

**ASSESSMENT OF INHALED AGRICULTURAL DUST HAZARD
AND MECHANISMS OF DISEASE USING AN ANIMAL
INHALATION MODEL IN COMBINATION WITH STUDIES OF
ISOLATED AIRWAYS**



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It is becoming increasingly clear that inhalation of some agricultural dusts in the workplace may cause pulmonary obstruction. We have been conducting biological experiments designed to both assess the potential hazard of agricultural dusts and to determine the mechanism(s) of the pulmonary response. This has been accomplished through the use of a computer-operated dust generation and animal inhalation exposure system (designed by David G. Frazer), which provides dust-exposed animals from which airways are then removed for additional study of the mechanisms of inhaled dust toxicity. Studies on isolated airways involve the isolated perfused guinea pig trachea. The perfused trachea is used because it contains respiratory smooth muscle, which is involved in narrowing of the airways in response to inhaled substances, and other cell types such as epithelium, which lines the airways and is known to be a target of the toxic effects of some agents. The isolated trachea also permits a detailed evaluation of the mechanisms of effect of suspected etiologic agents under carefully controlled laboratory conditions. We are able to ascertain the effect(s) of inhaled substances on respiratory smooth muscle and epithelium. The protocol used to examine dust effect(s) is to apply the bronchoconstricting drug, methacholine, to the fluid surrounding the trachea in order to establish the dose-response relationship for the diameter decrease caused by contraction of the smooth muscle. The methacholine easily reaches the muscle, which is situated on the outer surface of the trachea. These results are compared with the dose-response relationship obtained after the trachea is challenged with methacholine perfused through the lumen. The muscle contracts to luminal methacholine only after the drug has crossed the epithelium. The epithelium is a diffusion barrier and a metabolic site, and also releases modulatory factors which affect the responsiveness of the muscle. We have examined the effects of respirable cotton and barn dusts. A six-hour exposure to cotton dust caused pulmonary obstruction, the degree and duration of which depended on the level of dust in the air. The perfused trachea preparation revealed that a complex set of changes had occurred in the release of modulatory factors from the epithelium, which altered in a dust level- and post-exposure, time-dependent manner responsiveness of the muscle. Inhaled barn dust did not affect pulmonary function or tracheal reactivity. The use of these laboratory methods will continue to assist in the identification of inhaled dust hazards and disease mechanisms.

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