Inhaled Diacetyl Vapors And In Vivo Airway Reactivity To Methacholine (MCh) In Rats

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RATIONALE. Inhaled butter flavoring vapors are associated with fixed airways obstruction and decrements in pulmonary function (popcorn workers' lung, PWL) in workers who make or use flavorings. Previous investigations have implicated the α-diketone flavoring, diacetyl, as an etiologic agent in PWL. In these earlier studies rats inhaling diacetyl for 6 h developed vapor dose-dependent damage to the airway epithelium of the nose (site of most damage), larynx, trachea and intrapulmonary airways when examined 18 h after the exposure. The epithelium lining of the airways is an important barrier to the effects of inhaled toxic substances. Damage to the epithelium after inhalation of agents, such as ozone, results in airway hyperreactivity (AHR) to the contractile effects of inhaled MCh. Therefore, we hypothesized that diacetyl-induced morphological changes in epithelium would be accompanied by hyperreactivity to inhaled MCh. As well, we anticipated that no observable adverse effect limits (NOAELs) might be defined by diacetyl doses that did not result in AHR. METHODS. Male rats were exposed by inhalation for 6 h to diacetyl (60, 100, 200, 300 and 360 ppm). Eighteen h later the animals were anesthetized with ketamine/xylazine and prepared for measurement of airway resistance (Rl) and compliance (CDyn). After recording baseline values and saline vehicle controls, MCh aerosols were delivered in step-wise increasing concentrations (0.3 – 10 mg/ml MCh). RESULTS. There were no effects of any diacetyl exposure on basal Rl and Cdyn. In addition, reactivity to MCh, both in terms of Rl and Cdyn, was unaffected by any exposure to diacetyl. CONCLUSION. These findings indicate that the morphological damage seen in the epithelium of exposed rats following diacetyl exposure is not predictive of alterations in pulmonary function or airway reactivity changes. As such, the development of AHR in the rat is not a suitable marker for identification of NOAELs in this model. In addition, it remains possible that, in the rat, AHR is not among the sequelae of exposure to diacetyl.

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