Title of Research:

12_S01-03

Establishment of animal testing for the prediction of respiratory sensitizing potential of chemicals

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Summary of Research:

Respiratory allergy caused by occupational chemicals remains as a significant health concern for industrial workers. However, to date there are no proper animal models for effectively predicting their respiratory sensitizing potentials. The goals of this project are: (1) to develop the animal models for evaluating the relative hazard of respiratory sensitizing chemicals; and (2) to provide the useful information required for hazard assessment of these sensitizers in the workplaces. we developed a small device that enables intratracheal administration of testing substances in small animals such as mice. In this project, TDI, TMA and GA, three well-known respiratory sensitizing chemicals and chicken ovalbumin (OVA), were evaluated. Known contact sensitizing DNCB served as the negative control for respiratory allergens. Under light anesthesia with diethyl ether, mice were sensitized by administering individual agents, each at 4 doses including vehicle control, 5 times a week for a total of 3 weeks using a mouse intra-tracheal installation device. Three days following the last installation, these mice were daily challenged intratracheally with the corresponding agents for 3 days, and sacrificed 2 days thereafter. The degree of airway inflammation was evaluated using semi-quantitative histological grading systems. We found that histological scores, representing the degree of airway inflammation, increased with increasing doses of OVA and TDI used for sensitization. Similar trends were also noted for TMA- or GA-sensitized mice. They were also true for PAS staining in airway epithelial cells. In contrast, such changes were not observed in mice treated with DNCB. Thus, our testing system confirmed the relative sensitizing potency of these known respiratory sensitizers as previously reported in case-studies or epidemiologic studies. As the strategy for assessing the risk for respiratory sensitizing agents in workplace, although the relationship between airway sensitization onset (as determined by various endpoints) and exposure dose/concentration should be first investigated, these evidence for setting exposure limit vary in substances and exposure conditions. Thus, multi-factors, including experimental evidence, workplace exposure and clinical signs should be considered for properly and effectively controlling occupational respiratory allergy.

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Topics:

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