prominent and plural fibrosis also appeared at the day 90. This welding fume exposure induced lung fibrosis model could be helpful to solve whether welding fume exposure induced pneumoconiosis could be resolved after cessation of the exposure.

2017 HIGHLY-SOLUBLE STAINLESS STEEL WELDING FUME SLOWS THE PULMONARY CLEARANCE OF A BACTERIAL PATHOGEN AND SEVERELY DAMAGES THE LUNGS AFTER INFECTION.

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Acute respiratory tract infections are increased in terms of severity, duration, and frequency among welders as compared to the general population. The objective of this study was to determine the mechanism by which different welding fumes may affect pulmonary bacterial clearance and lung injury after infection. Fume was collected during gas metal arc (GMA) or flux-cored manual metal arc (MMA) welding using two consumable electrodes: stainless steel (SS) or mild steel (MS). The fumes were separated into water-soluble and insoluble fractions, and the metal composition determined. Sprague-Dawley rats were dosed intratracheally with saline (vehicle control) and the different welding fumes (1 mg/100 g b wt). Three days later, the rats were inoculated intratracheally with 5,000 Listeria monocytogenes. At 3, 5, and 7 days post-bacteria inoculation, left lungs were removed, homogenized, and the number of colony-forming units were counted after an overnight incubation. Animal weights and mortality were monitored over the course of the treatment period. The GMA-SS and GMA-MS fumes were found to be relatively insoluble, whereas the MMA-SS fume was highly water-soluble with the soluble fraction comprised of 87 % Cr and 11 % Mn. In contrast to the GMA-SS and GMA-MS groups, rats pre-exposed to MMA-SS fume lost significantly more weight and had an elevation in mortality after infection. Also, pre-exposure to the MMA-SS fume dramatically slowed the pulmonary clearance of L. monocytogenes as compared to the other groups. No difference in bacterial clearance was observed when comparing the GMA-SS, GMA-MS, and control groups. Extensive lesion formation, characterized by severe proteinaceous edema, significant inflammation, and consolidation, was present in the lungs of the MMA-SS group after infection. The significant reduction in bacterial clearance from the lungs after treatment with MMA-SS fumes is likely attributed to the presence of soluble metals and their effect on lung defense mechanisms.

2018 ACUTE INHALATION TOXICITY STUDY OF HCC-230FA IN MALE RATS.

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The acute inhalation toxicity of 1,1,1,3,3,3-hexachloropropane (HCC-230fa) was evaluated by exposure of male rats to 0, 0.50, 2.5, or 7.5 mg/L for a single, 1-hour period. Immediately following the exposure, 5 rats per group were bled for clinical pathology evaluation and necropsied. All surviving rats were kept for a 14-day, 1- or 3-month recovery period. Endpoints evaluated included body weights, clinical signs, hematology parameters, and limited pathology. There were no compound-related mortalities in the study. No toxicologically important hematology changes occurred during the study. Rats exposed to 2.5 or 7.5 mg/L had lower mean body weights and mean body weight gains the day after exposure when compared to controls. Immediately after exposure, rats in the 2.5 and 7.5 mg/L groups exhibited hunched posture, lethargy, irregular respiration, and ataxia (7.5 mg/L only). During the recovery period, clinical signs attributed to HCC-230fa included hunched posture, stained perinea, and nasal discharge in rats exposed to 7.5 mg/L. Pathologic examination revealed compound-induced minimal lymphoid necrosis in the spleens of 5/6 rats in the 7.5 mg/L group and in the thymuses of 2/5, 5/6, and 5/6 rats in the 0.50, 2.5, and 7.5 mg/L groups, respectively, that were necropsied immediately after the exposure. Microscopic examination of 1-month recovery rats revealed an adverse compound-induced change (minimal to mild degeneration/atrophy, seminiferous tubules) that was bilateral in the testes of 5/5 rats in the 7.5 mg/L group and unilateral in the testes of 1/5 rats in the 2.5 mg/L group. There were no compound induced microscopic changes in any rats at the 14-day or 3-month recovery. Based on microscopic pathology observations (lymphoid necrosis in thymuses), the no-observed-effect level for a single, 1-hour exposure to HCC-230fa in male rats was not established.

2019 INHIBITING CYCLOOXYGENASE (COX) ACTIVITY MODULATES MOUSE PULMONARY RESPONSES TO BUTYLATED HYDROXYTOLUENE (BHT).

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Oxidative metabolites of BHT generated in the lungs of mice following i.p. BHT administration cause reversible alveolar damage, an ensuing alveolitis characterized by macrophage infiltration, and promote lung tumorigenesis. We are studying how inflammation enhances tumor promotion in mice since chronic pulmonary inflammatory diseases increase the risk of developing lung cancer in humans. COX enzymes convert arachidonate to prostaglandins. Because COX-1 and COX-2 contents are elevated in response to a single (acute) and chronic (multiple) injections of BHT into BALB mice, and are highly expressed in lung tumors, modulation of this eicosanoid pathway was examined. In order to test the influence of a COX inhibitor on these pneumotoxicities, aspirin was added to an AIN-76A diet. Compared to standard lab chow, the lungs of mice fed AIN-76A were more severely affected by BHT, as measured by an increased lung weight/body weight ratio. Aspirin reduced the severity of the injury resulting from acute BHT and decreased bronchoalveolar lavage (BAL) macrophage content compared to mice treated with BHT alone. After chronic BHT treatment, several inflammatory parameters were reduced including the extent of macrophage and lymphocyte infiltration into alveolar airspaces and the amounts of PGE_2 and PGI_2 present in lung homogenates. However, aspirin only slightly decreased lung tumor multiplicity in a two-stage carcinogenesis protocol in which a single MCA (3-methylcholanthrene) injection was followed by chronic BHT administration. These results imply that the COX pathway is critical in the pneumotoxicity caused by BHT, while involvement of COX in tumor promotion needs further investigation. (Supported by CA33497)

2020 INTRATRACHEAL AMIODARONE ADMINISTRATION TO F344 RATS CAUSES ACUTE DAMAGE TO AIRWAY AND PARENCHYMAL CELLS; THE POSSIBLE ROLE OF FREE RADICAL GENERATION.

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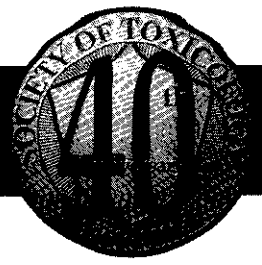
Intratracheal (i.t) instillation of the antiarrhythmic drug amiodarone (AD) leads to lung damage, inflammation, and fibrosis in F344 rats. To assess the direct effect of AD in this damage, male F344 rats were instilled with 6.25 mg/kg AD (3.125 mg/ml solution in sterile water) or the sterile water vehicle and subjected to bronchoalveolar lavage (BAL) at 15 min, 1 hr, and 3hr following i.t. treatment. The blood protein albumin was markedly elevated in the first BAL fraction of AD-treated animals at these time points, indicating an early damage to the alveolar-capillary barrier. Histopathologic alterations in AD-treated rats at these time points were characterized by multifocal, mild, acute, alveolar edema and hemorrhage with associated fibrinoid degeneration of alveolar septa and multifocal, marked, peracute, ulcerative bronchitis and bronchiolitis. To distinguish the affected cells in intact tissue, the lungs of rats euthanized at 15 min, 1 hr, and 3 hr following i.t. treatment were inflated with ethidium homodimer solution (4 μM). Laser-scanning confocal microscopy was used to visualize cells that lost membrane integrity and were positively stained with ethidium. Foci of massive damage to airway and alveolar cells were evident at all time points after i.t. AD treatment. To examine possible free radical production, AD solutions were analyzed using electron spin resonance. A carbon-based free radical signal was detected in AD solutions in water (25 mg/ml). Using the spin trap DMPO, the hydroxyl radical was detected in solutions of AD in water and AD in phosphate-buffered saline (both 3.125 mg/ml). Superoxide anion and hydrogen peroxide were implicated in the production of hydroxyl radicals. Thus, free radical production may be involved in the early damage to the airways and parenchyma after i.t. AD treatment.

2021 MECHANISM OF THE RESISTANCE TO BLEOMYCIN IN TRANSGENIC MICE OVEREXPRESSING IL-9.

M. Arras[1], F. Huaux[1], J. Louahed[4], A. Vink[4], V. Barbarin[1], M. C. Many[3], M. Delos[2], J. C. Renauld[4] and D. Lison[1]. [1]*UCL, Industrial Toxicology and Occupational Medicine Unit, Brussels, Belgium,* [2]*University Hospital of Mont Godinne, Laboratory of Pathology, Yvoir, Belgium,* [3]*UCL, Histology Laboratory, Brussels, Belgium and* [4]*UCL, Unit of Experimental Medicine and Ludwig Institue for Cancer Research, Brussels, Belgium.* Sponsor: R. Lauwerys.

Interleukin-9 is produced by TH2 lymphocytes and active on various immune and hematopoietic cells. We previously showed that IL-9 has a protective effect in an experimental model of lung fibrosis induced by silica particles. In order to further



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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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