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Organic Dust Exposures From Compost Handling: Case Presentation and Respiratory Exposure Assessment

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Inhalation of dust from contaminated organic materials may result in acute respiratory tract illness. Possible mechanisms include toxic and cellular reactions to microbial and other organic products or immunologic responses after prior sensitization to an antigen. A case is presented of a 52 year old male who developed fever, myalgia, and marked dyspnea 12 hr after shoveling composted wood chips and leaves. Inspiratory crackles, hypoxemia, and bilateral patchy pulmonary infiltrates were seen. Precipitating antibody tests for the usual antigens were inconclusive. He improved over 3 days.

In order to assess the environmental conditions the patient had experienced, we returned to the site to reproduce and measure respiratory exposures during hand loading of the compost. Visible clouds of fine particulate were easily generated during handling activities. Microscopic examination of these dusts indicated a predominance of spores. Endotoxin concentrations from inspirable and respirable dust samples ranged from 636 to 16,300 endotoxin units/m^3. Levels of contaminants found were consistent with those associated with respiratory illness in other agricultural settings.

Two respiratory disorders, hypersensitivity pneumonitis (HP) and organic dust toxic syndrome (ODTS), may occur after exposure to organic dusts containing fungal spores and endotoxins. Despite extensive clinical and environmental investigations, we were unable to differentiate these two disorders, and suggest they may represent parts of a spectrum of responses to complex organic dusts, rather than completely distinct clinical entities.

Key words: organic dust toxic syndrome, hypersensitivity pneumonitis, wood chips, compost handling, endotoxin

INTRODUCTION

Hypersensitivity pneumonitis (HP), also called extrinsic allergic alveolitis, is an inflammation of the lung parenchyma thought to be related to an immunologic reac-

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tion to a variety of inhaled materials. Agents associated with HP include a variety of airborne organic dusts and several low molecular weight chemicals [Cotes and Steel, 1987]. Symptoms of HP such as cough, dyspnea, fever, or myalgias develop in a minority of exposed persons, and may evolve insidiously or acutely. Repeated acute attacks are thought to predispose to chronic irreversible respiratory impairment. Organic dust toxic syndrome (ODTS) is described as a febrile response to high concentrations of airborne organic dust. High attack rates are considered typical, and similarly exposed individuals often develop comparable symptoms. Common signs and symptoms of ODTS include weakness, dyspnea, myalgias, and leukocytosis. Both HP and ODTS have been associated with exposures to molds, fungal spores, bacteria, and endotoxin [doPico, 1986]. Distinguishing these two disorders is thought to be important, since recurrent acute attacks of HP are recognized as a risk factor for development of chronic lung disease [Braun et al., 1979]. While ODTS has not been associated with chronic respiratory illness, the separation of HP and ODTS may be difficult in the clinical setting, in light of the overlapping clinical presentations.

We present a patient who developed an acute respiratory illness after shovelling mulch composed of composted wood chips and chopped leaves. The clinical findings met criteria for both HP and ODTS. Environmental studies of the compost pile were done to characterize the exposure which resulted in this patient's respiratory illness.

CASE PRESENTATION

A 52-year-old nonsmoking male landscape architect presented to the emergency department on July 10, 1989 with dyspnea, fever, headache, and myalgia progressing over 6 hr. Twelve hours prior to presentation, he had shovelled composted wood chips and leaves. The compost was produced from local tree pruning operations by power company contractors; compost materials included chopped leaves and branches added in successive layers to form compost piles, and were stored outdoors.

Examination revealed the patient in moderate respiratory distress, with a respiratory rate of 30, heart rate of 120, and an oral temperature 38.8°C. Lung auscultation showed fine bibasilar crackles without wheezing. Chest radiographs demonstrated bilateral infiltrates (Fig. 1). Arterial PO_2 breathing air was 53 mm Hg. The leukocyte count was 11.9 K/μl with 86 percent polymorphonuclear leukocytes and 6 percent immature forms.

Systemic steroid therapy was initiated. During the next twelve hr the pulmonary infiltrates and hypoxemia worsened, but then improved over the subsequent three days. Pulmonary function testing the morning after admission revealed mild restriction (FVC 3.37 liters, 68% predicted). The symptoms and infiltrates improved, and the patient was discharged on the third hospital day.

Serum samples drawn during the acute phase of the illness were sent to two laboratories. One laboratory reported no precipitating antibodies to 10 common hypersensitivity pneumonitis antigens, while the other reported elevated titers to *Aspergillus flavus* and *Aspergillus niger*. Serum from the patient did show precipitation with extracts of bulk samples of the compost material.

One month later the patient had no respiratory symptoms, and spirometry was normal. Serum was again sent to two laboratories, and titers were identical to the initial samples.

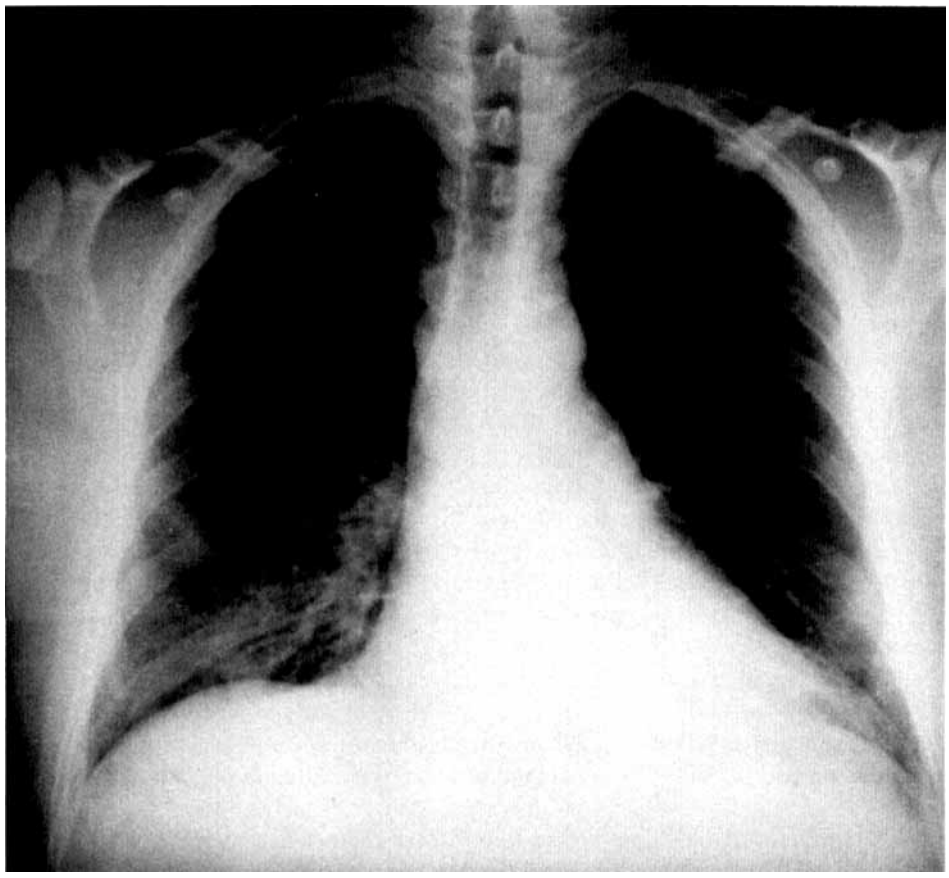

Fig. 1. Chest radiographic infiltrates on admission to hospital of patient with illness related to compost handling.

ENVIRONMENTAL STUDY METHODOLOGY

We returned to the compost pile and attempted to reproduce the exposure setting while making extensive environmental measurements [Kullman et al., 1990]. Industrial hygiene samples were collected to determine exposures to organic dusts and microorganisms generated during compost handling.

Bulk samples of compost were collected on July 11 and 13, 1989 to identify the types of microorganisms present. Bulk samples were suspended in phosphate buffered saline, serial 10-fold dilutions were made, and 0.1 ml portions of each dilution were plated in triplicate on the following media: 1) rose bengal streptomycin agar (RBS) for mesophilic fungi (25°C for >5 days); 2) tryptic soy agar (TSA) for mesophilic bacteria (35°C for 48 hr); 3) half-strength tryptic soy agar (TSA/2) for thermophilic actinomycetes (55°C for <7 days); and 4) eosin methylene blue agar (EMB) for Gram-negative bacteria (35°C for 48 hr) [Rogerson, 1958]. Fungal and bacterial colonies were counted and expressed as colony-forming units per gram of compost (CFU/g). The predominant fungi were identified on the basis of colony and microscopic morphology.

Air samples were collected on August 4, 1989 to assess inspirable and respirable dusts, particle size distributions, endotoxins, spores, viable microorganisms, and gases/vapors. Attempts were made to duplicate compost hand loading activities and related exposures as described by the patient. During compost handling, NIOSH investigators used respiratory protection.

Area samples were collected from three different sampling locations. To estimate the "routine" exposures from compost loading and unloading, some samples were collected by positioning the samplers in baskets suspended on a vertical stand at the breathing zone level. Samples were also collected to assess "worst-case" exposures by positioning the sampling equipment directly in visible clouds of dust generated by compost agitation. A third sampling station was positioned upwind from the compost pile to measure background concentrations of some environmental analytes. Airborne dust samples were collected with respirable and inspirable inlets on polyvinyl chloride filter media using portable sampling pumps operated at 1.7 liters per minute (lpm) and 2.0 lpm, respectively [Vincent and Mark, 1987; Hinds, 1982]. These samples were analyzed gravimetrically with an electrobalance. Respirable and inspirable dust samples were also analyzed for endotoxin content, expressed as endotoxin units per cubic meter of air (EU/m^3), by the chromogenic modification of the *Limulus* amebocyte lysate gel test [Olenchock, 1990].

Samples for airborne spores were collected on cellulose ester and polycarbonate filter media. In open-faced filter cassettes, spore counts were made by phase contrast light microscopy at approximately 500× magnification. Certain polycarbonate filters were stained with acridine orange and observed using fluorescence microscopy. Other filters were coated with metal and observed using scanning electron microscopy at approximately 4,000–5,000× magnification [Heikkila, 1988; Palmgren et al., 1986].

Samples for viable bacteria and fungi in air were collected using the All Glass Impinger (AGI) operated at 12.5 lpm with sterile, distilled water media [ACGIH, 1983; Brachman, 1964]. A cellulose ester filter was used in line as a backup to the impinger. Aliquots of impinger solution were spread across nutrient agar and incubated to grow fungi or bacteria to calculate airborne concentrations of bacteria and fungi in colony-forming units per cubic meter of air (CFU/m^3). The backup filter was analyzed for the presence of spores using phase contrast light microscopy.

Particle size distributions in air were measured using a five stage cascade impactor with effective aerodynamic cutoff diameters of 10 micrometers (μm)—stage 1, 5 μm—stage 2, 3 μm—stage 3, 1 μm—stage 4, and <1 μm backup filter. These samples were analyzed gravimetrically with an electrobalance [Jones et al., 1983].

Samples were taken for airborne gases and vapors during compost handling. Gas samples were collected in Tedlar bags using a portable sampling pump. These samples were analyzed within approximately three hr using infrared spectroscopy [Levine, 1989].

ENVIRONMENTAL RESULTS

The wood compost materials consisted of successive layers of chopped leaves, bark, and wood stored outdoors during a spring of high rainfall. Visible clouds of fine particulate were easily generated by agitation of these compost materials (Fig. 2). Bulk samples of the compost contained high concentrations of aerobic bacteria and

Fig. 2. Dust clouds generated during shovelling of wood compost.

fungi (Fig. 3). Sample 3 was collected from compost materials that appeared newly cut/mulched which may account for some of the differences in concentrations. Aspergillus and penicillium were the predominant fungi. Yeast colonies were also present in these samples (7.0×10^7 to 3.0×10^8 CFU/g). The mesophilic bacteria in the bulk samples were almost entirely Gram-negative (1.8×10^9 to 1.9×10^{10} CFU/g). Thermophilic actinomycete concentrations in these samples were lower (4.7×10^4 to 4.0×10^6 CFU/g). However, plate counts of thermophilic actinomycetes were problematic due to overgrowth by other thermophilic bacteria. These data show that the compost materials, stored outdoors in rainy environmental conditions, created a suitable substrate for the growth of many fungi and bacteria.

The inspirable and respirable dust measurements made during compost hand loading are reported in Table I. Dust concentrations measured during "worst-case" exposure conditions suggest a potential for brief periods of high organic dust exposures. Measurements taken to characterize the particle size distribution of these organic dusts indicated a mass median aerodynamic diameter (MMAD) of approximately 3 micrometers during "worst-case" exposure conditions.

Endotoxin was present in the airborne dusts at concentrations ranging from 636 to 16,300 EU/m^3 (Fig. 4). Fungal concentrations of air samples taken during compost handling operations were 1.4×10^6 CFU/m^3 during "routine" exposure and 4.7×10^8 CFU/m^3 during "worst-case" exposure. Total bacterial concentrations in air ranged from 6.3×10^5 to 7.7×10^8 CFU/m^3; background bacterial concentrations were below detectable limits. Most of the bacteria in these samples were Gram-negative, endotoxin-producing bacteria. The thermophilic actinomycete bacterial concentrations were lower. Microscopic examination of the impinger backup filter

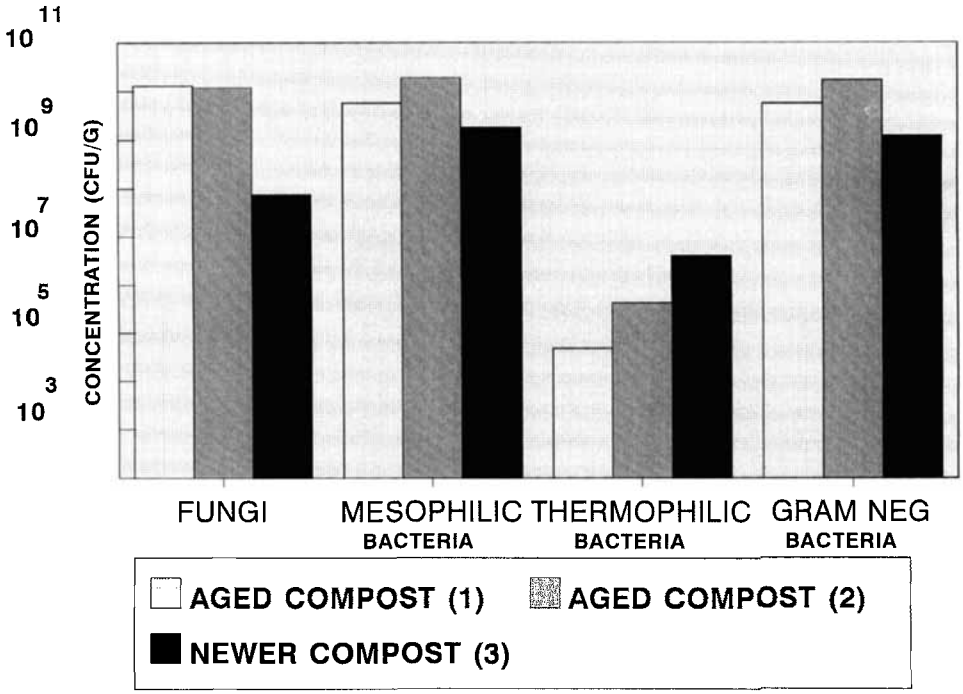

Fig. 3. Viable microorganisms isolated from bulk samples of three compost piles (colony-forming units/gram).

TABLE I. Inspirable and Respirable Dust Concentrations in Air During Compost Handling

Exposure	Sampling Time (minutes)	Inspirable dust mg/m^3	Respirable dust mg/m^{3a}
Routine	141	0.74	0.42
Worst-case	20	149	83
Background	232	0.32	—

[a]mg/m^3: Milligrams of dust per cubic meter of air.

revealed that some of the smaller fungal spores and bacteria (e.g., thermophilic actinomycetes) can penetrate the impinger, and the actual viable bacteria and fungal concentrations are likely higher than those reported here.

Airborne total dust samples analyzed by scanning electron microscopy, differential interference contrast microscopy, and epifluorescent microscopy with acridine orange staining indicate that fungal spores comprise a majority of airborne particles. The spore concentration from the six routine exposure estimates was $1.3 \pm 2.2 \times 10^8$ spores/m^3, while spore counts from "worst-case" exposure samples were $3.7 \pm 2.5 \times 10^9$ spores/m^3.

The infrared spectra from the gas sample collected at the job site were similar to the spectra obtained from the sample collected upwind of the site suggesting that, in this outdoor setting, there is sufficient dilution to prevent buildup of any gases from compost decomposition.

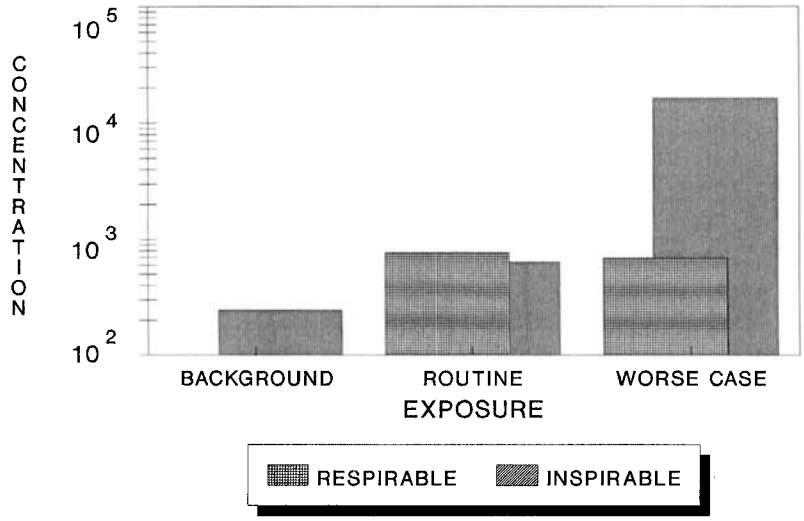

Fig. 4. Airborne respirable and inspirable endotoxin concentrations during compost handling (endotoxin units/m^3).

DISCUSSION

ODTS was initially described as "pulmonary mycotoxicosis" by Emanuel [1975]. Symptoms usually develop 4–6 hr after exposure. Fever and cough are almost always associated with the onset of symptoms. Hypoxia and bibasilar crackles on chest auscultation are also commonly noted [Merchant, 1987]. Patients may show patchy infiltrates on chest radiographs, and some may also have elevated serum precipitins [Rask-Anderson and Malmberg, 1990]. ODTS is probably not mediated through a classical immunological response, but may be mediated by interleukins [Malmberg et al., 1988]. Neutrophils may predominate early in the lung inflammatory response, but lymphocytosis can be seen later [Lecours et al., 1986]. After recovery from the acute illness, the development of chronic lung impairment in patients with ODTS has not been reported.

HP was recognized by Ramazzini [1713] and has now been described in many occupational and nonoccupational groups, including bird breeders, office workers exposed to humidifier systems contaminated with fungal spores or amoeba, and farmers exposed to moldy hay and decaying vegetable matter or wood products [Campbell, 1932; Finnegan et al., 1985; Salvaggio, 1987]. Several authors have reported HP following exposure to moldy wood planks or wood chips [Belin et al., 1987; Dykewicz et al., 1988; Kolmodin-Hedman et al., 1987; Enarson et al., 1990; Jappinen et al., 1987]. Previous exposure, with immunologic sensitization, is thought to be required prior to the development of HP.

The reported incidence of HP in individuals chronically exposed to potential antigens is generally low, consistent with a hypersensitivity reaction, 0.03 percent in Swedish farmers [Malmberg et al., 1988] and 0.42 percent in a Wisconsin farming population [Gruchow et al., 1981]. However, it has been reported in 15 percent of office workers exposed to contaminated ventilation systems [Finnegan et al., 1985].

The acute syndrome, as in ODTS, generally develops 4–6 hr after exposure.

Symptoms may last several days, almost always less than two weeks, and often recur with re-exposure. Fever, cough, dyspnea, and hypoxemia, along with generalized body aches and weakness, are the most commonly associated findings. Three major diagnostic criteria include exposure, flu-like symptoms, and infiltrative changes on chest radiograph not associated with other disease processes [Terho, 1986].

The pathogenesis of HP is not well understood. The reaction initially was thought to involve a type III antigen-antibody hypersensitivity reaction, or "Arthus" response [Nicholson, 1972], although lymphocytosis and evidence of type IV, cell-mediated immunity is currently thought to indicate the primary mechanism of disease [Reynolds, 1988]. Even without a previous sensitizing exposure, laboratory animals may show an inflammatory lung response after inhalation of these same compost dusts [Frazer et al., 1990].

Measurement of serum precipitins to potential etiologic agents is neither sensitive nor specific. In one study of asymptomatic pigeon breeders, precipitating antibodies against pigeon antigens were identified in forty percent of the subjects [Fink et al., 1972]. In a study of Swedish farmers with HP, precipitating antibodies were identified in only forty percent of symptomatic individuals [Malmberg et al., 1988]. The high rates of false positivity and false negativity in measurements of precipitating antibodies in HP may be related to uncertainty in identification of the etiologic antigens. Our patient did show serum precipitation to extracts of bulk samples of the compost material, but this test is not widely available, and its significance is unknown. It has been suggested that precipitating antibodies simply represent evidence of exposure to specific agents and not necessarily the mechanism of disease [Burrell and Rylander, 1981].

The compost implicated in this illness was remarkable in the almost explosive release of dust on minimal handling. The respirable size of these airborne dusts would permit penetration to the pulmonary air spaces which may be necessary to elicit certain respiratory illnesses [May et al., 1986]. Viable fungal concentrations in air exceeded 10^6 CFU/m^3 and airborne spore counts were even higher with an average concentration of 3.7×10^9 spores/m^3 during "worst-case" exposure conditions. These concentrations are high in comparison to agricultural settings [May et al., 1986; Donham, 1986]. Aspergillus and penicillium, the predominant genera of fungi, are described as a cause of hypersensitivity pneumonitis in other occupational settings and these fungi may possibly contribute to other pulmonary responses [May et al., 1986; Malmberg et al., 1990]. Gram-negative bacteria and bacterial endotoxin were also a significant exposure hazard in airborne dusts generated during handling of these compost materials. Concentrations of viable, thermophilic bacteria were lower than Gram-negative and total mesophilic bacteria in both air and bulk compost samples.

Numerous studies have demonstrated a relationship between endotoxin exposure and acute respiratory symptoms [Castellan et al., 1987; Rylander et al., 1985; Jacobs, 1989]. Studies of inhalation exposure to endotoxins in cotton dusts demonstrate a threshold for human ventilatory responses of approximately 90 EU/m^3 [Castellan et al., 1987]. Endotoxin concentrations measured during compost handling ranged from 636 to 16,300 EU/m^3, all in excess of this estimated threshold level. Based on endotoxin concentrations alone, these compost dusts would present a health risk. The high concentrations of viable fungi and spores in these materials add to the potential health hazards from exposure to this compost.

CONCLUSIONS

This case demonstrates many of the difficulties encountered when attempting to differentiate acute HP and ODTS. The exposure settings associated with these conditions, as well as the onset, duration, and type of symptoms, may be similar. Reported attack rates in ODTS are generally high, but in HP have been both low and high. Thus, the prevalence of illness in coworkers may not be helpful. The lack of specificity in the measurement of serum precipitins makes it likely that precipitating antibodies will be detected in some patients who have nonimmunologically mediated febrile responses to organic dusts. It is also not likely that skin testing would be useful to differentiate these syndromes, although this has not been studied.

Findings on physical examination and chest radiography are not helpful in differentiating HP and ODTS, as patients with both conditions have been described with fever, bibasilar lung crackles, and patchy infiltrates on chest radiograph. Although radiographic infiltrates are thought uncommon in ODTS, few studies are available. Certain authors have even excluded the diagnosis of ODTS if the chest film is abnormal [May et al., 1986].

An extensive environmental exposure characterization was performed in this case. High concentrations of airborne Gram-negative bacteria, endotoxins, and fungal spores were measured during compost handling activities. We were able to define neither a specific etiologic agent nor a particular disease process. However, respiratory illness from exposure to these organic dust constituents is well described, and it seems likely that the illness was caused by the exposure. It is certainly advisable that individuals handling similar substances exercise caution, and avoid inhaling dusts generated from these compost materials.

HP and ODTS are difficult to differentiate. When epidemiologic information is available it may be helpful in differentiating HP and ODTS, as there is much clinical overlap in these two syndromes. Current knowledge suggests they may in fact represent parts of a spectrum of responses to complex organic dusts, rather than completely distinct clinical entities.

REFERENCES

American Conference of Governmental Industrial Hygienists (1983): "Air Sampling Instruments, 6th Ed." Cincinnati: ACGIH, pp E1–9.

Belin L (1987): Sawmill alveolitis in Sweden. Int Arch Allergy Appl Immunol 82:440–443.

Brachman PA (1964): Standard sampler for assay of airborne microorganisms. Science 144(3634):1295.

Braun SR, doPico GA, Tsiatis A, Horvath E, Dickie HS, Rankin J (1979): Farmer's lung disease: Long-term clinical and physiologic outcome. Am Rev Respir Dis 119:185–191.

Burrell R, Rylander R (1981): A critical review of the role of precipitins in hypersensitivity pneumonitis. Eur J Respir Dis 62:332–1343.

Campbell JM (1932): Acute symptoms following work with hay. Br Med J 2:1210–1212.

Castellan RM, Olenchock SA, Kinsley KB, Hankinson JL (1987): Inhaled endotoxin and decreased spirometric values: An exposure-response relation for cotton dust. New Engl J Med 317:605–610.

Cotes JE, Steel J (1987): "Work-Related Lung Disorders." Oxford: Blackwell.

Donham KJ (1986): Hazardous agents in agricultural dusts and methods of evaluation. Am J Ind Med 10:205–220.

doPico GA (1986): Report on diseases. Am J Ind Med 10:261–265.

Dykewicz MS, Laufer P, Patterson R, Roberts M, Sommers HM (1988): Woodman's disease: Hypersensitivity pneumonitis from cutting live trees. J Allergy Clin Immunol 81:455–460.

Emanuel DA, Wenzel FJ, Lawton BR (1975): Pulmonary mycotoxicosis. Chest 67:293–297.

Enarson DA, Chan-Yeung M (1990): Characterization of health effects of wood dust exposures. Am J Ind Med 17:33–38.

Fink JN, Schlueter DP, Sorsmon AJ, Unger GF, Borboriak JJ, Rimm AA, Arkins JA, Dhaliwal KS (1972): Clinical survey of pigeon breeders. Chest 62:277–281.

Finnegan MJ, Pickering CA, Davies PS, Austwick PK (1985): Factors affecting the development of precipitating antibodies in workers exposed to contaminated humidifiers. Clin Allergy 15:281–292.

Frazer DG, Jones W, Petsonk EL, Kullman G, Barger MW, Afshari A, Jones T, Castranova V (1990): Pulmonary response to the guinea pig animal model to inhalation of leaf/wood compost. Am Rev Respir Dis 141:(4);A588.

Gruchow HW, Hoffman GR, Marx JJ, Emanuel DA, Rimm AA (1981): Precipitating antibodies to farmer's lung antigens in a Wisconsin farming population. Am Rev Resp Dis 124:411–415.

Heikkila P (1988): Identification and counting of fungal spores by scanning electron microscope. Ann Occup Hyg 32:241–248.

Hinds WV (1982): "Aerosol Technology." New York: John Wiley & Sons, pp 69–126.

Jacobs RR (1989): Airborne endotoxin: An association with occupational lung disease. Appl Ind Hyg 4:50–56.

Jappinen P, Haahtela T, Liira J (1987): Chip pile workers and mold exposure. J Allergy 42:545–548.

Jones J, Jankovic J, Baron P (1983): Design construction and evaluation of a multi-stage "cassette" impactor. Am Ind Hyg Assoc J 44:409–418.

Kolmodin-Hedman B, Blomquist G, Lofgren F (1987): Chipped wood as a source of mould exposure. Eur Resp J 154:44–51.

Kullman GJ, Jones WG, Olenchock SA, Sorenson WG, Marcelo-Baciu R, Petsonk EL, Parker JE (1990): Organic dust exposures from compost handling operations. Presented at the Conference of the American Industrial Hygiene Association.

Lecours R, Laviolette M, Cormier Y (1986): Bronchoalveolar lavage in pulmonary mycotoxicosis (organic dust toxic syndrome). Thorax 41:924–926.

Levine P (1989): Advantages and disadvantages in the use of fourier transform infrared (FTIR) and filter infrared (FIR) spectrophotometers for monitoring airborne gases and vapors of industrial hygiene concern. Appl Ind Hyg 4:180–187.

Malmberg P, Rask-Andersen A, Hoglund S, Kolmodin-Hedman B, Guernsey JR (1988): Incidence of organic toxic dust syndrome and allergic alveolitis in Swedish farmers. Int Arch Allergy Appl Immunol 87:47–54.

Malmberg P, Rask-Andersen A, Lundholm M, Palmgren U (1990): Can spores from molds and actinomycetes cause an organic dust toxic syndrome and reaction? Am J Ind Med 17:109–110.

May JJ, Stallones L, Darrow D, Pratt D (1986): Organic dust toxicity (pulmonary mycotoxicosis) associated with silo unloading. Thorax 41:919–923.

Merchant JA (1987): Agricultural exposures to organic dusts. In Rosenstock L (ed): "Occupational Medicine, State of the Art Reviews." 2:409–425.

Nicholson DP (1972): Extrinsic allergic pneumonias. Am J Med 53:131–136.

Olenchock SA (1990): Endotoxins in various work environments in agriculture. In Pierce GE (ed): "Developments In Industrial Microbiology." Vol 31. Society for Industrial Microbiology, Amsterdam: Elsevier, pp 193–197.

Palmgren U, Strom G, Malmberg P, Blomquist G (1986): The nuclepore filter method: A technique for enumeration of viable and nonviable airborne microorganisms. Am J Ind Med 10:325–327.

Ramazzini B (1713): "De Morbis Artificum Diatriba." Chicago: University of Chicago Press, 1964.

Rask-Anderson A, Malmberg P (1990): ODTS in Swedish farmers: Symptoms, clinical findings, and exposure in 98 cases. Am J Ind Med 17:116–117.

Reynolds H (1988): Hypersensitivity pneumonitis: Correlation of cellular and immunologic changes with clinical phases of disease. Lung 166:189–208.

Rogerson CT (1958): Kansas aeromycology. I. Comparison of media. Trans Kans Acad Sci 61:155–162.

Rylander R, Haglind P, Lundolm M (1985): Endotoxin in cotton dust and respiratory function decrement among cotton workers in an experimental carding room. Am Rev Respir Dis 131:209–213.

Salvaggio JE (1987): Hypersensitivity pneumonitis. J Allergy Clin Immunol 79:558–571.

Terho EO (1986): Diagnostic criteria for farmer's lung disease. Am J Ind Med 10:329.

Vincent JH, Mark D (1987): Comparison of criteria for defining inspirable aerosol and the development of appropriate samplers. Am Ind Hyg Assoc J 48:454–457.