treated with cerium-144 in activity 1,85 kBq/g (I group), 9,25 kBq/g (II group), 18,5 kBq/g (III group). In the second step all groups were external irradiated with gamma-ray in doses 105 cGy/kg. On the 15th day, and 1st,2nd,3rd,6th and 9th months were determined proline, hydroxyproline, and hexosamine in the dry rats lung. The absorbed dose in the rats lung after incorporated 144-Ce in activity 185 kBq/g on the 3rd months was 36 Gy. The results show that the combination of 105 cGy/kg external radiation and 70 Gy internal dose generated in lung for 9th months (from Ce-144) give the additive fibrous effect. From the experimental data obtained one draw the conclusion that the pathological effect from the combination of both radiation factors may become grave in doses causing approximately equal biological changes.
Acknowledgements: We thank colleagues Cr.Lalova and G.Kiradjiev for their support in biochemical analyses.

1044 TIME COURSE OF LUNG RESPONSE IN THE MOUSE TO PANCREATIC ELASTASE

E. N. Potts, J. A. Voynow and W. M. Foster. *Duke University Medical Center, Durham, NC.*

Treatment of the lung with elastase, a serine protease, leads to inflammation and mucous cell metaplasia. The goal of this study was to determine if elastase has additional effects upon respiratory mechanics. Adult C57Bl/6 male mice (n=36) were put into Control (0.9 % NaCl), Low (0.5 ug) and High (5.0 ug) dose mouse pancreatic elastase (mPE) groups. Treatment was delivered by oro-pharyngeal aspiration on days 1 and 4, and total lung resistance (low-frequency forced oscillation technique) was monitored on days 8 or 11. Additional mice (n=20) were euthanized on days 8 or 11, followed by tracheal catheterization and collection of alveolar lavage (BAL).
Results: mPE treatment led to lung inflammation by day 8 as evidenced by cellularity of BAL (20,000 cells/ml on average in Control group vs. 108,000 cells/ml in High dose mPE; and a neutrophil (PMNs) influx of <500 PMN/ml in Control group vs. 105,000 PMN/ml in High mPE). At day 8 lung inflammation was increased by Low dose mPE, but to a lesser degree than found in High dose mice. By day 11, cellularity and inflammation had begun to ebb: BAL cells/ml and PMN/ml were still elevated for Low and High mPE, but had decreased on average to approximately 75% and 55%, respectively, of the day 8 values. Airway reactivity, indexed as total lung resistance to an IV methacholine (Mch) challenge, was increased after mPE: for Control group (n=12) the average total lung resistance (RTa) increased above baseline by 48% in response to the highest dose of Mch, whereas RTa had increased by 83% and 99% after High mPE on days 8 and 11. Low mPE also altered Mch sensitivity as RTa increased above baseline by 53% and 60% on days 8 and 11.
Conclusion: exogenous delivery of mPE to the lower respiratory tract in the mouse leads to a dose-related inflammatory response (BAL cellularity and influx of PMNs) and enhances airway reactivity to Mch. Interdependence among phenotypic airway responses to elastase, i.e., inflammation, reactivity to Mch, and epithelial remodeling, is unclear at this point and requires further investigation. Supported by NIH: HL 62641, HL 65611, and ES011961.

1045 INFLUENCE OF PARTICLE SHAPE ON SILICA TOXICITY *IN VITRO*: IMPACT OF SIMULATED LUNG MECHANICS, SURFACE TREATMENT, AND AGGREGATION

S. C. Brown[1], M. A. Kamal[2], N. Nasreen[2], V. B. Antony[2] and B. M. Moudgil[1]. [1]*Materials Science and Engineering, and Particle Engineering Research Center, University of Florida, Gainesville, FL and* [2]*Department of Medicine, University of Florida, Gainesville, FL.* Sponsor: S. Roberts.

We have synthesized spherical and rod-shaped amorphous silica particles of equivalent radii (50nm and 100nm) to determine the influence of simulated lung mechanics on shape-dependent particle toxicity. Human pleural mesothelial cells (MET-5A) were subjected to cyclic stretch at 5% elongation to simulate normal lung mechanics. Cell cultures were exposed to spheres and rods at equal surface area dosages. To modulate cell-particle interactions, spheres and rods were treated with fibronectin and polyethylene glycol (PEG) to enhance and mitigate particle-cell adhesion, respectively. Cell membrane integrity was monitored by lactate dehydrogenase (LDH) release, and inflammatory response was analyzed using an Interleukin-8 (IL-8) ELISA. Min-U-Sil quartz was used as a positive control in this study. Results indicate that native particle cytotoxicity and IL-8 release are mildly enhanced in the presence of cyclical stretch regardless of particle shape. PEG surface modification inhibited this effect, indicating that it is driven by particle-cell adhesion. No significant deviation in LDH or IL-8 release was noted for silica spheres versus rods; however, it was evident that these two materials have significantly different aggregation potentials. Silica nanorods were observed to form 'super-cluster' aggregates much larger than the size of the cells and orders in magnitude larger than those formed by the spheres. This implies that the effective dosages available for cellular interaction and uptake may have been largely different for the spheres versus rods. The influence of aggregation on effective dosage was evaluated using dispesed and hard-aggregated sub-micron sized fractions of Min-U-Sil 5 quartz particles. The aggregated particles resulted in lower cytotoxicity. These results indicate that shape-dependant deviations in particle aggregation need to be accounted for in comparative particle dosimetry.

1046 DOES SANDBLASTED METAL ATTENUATE OR ENHANCE THE TOXICITY OF SILICA SAND?

V. Robinson, V. Castranova, S. Leonard, M. Barger, D. Pack, G. Feather and V. Vallyathan. *HELD, NIOSH, Morgantown, WV.*

It is well known that freshly fractured silica sand resulting from sandblasting operations causes pulmonary toxicity and inflammation. However, it is unclear what contribution, if any, the material that is blasted may have upon the toxicity of silica sand. Two alternative hypotheses were proposed: 1) that the addition of freshly fractured metals, such as iron, would make the metal/sand mix more potent via the Fenton reaction, or 2) that metal, such as aluminum, would coat the silica particles, mask reactive sites on the silica surface and attenuate the toxicity. In this study, plates of several pure metals (iron, aluminum, copper, tungsten, titanium, chromium, tin or nickel) were blasted with silica sand using an automated sandblasting apparatus. The resulting aerosolized silica sand/metal dust mixture was collected on filters, then characterized by ESR, chemical analysis and microscopy. Additional samples of the dust (1.0 mg) were instilled intratracheally into Sprague Dawley rats, followed by lavage at either one or three days post instillation. The resulting studies of inflammatory indices indicate that the addition of metal does not make the dust mix more toxic than the silica sand alone, rather, toxicity is depressed.
The findings and conclusions in this report (abstract/presentation) have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

1047 REPEATED INHALATION TOXICITY OF SYNTHETIC AMORPHOUS SILICAS IN RATS: EVALUATION OF THEIR TOXICITY UP TO 3 MONTHS AFTER EXPOSURE

J. Arts, H. Muijser, E. Duistermaat, K. Junker and F. Kuper. *Toxicology and Applied Pharmacology, TNO Quality of Life, Zeist, Netherlands.* Sponsor: A. Nordone.

The inhalation toxicity of three synthetic amorphous silicas (SAS), precipitated silica Zeosil 45, silica gel Syloid 74, and pyrogenic silica Cab-O-Sil M5 was studied in Wistar rats. Rats were exposed nose-only to 1, 5 or 25 mg/m3 of one of the SAS, 6 h/day for 5 days. Positive controls were exposed to 25 mg/m3 crystalline silica (quartz dust), negative controls to clean air. Animals were necropsied the day after the last exposure, or 1 or 3 months later. All exposures were tolerated without serious clinical effects, changes in body weight or food intake. Silicon levels in tracheobroncheal lymph nodes were below the detection limit in all groups. Silicon was found in the lungs of all high concentration SAS groups after one day, and was cleared 3 months post-exposure. Exposure to all three SAS at 25 mg/m3 induced elevations in biomarkers of cytoxicity in bronchoalveolar lavage fluid (BALf), increases in lung and tracheobronchial lymph node weight, and histopathological lung changes at 0 months. Exposure to 5 mg/m3 changes induced histopathological changes and changes in BALf only. With all three SAS these effects were transient and, with the exception of slight histopathological lung changes at the higher exposure levels, were reversible during the 3-month recovery period. No adverse changes were observed in animals exposed to 1 mg/m3 SAS.
In animals exposed to quartz, silicon was found in the lungs at comparable levels 0, 1 and 3 months post-exposure. Pulmonary changes differed significantly compared to those induced by SAS, both with regard to the type and severity as well as in the time-response profile. Effects were minimal at 0 months, present at 1 month, and progressively more severe at 3 months. The results of the present study indicate that lung clearance is a key factor in the development of silicosis.
This research is funded by CEFIC-ASASP, Brussels, Belgium.

1048 PATHOLOGICAL STUDY ON THE PULMONARY TOXICITY INDUCED BY THE INTRATRACHEALLY INSTILLED YELLOW SAND IN MICE

A. Shimada, O. Mina, K. Theerayuth, T. Morita and H. Inoue. *Veterinary Pathology, Tottori University, Tottori-shi, Japan.*

The frequency and volume of yellow sand are increasing in Japan, resulting in one of the air pollution related threats to human health. There are, however, few reports on the pathological study of the pulmonary toxicity induced by yellow sand. In this study, we examined inflammatory changes in the bronchoalveolar lavage fluids (BALF) and lung tissues of mice intratracheally instilled with yellow sand.

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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, and poster sessions of the 45th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, San Diego, March 5–9, 2006.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

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

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