or CN. In the in vivo study, a subset of TJ rats demonstrated acute respiratory distress and 3/40 animals from the TJ group and 1/40 CV died within 30 min of dosing. Body weight gain changes in treated rats compared with CN were not significant. Total BALF cell counts showed significant increases in the AF/8h and TJ/4wk group. BALF LDH activity was significantly increased compared to CN for TJ/72h. BALF protein values were unaffected by MED extract exposure. Metal analysis of the extracts demonstrated different metal profiles that likely contributed to these observed differences in response. Our data indicate that the inflammatory response seen in rats exposed to MED extracts was complex, depending on geographic region of the MED and sampling time. Cytokine, histopathology and tissue metal analyses are underway and may prove helpful in further characterizing the effects of MED extract.

PS 574 THE CIGARETTE ADDITIVE MENTHOL BLOCKS THE RESPIRATORY TRACT IRRITATION RESPONSE TO ACROLEIN, A PRIMARY IRRITANT IN CIGARETTE SMOKE.

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Menthol, a compound derived from peppermint, produces a cooling sensation which is thought to be mediated via neuronal TRPM8 channels. Menthol is widely used in preparations for the treatment of cough, pain and itch and is a common additive to cigarettes. The current study was performed to characterize the effects on menthol on the respiratory tract irritation response induced by two irritants in cigarette smoke: acrolein and acetic acid. Acrolein is an electrophilic irritant which acts through the TRPA1 receptor. Acetic acid is an acidic irritant that likely acts through the ASIC receptor. Towards these ends female C57Bl/6J mice were exposed to menthol, irritant, or the combination of the two for 15 minutes during which time respiratory parameters were measured. The primary response to irritant vapors in the mouse is sensory irritation. The response, mediated by the trigeminal nerve, is characterized by reduced breathing frequency due to braking at the onset of each expiration. The average duration of braking (DB) during exposure was used to quantify this response. At a concentration of 16 ppm menthol exerted a minimal transient sensory irritation response (50 msec DB). Acrolein (2 ppm) exerted a strong irritation response (200 msec DB). The response to acrolein was blocked by concurrent exposure to 16 ppm menthol. This level of menthol is significantly lower than that present in smoke from mentholated cigarettes. Menthol partially diminished the irritation response to acetic acid, another irritant present in cigarette smoke. It is not known if the counter-irritating effects of menthol are mediated via interactions of menthol with the TRPA1 and/or ASIC receptor and/or via TRM8-mediated pathways. The inhibition of the irritation response to two irritants present in cigarette smoke suggests that mentholated cigarette smoke may contain pharmacologically active concentrations of menthol vapor.

PS 575 THE USE OF E-CADHERIN IMMUNOFLUORESCENCE IN PULMONARY TOXICOLOGIC PATHOLOGY STUDIES.

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E-cadherin is a calcium dependent adhesion molecule with important roles in epithelial intercellular adhesion and cellular structure. Immunofluorescent staining can localize and quantify protein expression in cells or tissues. Co-localization of 2 or more different proteins used in combination with fluorochromes of different colors can reveal the location of each protein. We investigated the use of e-cadherin immunofluorescence in different species (rat and mouse), with different fixatives (10% neutral buffered formalin, 4% paraformaldehyde, and 2.5% glutaraldehyde), with and without antigen retrieval, and as a dual label with immunofluorescence for other proteins. Mouse monoclonal anti-e-cadherin antibodies (BD Biosciences, San Jose, CA) in conjunction with fluorochrome-conjugated donkey anti-mouse antibodies clearly delineated sites of e-cadherin expression in lungs of rats or mice. EDTA heat-induced epitope retrieval was required to restore antigenicity to fixed tissues. E-cadherin could be demonstrated in formalin or paraformaldehyde fixed tissues but not in glutaraldehyde fixed tissue. Immunofluorescent double-labeling with e-cadherin can be used with immunofluorescent detection of podoplanin, a lymphatic endothelial cell marker that is also expressed by alveolar type I cells in the lung. Low levels of e-cadherin expression in type I cells allowed the double labeled type I cells to be distinguished from lymphatic endothelium and facilitated diagnosis of lymphangiectasia. E-cadherin immunofluorescent double labeling can also be used with activated caspase 3 or β-catenin immunofluorescence to localize the expression of these proteins in damaged airways. Thus, in the lung, e-cadherin immunofluorescence can demonstrate abnormal and normal epithelial cell junctions, facilitate demonstration of airway epithelial changes, and distinguish podoplanin-expressing alveolar type I cells from lymphatic endothelium.

PS 576 TELEMETERED THORACIC IMPEDANCE PNEUMOGRAPHY: COMPARISON WITH AMBULATORY RESPIRATION MEASUREMENT STANDARDS IN THE ANESTHETIZED BEAGLE DOG AND PHARMACOLOGICAL VALIDATION.

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Recent developments in thoracic-impedance-pneumography (TIP) as a telemetry based approach to measure respiratory activity seems very suitable for assessment of pharmacological effects of drugs in non-restrained conditions, and for combination with ambulatory telemetered cardiovascular investigations in toxicology studies. As a first validation step, we have implemented TIP in the anaesthetized beagle dog and compared the respiratory parameters with existing, non-restrained respiratory assessment methods. Four dogs were implanted with DSI D70-PCTR transmitters whose pressure catheters were placed intrathoracically for pleural pressure (PP) measurement. Four weeks later, the animals were isoflurane-anesthetized and instrumented with a tracheal pneumotachometer (PNT) used as the reference method, and a JET® RIP (Respiratory Inductive Plethysmography, DSI) system. One hour after induction, baseline data was collected for 15 min, followed by experimental modifications of the respiratory function: three hypercapnia levels (5.3, 5.8 and 6.1 % ETCO2, 15 min recovery/level) followed by a subcutaneous bolus of Morphine (M) at 2 mg/kg. Three days later the same procedures were repeated replacing Morphine with Buspirone intramuscularly administered at 3 mg/kg. Regression analysis was conducted for the PNT, RIP, TIP and PP based tidal volume (TV), respiratory rate (RR), and minute ventilation (MV) values. When comparing values between RIP, TIP or PP versus PNT, correlation coefficients (R2)

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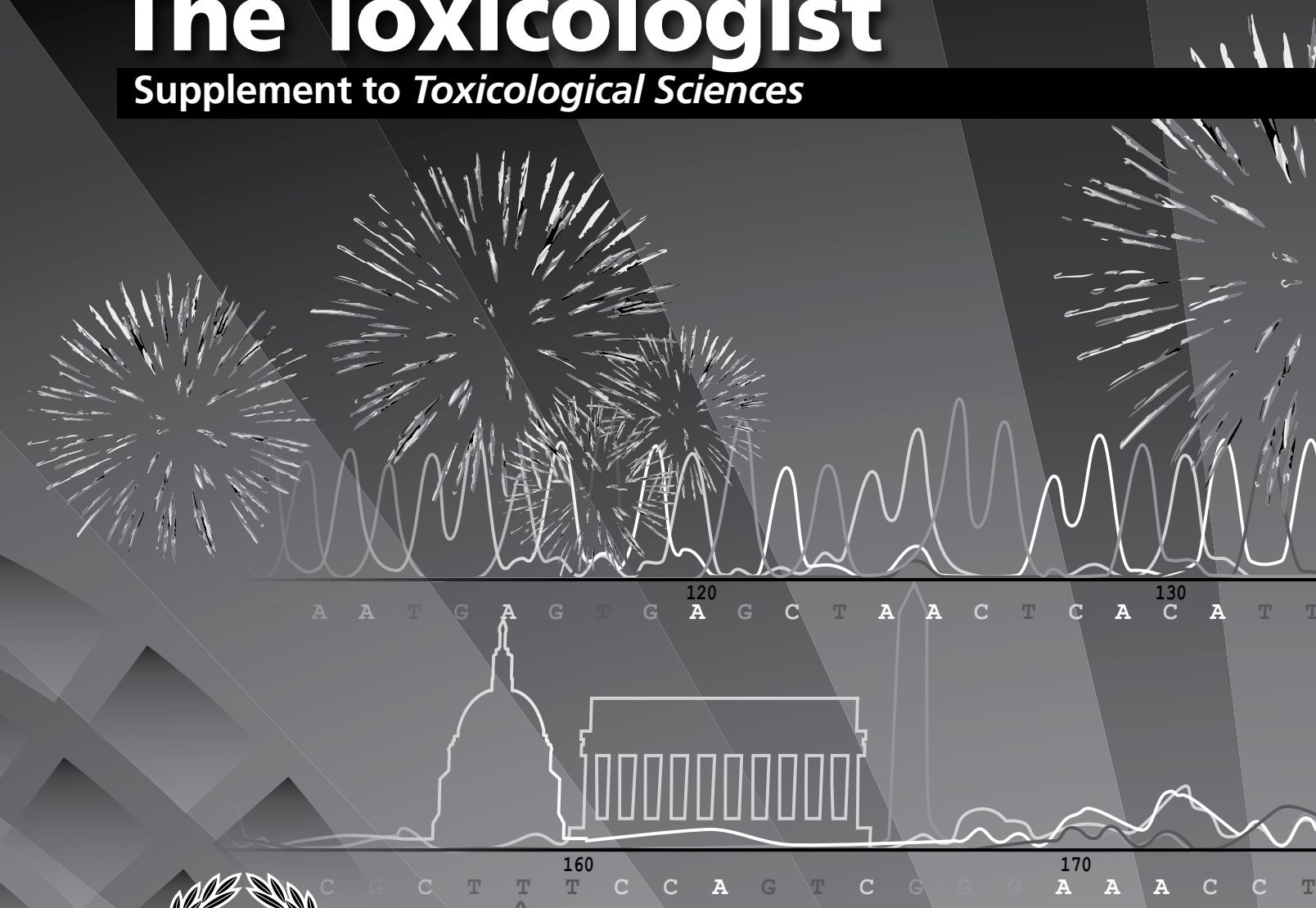

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

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

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