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Organic Dust Exposure From Compost Handling: Response of an Animal Model

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The objective of this investigation was to elucidate the pulmonary responses of an animal model to dust generated from leaf/wood compost which had caused a severe case of acute respiratory illness in an individual. Guinea pigs were exposed for 4 hr to 30 mg/m^3 of aerosolized leaf/wood compost dust. Inhalation resulted in significant cellular activation and changes in pulmonary mechanics. Maximal elevation in breathing rate (↑ 36%) was observed 12–18 hr postexposure. Similarly, maximal granulocyte infiltration (↑ 1,600%) and activation of alveolar macrophages (↑ 65%) occurred 18 hr postexposure. In contrast, maximal airway obstruction (↑ 120%) occurred immediately after exposure and returned toward normal (↑ 53%) by 18 hr postexposure. In several respects, the airway obstruction and pulmonary inflammation described in the animal model were comparable to the human response to compost dust. Therefore, this animal model may be useful in predicting the potential respiratory hazard associated with exposure to various organic dusts. © 1993 Wiley-Liss, Inc.*

Key words: organic dust, animal model, pulmonary inflammation, airway obstruction, inhalation exposure, leaf/wood compost

INTRODUCTION

It has long been documented that exposure to cotton dust results in chest tightness and respiratory impairment [Schilling et al., 1955]. This occupational syndrome in textile workers has been classified as byssinosis [Rylander et al., 1987]. Recently, it has been proposed that the health effects of cotton dust exposure are not unique but rather are representative of responses to organic dusts in general [Rylander, 1990]. Indeed, acute reactions characterized by fever, malaise, leukocytosis, headache, and decreased pulmonary function have been described in dairy farmers, swine confinement workers, grain handlers, and wood workers [Malmberg, 1990; Donham, 1990; Hurst and Dosman, 1990; Enarson and Chan-Yeung, 1990].

Organic dusts commonly contain a variety of agents which potentially could cause adverse health effects. Organic dusts are normally contaminated with bacteria.

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Endotoxins, i.e., products from Gram-negative bacteria, have been found in organic dusts at relatively high levels [Olenchock et al., 1987] and have been associated with pulmonary function changes in swine confinement workers [Donham, 1990] as well as human volunteers and animals exposed to cotton dust [Castellan et al., 1987; Gordon, 1990]. Organic dusts are often contaminated with fungi and associated mycotoxins [Palmgren and Lee, 1986; Sorenson, 1990], and mycotoxins have been shown to be toxic to alveolar macrophages [Sorenson et al., 1986]. In addition, fungal spores have been associated with adverse health effects in farmers exposed to moldy dusts [Malmberg et al., 1986].

Recently, NIOSH scientists investigated a case in which a landscape architect was admitted to the hospital with dyspnea, fever, headache, hypoxemia, and myalgia approximately 12 hr after shoveling compost containing chopped leaves and branches [Weber et al., 1990]. Environmental sampling at the site indicated that inhalable and respirable dust levels of 149 and 83 mg/m^3, respectively, could be generated during compost handling. Analysis of this dust yielded high spore counts (10^6–10^9 spores/m^3), substantial fungal and bacterial contamination, and airborne endotoxin levels as high as 16,300 endotoxin units/m^3 [Kullman et al., 1990]. Although a great deal of information has been collected in this case, a distinction between hypersensitivity pneumonitis and organic dust toxic syndrome could not be made.

Recently, our laboratory has conducted an extensive effort to develop an animal model which would correlate with human responses to inhalation of organic dusts. For example, time course and dose-response information have been published previously which demonstrate that pulmonary reactions of the guinea pig to cotton dust exposure are comparable to those of textile workers [Castranova et al., 1987, 1990; Robinson et al., 1988]. Therefore, the objective of the present investigation was to systematically describe the pulmonary responses to inhalation of compost dust in this animal model.

METHODS

Dust Collection

Samples of compost consisting of chopped leaves and branches were collected from a small scale recycling operation, i.e., the site of exposure which recently resulted in an adverse health response in a worker [Weber et al., 1990]. Environmental measurements made while collecting these samples indicated a worst–case exposure of 149 mg/m^3 (inhalable dust) and 83 mg/m^3 (respirable dust). Analysis of this dust revealed high spore counts (10^6–10^9 spores/m^3), substantial fungal and bacterial contamination, and airborne endotoxin levels as high as 16,300 endotoxin units/m^3 in the inspirable dust sample [Kullman et al., 1990]. Compost samples were stored at 2°C until use. Animal exposures were conducted within three weeks of sample collection.

Generation of Dust for Inhalation Exposure

A modified Pitt-3 (MP-3) dust generator similar in design to the one described by Weyel et al. [1984] was constructed on a larger scale using a 15-in loud speaker acoustically coupled to a 13-in diameter, 16-in long vertical plexiglass cylindrical chamber enclosed on both ends by flexible rubber diaphragms. The generator was used to separate and resuspend small respirable particles contained in a bulk compost

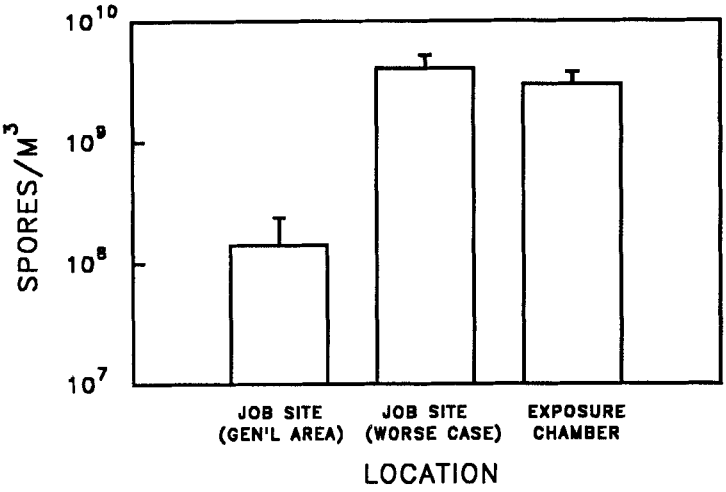

Fig. 1. Airborne spore counts from samples taken at the job site and in the exposure chamber. Worst-case samples were taken directly in the dust cloud while general area samples were taken in the general vicinity of the operation. Data are means ± standard errors of 3, 6, and 6 samples for the exposure chamber, worst-case, and general area, respectively.

sample that was placed inside the generator chamber. The optimal operating conditions for the new generator were determined using the procedures previously described by Frazer et al. [1987]. The generator's output performance was optimized when it was driven at 12 VRMS with a frequency modulated signal that linearly increased and decreased between 10 and 24 H_z at a rate of 30 times/min. Air flow through the generator was maintained at 20 L/min.

Animal Exposure

Upon generation, the compost dust was passed through a static charge neutralizer (TSI Model #3054), a 25 L plexiglass settling tank, and an air mixing chamber. The respirable compost dust was then instilled into an animal exposure chamber holding 8 guinea pigs. The exposure chamber was held at 26 ± 2°C and an average relative humidity of 48 ± 3%. A miniram (Miniature Real-time Aerosol Monitor, GCA Model #PDM-3) was placed inside the exposure chamber to estimate the mass concentration of the aerosol exposures at 10 sec intervals. The miniram signal was used to maintain mass concentration at 30 mg/m^3 by automated feedback control of diluent air in the mixing chamber. The actual mass concentration of each exposure was determined gravimetrically at one-half hour intervals using cassettes containing VM-1 filters to collect dust samples at a flow rate of 1 liter/min.

In this study, English short hair guinea pigs were obtained from Camm Research Laboratory Animals, Wayne, NJ. Animals were exposed to 30 mg/m^3 compost dust for 4 hr and studied 0 and 18 hr after the end of this exposure. This exposure dose was chosen to mimic spore counts measured in the dust cloud generated at the job site (Fig. 1).

Analysis of Dust in the Exposure Chamber

Air samples were taken from the exposure chamber at various times. The mass median aerodynamic diameter of the dust was determined with a cascade impactor [Jones et al., 1983]. Dust samples were analyzed for spores under a light microscope.

Pulmonary Mechanics

Breathing rate was determined using methods similar to those previously described [Ellakkani et al., 1984]. Briefly, an animal was placed in a glass plethysmograph in which small differences in pressure were created by changes in the humidity, temperature, and compression of gas entering and leaving the lungs. These pressure changes, which were proportional to the animal's breathing pattern, were measured with a sensitive pressure transducer (Setra Model #239). The spectral content of the pressure signal, which included the fundamental breathing frequency and harmonics, was computed with a high resolution signal analyzer (B&K, Model #2033). Breathing frequency was measured during a challenge with 10% CO_2.

Postmortem pulmonary hyperinflation due to gas trapping and wet/dry weights were assessed on the exposed animals not used in the lung cellular analysis. These measurements were made prior to exposure to compost dust (n = 6), immediately following exposure (n = 6), and 18 hr after exposure to compost dust (n = 6) using the technique described by Stengel et al. [1980]. Animals were injected intraperitoneally with 1.0 ml of sodium pentobarbital; they died within a few minutes of injection. The abdomen was opened, the diaphragm sectioned, and the lungs allowed to deflate passively. Next, the trachea was exposed, and a 1.25-in polyethylene tracheal cannula was tied in place. The lungs were excised and placed in a beaker containing physiological saline. In less than 5 min, the lungs were weighed in air (W_t), then weighed a second time while inverted in saline using a balance (Mettler H2OT). The lung cannula was securely fastened to a solid metal tube embedded in a brass weight. The buoyant force on the lung containing trapped gas could be determined by the change in weight of the brass weight (ΔW_T) with and without the lung in place. The volume of gas within the excised lung (ELGV) could then be calculated using the following relationship:

$$ELGV = \{\Delta W_T - W_t [1 - SG_{H_2O}/SG_T]\} 1/SG_{H_2O},$$

where SG_{H_2O} is the specific gravity of physiological saline and SG_T is the specific gravity of lung tissue. For purposes of comparison, the ELGV measurements were normalized with respect to body weight (ELGVN). These trapped gas values have been shown to reflect the degree of airway obstruction in guinea pigs [Stengel and Silbaugh, 1986; Amdur and Mead, 1981].

Immediately following each ELGVN measurement, the lung W_{WET}/W_{DRY} weight ratio was determined by weighing the lung lobes (W_{WET}), then placing them in a drying oven at 80°C for 48 hr to remove the water, and weighing them a second time (W_{DRY}).

Cellular Responses

Alveolar macrophages and pulmonary leukocytes were harvested by bronchoalveolar lavage using a Ca^{2+} and Mg^{2+}-free Hank's balanced salt solution [Miles et al., 1978]. Briefly, an animal was anesthetized with sodium pentobarbital, the trachea cannulated, and the lungs lavaged (7–8 ml/lavage) until a total of 80 ml of lavage fluid was collected. Cells were then centrifuged, washed, and resuspended in HEPES-buffered medium (145 mM NaCl, 5 mM KCl, 1 mM $CaCl_2$, 5.5 mM glucose, and 10 mM Na HEPES (pH = 7.4)).

Differential cell counts were made using an electronic cell counter (Coulter Counter Z_{BI}) with a cell sizing attachment (Channelizer 256; Coulter Electronics, Inc., Hialeah, FL). Using this system alveolar macrophages, lymphocytes, and granulocytes can be distinguished by their characteristic volume distributions [Castranova et al., 1990]. These differential cell counts were verified microscopically on selected samples using a Wright-Giemsa stain.

Superoxide anion release was measured at rest and after stimulation with unopsonized zymosan (2 mg/ml) by monitoring the reduction of cytochrome C spectrophotometrically at 550 nm [Miles et al., 1978]. Assays contained 3.11×10^6 alveolar macrophages in 6 ml of HEPES-buffered medium. Experiments from our laboratory indicate that contaminating leukocytes do not secrete significant levels of superoxide in response to unopsonized zymosan (data not shown).

Statistical Analysis

Statistical analysis employed the t test with significance set at $p \leq 0.05$. All data points represent the mean of at least six experiments using separate animals.

Disclaimer

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RESULTS

Aerosolized compost dust in the animal exposure chamber was characterized for spore count (Fig. 1) and mass median aerodynamic diameter (Fig. 2). Spore concentrations in the exposure chamber (approximately 2×10^9 spores/m^3) were similar to those found directly in the dust cloud generated at the workplace during shoveling and bagging of the leaf/wood compost. Similarly, both dust in the exposure system and at the job site exhibited a mass median aerodynamic diameter of approximately 3 μm.

Inhalation of compost dust resulted in significant changes in the pulmonary parameters of guinea pigs. Changes in breathing rate of guinea pigs at various times after exposure are shown in Figure 3. Immediately after exposure to compost dust, breathing rate increased significantly (↑ 17%). Breathing rate continued to rise to 36% above the control level at 12 hr postexposure and remained near this level at 18 hr postexposure.

Wet/dry weight of excised guinea pig lungs did not change significantly following exposure to compost dust (Fig. 4). In contrast, a significant increase (120%) in trapped gas, reflecting airway obstruction, was noted immediately following exposure (Fig. 5). This airway response declined with time after inhalation of compost dust, being only 53% above control 18 hr postexposure.

The yield of lavagable macrophages, lymphocytes, and granulocytes is given in Figure 6A–C, respectively. The number of alveolar macrophages or lymphocytes harvested by lavage was not significantly affected by inhalation of compost dust. In contrast, granulocyte infiltration was dramatic, i.e., increasing 5.5-fold immediately after a 4 hr exposure to compost dust and increasing 16-fold 18 hr postexposure.

The state of activation of alveolar macrophages after compost dust exposure was monitored by measuring superoxide anion secretion at rest (Fig. 7A) and after stimulation with zymosan particles (Fig. 7B). Resting superoxide secretion was unaf-

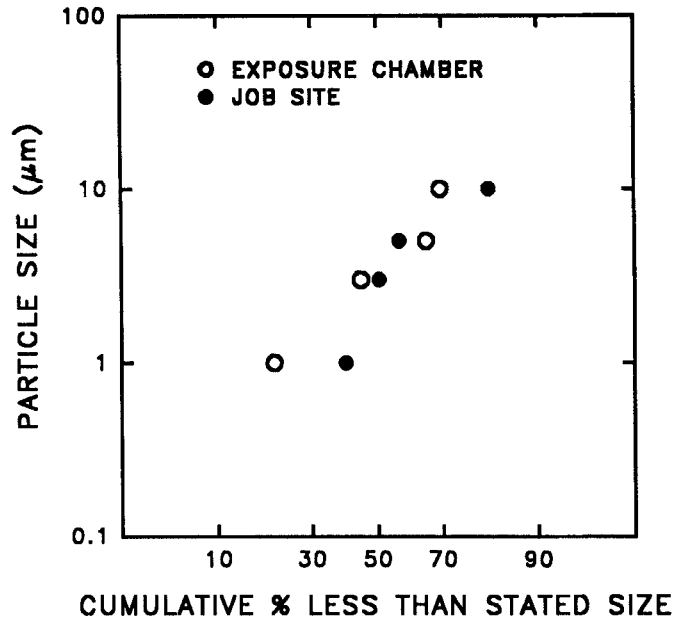

Fig. 2. Cumulative particle size distributions of compost aerosols collected at the job site and in the exposure chamber.

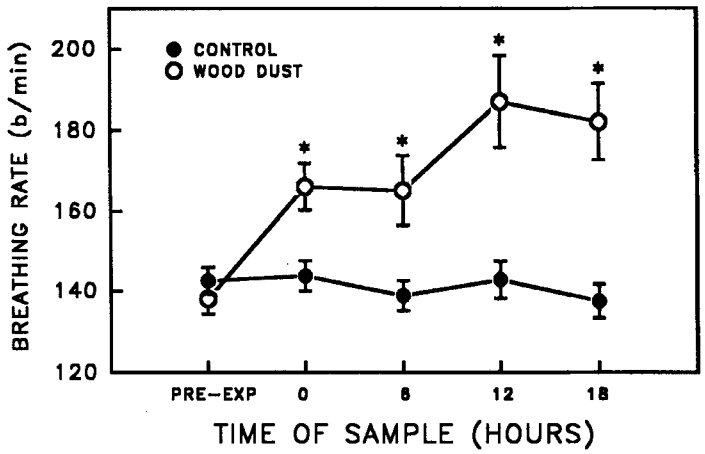

Fig. 3. Effect of inhalation of compost dust on the breathing rates of guinea pigs challenged with 10% CO_2. Values are means ± standard errors of data from at least six separate animals. *indicates a significant increase above the unexposed level ($p \leq 0.05$).

fected by inhalation of compost dust. In contrast, particle-stimulated superoxide release was significantly elevated (↑ 65%) 18 hr postexposure.

DISCUSSION

This investigation describes the pulmonary responses of a guinea pig animal model to inhalation of leaf/wood compost dust. The dust used in the exposure study

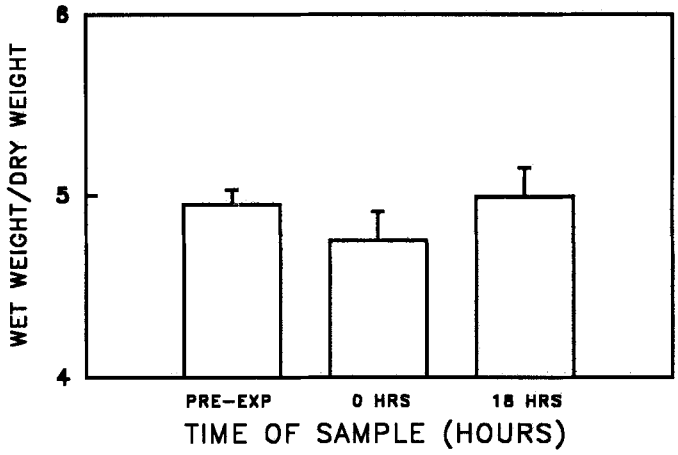

Fig. 4 Effect of inhalation of compost dust on wet/dry weight of excised guinea pig lungs. Values are means ± standard errors of six experiments.

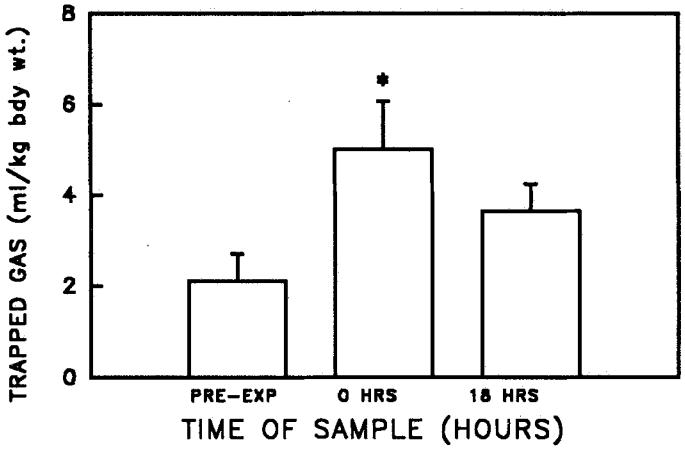

Fig. 5. Effect of inhalation of compost dust on trapped gas (normalized excised lung gas volume) of guinea pigs. Trapped gas reflects airway obstruction. Values are means ± standard errors of six experiments. * indicates a significant increase above the unexposed level ($p \leq 0.05$).

was similar in spore concentration and particle size to that generated at a job site where a worker became ill.

After inhalation of compost dust, guinea pigs exhibited an increased breathing rate, airway obstruction, infiltration of granulocytes, and stimulation of superoxide secretion from alveolar macrophages exposed to zymosan particles. With the exception of airway obstruction, all of the above parameters were maximally affected approximately 18 hr postexposure. In contrast, airway obstruction was most pronounced immediately after exposure and declined towards normal with time.

There are several similarities between the responses of the animal model to inhalation of compost dust and those of the affected worker [Weber et al., 1990]. Upon admission into the hospital, i.e., 12 hr after exposure, the patient exhibited

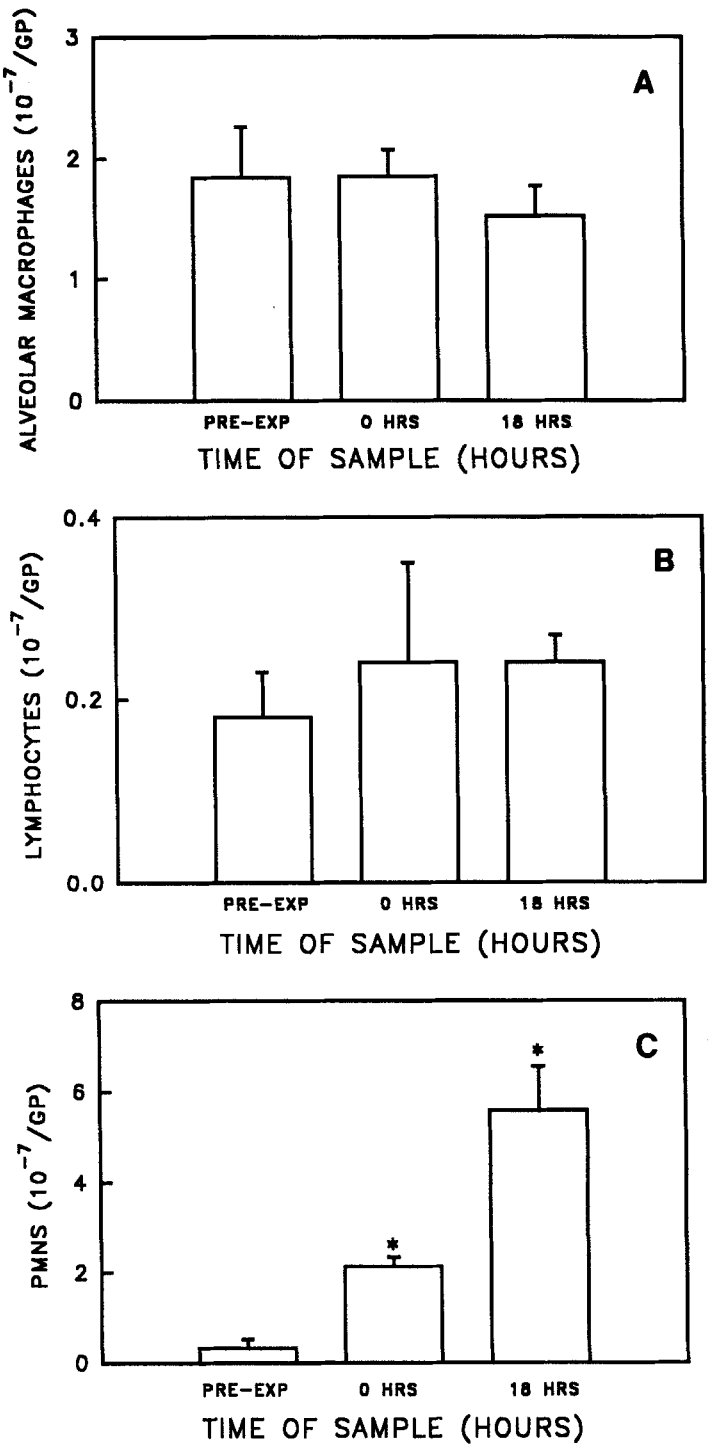

Fig. 6. Effect of inhalation of compost dust on the number of alveolar macrophages (**A**), lymphocytes (**B**), or granulocytes, i.e., mostly polymorphonuclear leukocytes (**C**), harvested by bronchoalveolar lavage of guinea pigs. Values are means ± standard errors of six experiments. * indicates a significant increase above the unexposed level ($p \leq 0.05$).

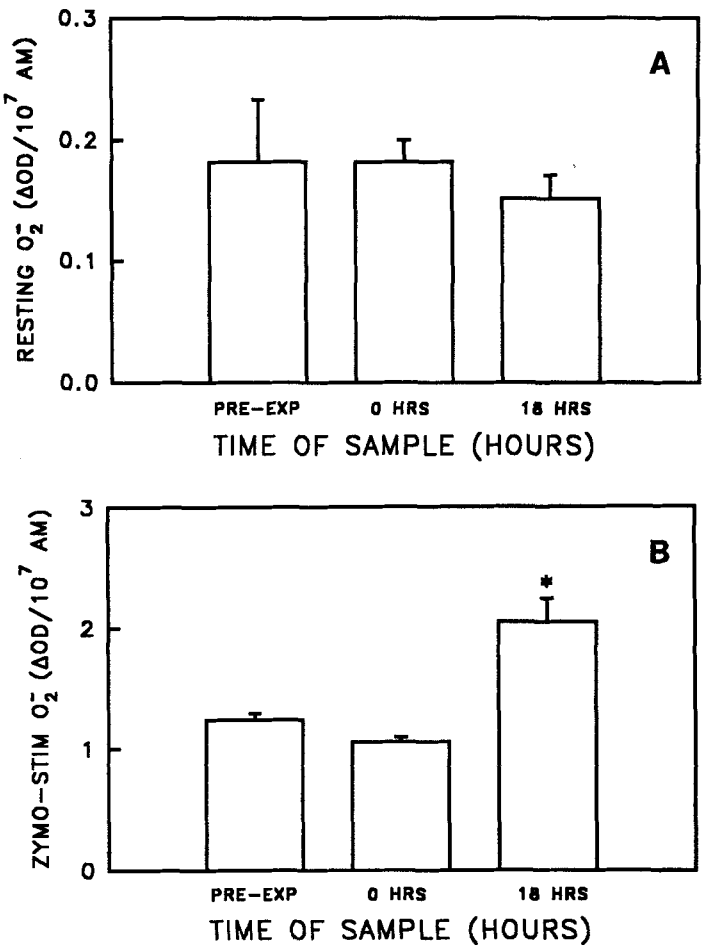

Fig. 7. Effect of inhalation of compost dust on resting (**A**) and zymosan-stimulated (**B**) superoxide release from alveolar macrophages. Values are means ± standard errors of six experiments. *indicates a significant increase above the unexposed level ($p \leq 0.05$).

labored breathing. His respiratory rate (30 b/min) and peripheral leukocyte count (11.9 K/μl) were elevated. These reactions were significantly diminished by the next morning.

The responses of the guinea pig model to inhalation of compost dust are nearly identical to those reported by our laboratory in previous studies with cotton dust [Robinson et al., 1988; Castranova et al., 1987, 1990; Frazer et al., 1989]. The only exceptions noted are that lymphocytes and wet/dry weight are elevated after exposure to cotton dust while being unchanged after compost dust inhalation. Such similarity in the animal model argues in favor of the proposal by Rylander [1990] that there is a commonality in the responses to a variety of organic dusts. Indeed, Von Essen et al. [1988] have shown that neutrophil infiltration occurs after exposure to grain dust.

Endotoxin has been proposed as the etiologic agent for neutrophil recruitment after exposure to organic dust [Rylander and Fischer, 1986]. However, grain dust and

cotton dust extracts still cause leukocyte infiltration after endotoxin has been removed [Von Essen et al., 1988; Ainsworth et al., 1981]. Recently, our laboratory has shown that cotton dust contains the chemotactic peptide (n-formyl-methionyl-leucyl-phenylalanine) [Fedan et al., 1990]. This peptide is a bacterial product which should be common to all bacterially contaminated organic dusts. We have shown that this agent is not only a chemoattractant for leukocytes, but also directly causes contraction of airway smooth muscle [Fedan et al., 1990]. Therefore, it may play an important role in the pulmonary response to organic dust inhalation.

As with cotton dust, inhalation of compost dust increased zymosan-stimulated superoxide release from alveolar macrophages but did not affect resting release. We have reported analogous results with macrophages treated with platelet-activating factor (PAF), i.e., PAF did not stimulate resting alveolar macrophages but potentiated the response of macrophages to particle stimulation [Kang et al., 1991]. Evidence indicates that cotton dust and endotoxin can stimulate phagocytes to release PAF [Kang et al., 1991; Leaver et al., 1990; Rylander and Beijer, 1987]. Therefore, PAF may play a role in the activation of alveolar macrophages seen after exposure to organic dust.

In conclusion, the results indicate that the guinea pig model is responsive to inhalation of leaf/wood compost as well as to cotton dust. This animal model may prove useful in determining the potential human toxicity of organic dusts and in elucidating the mechanisms controlling pulmonary reactions to organic dust exposures.

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