as positive and negative controls, respectively. **Results:** Results revealed that the toxicity of lunar and Martian regolith simulants was intermediate between that of TiO2 and crystalline silica. Furthermore, measurements of inflammatory cytokines IL-1β and IL-18 indicated comparable levels of NLRP3 inflammasome activation. Here we show that while lunar and Martian dust simulants do exhibit toxicity, their levels fall between those of TiO2 and crystalline silica. **Conclusions:** Thus, significant levels of inflammation and chronic diseases would require higher concentrations or extended exposure to these simulants compared to crystalline silica. Accordingly, mitigation measures should be implemented for lunar and Martian dusts, although the level of concern need not equal crystalline silica. These findings provide crucial insights into health considerations for future space exploration endeavors. Funding provided by R25ES022866. SOT Intern support.

PS 4273 Inhaled household dust induced local and systemic toxic effects

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Background and Purpose: The potential adverse health effects of inhaled household dust (HD) have been more importantly considered since the coronavirus pandemic. In particular, given that health-vulnerable groups, such as the elderly, pregnant women, and infants, spend more time at home than healthy people, the health impact has received greater attention. **Methods:** In this study, we obtained filters instilled into air purifiers that were being used in ten homes. The filters were sonicated in autoclaved distilled water to collect HD, and the extract containing HD was freeze-dried. The HD was resuspended in autoclaved distilled water and sterilized before toxicity tests. **Results:** The HD included plastic (polypropylene, polyethylene, polystyrene, and PET) and non-plastic (cellulose and proteins) particles of various sizes, and heavy metals including copper, vanadium, zinc, barium, strontium, and antimony were detected at the meaningful level in HD suspension. When dosed HD by pharyngeal aspiration to mice for 13 weeks, HD was found in the lung tissue with the cytosol of the alveolar macrophages, and the pulmonary level of inflammatory mediators increased in a dose-dependent manner. In addition, we observed the cell density of the heart tissue is markedly decreased in mice exposed to HD. **Conclusions:** Chronic inhalation of HD may cause adverse health effects locally and systemically due to the postponed lung burden.

PS 4274 Pulmonary exposure to dusts from grinding stone countertop products induces lung inflammation and fibrosis

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Background and Purpose: Engineered stone (ES) is a manmade composite material that may contain crystalline silica (CS, e.g., quartz), resins, and pigments. It is becoming increasingly popular for countertops, backsplashes, and other surfaces due to its durability, non-porous nature, low maintenance, and aesthetic qualities. However, the engineered stones that contain a high percentage of CS can release a large amount of respirable crystalline silica (RCS) dust during cutting, grinding, and polishing tasks performed by workers. Overexposure to RCS causes silicosis, a debilitating and potentially deadly lung disease. Outbreaks of an accelerated form of silicosis have been reported in populations of stone countertop workers in Italy, Australia, South Korea, and the United States. **Methods:** To better understand the pulmonary risks of workers in the stone countertop industry, we exposed adult male rats to dusts generated by grinding one of three types of ES products or granite (40% CS), Min-u-sil® 5 (MS5, positive control, 99.2% CS), or saline vehicle control via a single intratracheal instillation. The three different types of ES products contain high (H), medium (M), and low (L) CS content (90%, 50%, 0.02%, respectively). All exposures occurred after a 1-week acclimation period. The exposure concentrations were 10 mg/rat of test article dispersed in USP 0.9% saline vehicle, n = 8/group. Animals were euthanized at 1-, 21-, and 84-days post-exposure to characterize the development and resolution of acute and chronic inflammation, as well as determine the fibrogenic potential of these materials. Immediately following euthanasia, the left lung lobe and cardiac lobe of the right lung were tied off and reserved for histopathology and molecular analyses, respectively. Bronchoalveolar lavage (BAL) was performed, and the fluid reserved for cytology and molecular analysis. Blood was drawn from the abdominal vena cava and reserved for cytology and plasma chemistry analysis. Values were presented as % of saline vehicle control ± standard deviation. **Results:** Bronchoalveolar lavage fluid (BALF) lactate dehydrogenase (LDH), an indicator of cell damage and lung injury, was elevated in all test groups at 1-day post-exposure (MS5 = 215.22±10.93%, granite = 142.71±11.03%, H = 163.94±13.00%, M = 146.86±9.01%, L = 132.16±9.00%, $p < 0.05$). At day 21, only the MS5 (117.31±13.29%) and the H (127.75±15.63%) ES group's LDH activities were elevated ($p < 0.05$). At day 84 post-exposure, BALF LDH activities in the MS5 (296.20±32.31%), H (287.57±14.64%) and M (143.67±9.17%) ES were elevated ($p < 0.05$) and, furthermore, were higher than at day 1 or day 21 ($p < 0.05$), while LDH levels returned to baseline in the other groups. Total cell count (TCC) in the BALF was increased for MS5 (609.27±202.88%) and all ES groups (H = 268.81±106.76%, M = 183.85±50.05%, L = 168.60±74.40%) at 1-day post-exposure ($p < 0.05$). At 21 days, TCC in MS5 (734.90±325.68%), and the H (304.27±138.50%) and M (155.83±60.37%) ES groups remained elevated ($p < 0.05$). By 84 days post exposure, TCC in all test groups was elevated (MS5 = 4339.88±2179.17%, granite = 287.43±123.52%, H = 809.17±431.07%, M = 257.85±68.78%, L = 187.52±45.45%, $p < 0.05$), with H being significantly higher than the other types of ES ($p < 0.05$). Gross histologic examination revealed large legions on the surface of exposed lungs in the MS5 and ES exposed lungs that did not resolve at day 84. At day 84, MS5 and the H ES caused greater alveolar lipoproteinosis, granulomatous inflammation, alveolar epithelial cell hypertrophy and hyperplasia, and interstitial fibrosis than other exposures. These groups were also associated with granulomatous inflammation in the bronchus-associated lymphoid tissue and granulomatous inflammation and fibrosis in the tracheobronchial lymph node. **Conclusions:** These findings indicate that exposure to RCS dust from both granite and ES may pose a significant pulmonary hazard including interstitial fibrosis. It appears that the observed toxicity is largely driven by the crystalline silica content of the stone countertop products. **Disclaimer:** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. Mention of brand name does not constitute product endorsement.

PS 4275 Development and Validation of a Preclinical Inhalation Model to Test Vaporized Cannabis Distillates

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Background and Purpose: The legalization of cannabis is becoming more common in many jurisdictions, contributing to a rise in its use. A wide array of products have emerged, with vaporizers gaining favour among users. This includes cannabis vape cartridges that utilize battery-powered devices to heat and aerosolize cannabis derived liquids. These cartridges contain purified distillate with high concentrations of specific compounds from the cannabis plant, particularly the psychoactive cannabinoid tetrahydrocannabinol (THC). Despite their growing popularity, the effects of inhaled cannabis distillates on the respiratory tract are unknown. The purpose of this study was to address this gap in knowledge by creating a standardized mouse model for vaporized cannabis distillate exposure to test the pulmonary immune response upon inhalation using two commonly used in-bred mice strains and using commercially available and regulated cannabis products. **Methods:** First, C57BL/6 and Balb/c mice were subjected to a nose-only exposure of vaporized THC distillate using the SCIREQ inExpose and a 510 Thread Cartridge device containing 96% THC. A dose response to increasing exposure length and intensity was characterized with 10, 20 and 30-minute exposures at 1 puff per minute, or 1, 2, and 4 puffs per minute exposures for 10 minutes, respectively (n = 6 per group). Blood was collected immediately following the exposures and serum levels of the THC metabolite THC-COOH were measured using a THC Forensic ELISA kit. Then, to assess the immunological effects, C57BL/6 and Balb/c mice were subjected to an acute 3-day nose-only exposure of vaporized THC distillate (n = 12 per group). Lung tissue was collected immediately following the exposure and innate immune cell populations were quantified using flow cytometry. **Results:** In both C57BL/6 and Balb/c mice, there was a time-dependent increase in blood THC-COOH levels, with a mean concentration of 20.5 ng/mL following a 10-minute exposure and 28.9 ng/mL following a 30-minute exposure. There was also a dose-dependent increase with concentrations of 13.8 ng/mL at 1 puff per minute and 29.1 ng/mL at 4 puffs per minute. No significant differences in serum THC-COOH concentrations were observed between the two strains. However, we did observe strain-related differences in immune response. In C57BL/6 mice exposed to vaporized THC distillate for three days, lung monocyte and eosinophil populations significantly increased from 2.87% to 5.69% ($p < 0.02$) and from 1.37% to 2.92% ($p < 0.05$), respectively. Values are expressed as a percentage of total immune cells. There were no significant changes in lung neutrophil, macrophage, or dendritic cell populations. In contrast, the innate immune cell populations in the lungs of Balb/c mice remained unchanged. **Conclusions:** To our knowledge, this is first study to investigate how inhalation of vaporized cannabis distillates impacts immunomodulation in the lungs. Development of this preclinical model will permit investigation of the pulmonary and systemic responses to inhaled vaporized cannabis distillates, allowing for rigorous toxicologic evaluation. Strain-dependent differences in response to cannabis underscore the importance of model selection in experimental design and parallel the variability in the effects of cannabis in humans.

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