Organic dust toxic syndrome: A noninfectious febrile illness after exposure to the hog barn environment

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Organic dust toxic syndrome (ODTS), also called "toxic alveolitis" and "pulmonary mycotoxosis" in the current medical literature, is a very common noninfectious febrile illness that is seen after inhalation exposure to organic dust.[1–3] This problem occurs in a variety of work settings, but has been reported most often in individuals working in various aspects of production agriculture, including the hog confinement barn environment.[4] The worker's response to inhalation of organic dust consists of lung inflammation and a self-limiting systemic inflammatory reaction, usually lasting several days. Medical treatment is not required in most cases. However, people who have experienced ODTS symptoms are at increased risk both for respiratory symptoms with subsequent exposures to organic dust, and for developing chronic bronchitis.

Exposures linked to ODTS

Organic dust toxic syndrome was initially described in farmers heavily exposed to organic dust while unloading silos.[5] Fungal spores were seen on lung biopsy specimens of individuals who were quite ill with ODTS.[6] For this reason, the disorder was initially called "pulmonary mycotoxicosis" or "silo unloader's syndrome." Subsequently, ODTS was reported in persons handling stored grain, particularly grain that appeared to be heavily contaminated with bacteria or molds.[7,8] A study indicated that pig farmers are also at increased risk for developing ODTS.[9] The use of wood shavings as bedding in hog barns was clearly a risk factor. Exposure to moldy straw or wood chips in other farm settings has been linked to this illness. Symptoms of ODTS have also been reported in individuals who work with poultry, handle compost, and sort garbage or process cotton.[10–15]

Exposure to endotoxin is a factor common to these otherwise diverse occupations. Endotoxin levels are high in hog confinement barns, during silo unloading and chicken processing, and in other settings where ODTS occurs.[16] Experimental exposure of humans to endotoxin from the cell walls of gram-negative bacteria causes clinical signs and laboratory findings consistent with ODTS.[17] Challenge of laboratory animals with endotoxin causes neutrophilic inflammation of the lower respiratory tract, with evidence of systemic inflammation, much as in human subjects.[18] It is of note that hog barn dust is rich in endotoxins, and that endotoxin exposure has been implicated as one of the causes of airway disease in people who work in hog confinement barns.[19]

Exposure to materials that appear moldy has also been associated with ODTS. In a Swedish study,[20] higher mold spore counts were found on farms where workers had experienced ODTS symptoms than on farms where no ODTS symptoms had been reported. Inhalation challenge of laboratory animals with *Aspergillus fumigatus*, a mold commonly found in agricultural settings, caused neutrophilic lung inflammation similar to that seen after endotoxin challenge.[21] Human inhalation challenge with mold spores has not been performed for ethical reasons. However, molds have been cultured from the lung-biopsy specimens of patients with ODTS.[22] These observations, as well as reports from persons who had developed ODTS, suggest that inhalation exposure to mold spores is another cause of this syndrome. Although molds have been identified in hog confinement barns, it is not clear if the mold spore counts are sufficiently elevated to cause ODTS.[23,24] Therefore, inhalation exposure to endotoxin is considered the most likely cause of ODTS symptoms experienced by individuals who work in hog barns.

Diagnosis

A careful occupational exposure history, with an emphasis on work activities during the previous 48 hours, is key for making the diagnosis of ODTS. This history will often elicit a description of heavy inhalation exposure to organic dust, frequently without use of a respirator. If the task involves handling grain or fodder, these materials are frequently, but not always, described as being spoiled. Several persons working together may all become ill with ODTS.

Obtaining a detailed history of present illness and performing selected medical tests comprise the second component in diagnosing ODTS. Complaints commonly voiced include a nonproductive cough, fever, chills, malaise, chest tightness, and headache.[2] If medical attention is sought, auscultation of the thorax may be unremarkable. Alternatively, rales may be heard. Lung function test results may be normal or may show mild restriction and decrease in the diffusing capacity for carbon monoxide. Thoracic radiographs are often normal, but may show minimal interstitial infiltrates. Oxygen saturation level is in the normal range. The complete blood count (CBC) is often remarkable for leukocytosis with neutrophilia.

Seeing an elevated white blood cell count may cause the medical care provider to incorrectly conclude that the illness is infectious in nature. The history and CBC result of patients with ODTS may also be confused with those of acute hypersensitivity pneumonitis, also known as farmer's lung. However, patients with acute farmer's lung are more likely to have radiographic abnormalities, low blood oxygen levels, and restriction

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and a low diffusing capacity for carbon monoxide on lung function testing. Measuring serum allergic precipitins (ie, IgG antibodies to antigens in the agricultural setting that commonly cause farmer's lung) may also be useful in making the distinction between ODTS and farmer's lung. It is of note that farmer's lung has not been described in association with work in hog confinement barns. However, hypersensitivity pneumonitis can result from other farm exposures and from inhaling mold spores or thermophilic bacteria present in residential structures or office buildings.

On the very rare occasions where respiratory failure is suspected to have occurred secondary to the inflammatory response of ODTS, performing an open lung biopsy may be helpful. It is likely to show changes of acute inflammation, with infiltration of neutrophils and macrophages, in the terminal bronchioles of the lung, alveoli, and lung interstitium.[6] Fungal spores have been identified in the lung, but are not thought to represent an infection even though the organisms at times can be cultured from the biopsy specimen.

Pathophysiology

Organic dust toxic syndrome results from the response of the innate immune system to organic dust inhalation.[25] This reaction does not require prior sensitization and is not a specific response of the adaptive immune system. Neutrophil recruitment to the lung after organic dust exposure is a complex process. Neutrophil chemotaxis is facilitated by several mechanisms, including direct recruitment and, in response to swine-barn-dust or grain-dust challenge, through release from alveolar macrophages and bronchial epithelial cells of substances chemotactic for neutrophils, including the complement cascade component C5a, and interleukin-8 (IL-8).[26–28]

Fever is a prominent symptom in ODTS. Pyrogenic cytokines known to be released in response to exposure to swine-barn dust include IL-1 and IL-6.[27–29] It is very likely that release of these mediators contributes to fever and other inflammatory effects. Cytokine release has been studied in persons experimentally exposed to moldy wood chips in order to induce ODTS.[30] Neutrophils recovered by bronchiolar lavage increased in number in response to this challenge; in addition, IL-8, IL-6, and tumor necrosis factor increased.

Long-term effects

In a cross-sectional survey of Midwestern farmers, 30% reported having had ODTS symptoms.[8] There was a strong association between ODTS symptoms and cough or chest tightness with subsequent organic dust exposure (odds ratio 4.9 in men; 95% confidence interval, 2.5 to 9.9). These investigators did not find an association between ODTS symptoms and lung-function test abnormalities. There has been a strong association identified between reporting a history of ODTS and occurrence of chronic bronchitis in feed mill workers[31] and greenhouse workers.[32] The prevalence of chronic bronchitis is relatively high in workers exposed to swine confinement barns, with 13% to 20% of these individuals reporting chronic bronchitis symptoms.[9,33] It is possible, but as yet unproven, that the relatively high prevalence of chronic bronchitis in persons who work in this environment is in part related to a history of ODTS.

Epidemiology

Investigation of an outbreak of ODTS in a group of college students heavily exposed to dust from straw used to cover a dance floor at a party revealed that as many as 82% of a group of persons at risk for ODTS secondary to heavy organic dust exposure may become ill.[34] A survey of 6702 Swedish farmers revealed that 6% had a convincing history of a febrile illness after organic dust inhalation, usually reported after handling material that was clearly moldy.[12] Organic dust toxic syndrome was felt to be the cause of these reactions in 97% of subjects. A survey of pig farmers in the Netherlands yielded similar prevalence data.[9] Vogelzang et al[4] reported that 6.4% of a group of 239 pig farmers had experienced ODTS symptoms.

A written survey of veterinarians attending the 2002 American Association of Swine Veterinarians annual meeting included questions concerning the respondent's history of ODTS symptoms.[35] All veterinarians attending this meeting were invited to take part in the study. Participants included 122 of 536 registrants (mean age, 42.5 years). Interestingly, 49% of participants who had a veterinary practice limited to swine reported having had ODTS symptoms after working in hog barns.[36] Veterinarians who had worked in hog barns for > 20 years were significantly more likely to have reported this illness than were those who had a shorter work history. Lung function testing (spirometry) was performed on all study participants. There was no association between having a history of ODTS and having an abnormal spirogram. Also, swine veterinarians with a history of ODTS symptoms were not more likely to report symptoms of chronic bronchitis than those with no history of ODTS symptoms.

Treatment and prevention

The symptoms of ODTS are usually self-limiting, and many affected persons do not seek medical care. The recommended treatment for ODTS-associated fever and myalgia is acetaminophen or nonsteroidal anti-inflammatory agents. The rare individual who develops respiratory failure should be managed with supportive care. There is no evidence that treatment with corticosteroids is helpful, in contrast to the treatment recommendations for managing acute or subacute hypersensitivity pneumonitis.[37]

The use of respirators can reduce endotoxin exposure by more than 90% in healthy, normal study subjects inside a swine confinement barn.[38] The neutrophilic inflammatory response in the respiratory tract was significantly attenuated by use of respirators, as was the tendency for bronchospasm as measured by methacholine challenge. Interleukins 6 and 8, measured in nasal lavage fluid, were also significantly lower in subjects who had worn respirators. Other investigators have made similar observations from use of N-95 respirators, which are readily available.[39] However, use of respirators by a group of veterinary students visiting a commercial swine farm did not prevent ODTS symptoms.[40] Compliance with use of respirators in swine confinement barns is limited, but can be improved with education interventions.[41,42] Some workers may find wearing respirators uncomfortable, or may avoid their use because they limit verbal communication.

Use of engineering controls and best-management practices for maintaining good air quality in swine confinement buildings is the preferred means of preventing both ODTS and the airway disease common in persons who work in this environment. Previous studies of air quality in swine barns demonstrated that endotoxin levels are important in the causation of subacute airway disease in swine-confinement workers.[43] Currently, there are no published recommendations for an upper limit for

endotoxin levels in swine confinement barns to prevent ODTS. Because ODTS usually occurs after intense organic dust exposures, it is possible that keeping endotoxin levels in swine barn dust as low as possible will also prevent this disorder. Measures to reduce endotoxin exposure include sprinkling of oil to reduce dust in swine confinement barns,[29] which results in less respiratory tract inflammation in workers.

Routine monitoring of endotoxin levels in swine confinement barns would be ideal. Visual inspection alone is not adequate as a means of judging the cleanliness of a barn. In a recent study, there was no difference between barns that were rated very clean by visual inspection and those that were not described as being clean, in terms of the respiratory inflammatory response of normal volunteers who spent time there.[44] Unfortunately, frequent monitoring of endotoxin levels in swine confinement barns is not yet practical outside the research setting.

Conclusions

Organic dust toxic syndrome is a very common medical condition experienced by persons who work in swine confinement barns and in a number of other agricultural settings. It is an acute, usually self-limiting, febrile illness that may resemble infectious illnesses and hypersensitivity pneumonitis, in terms of clinical presentation and laboratory findings. A careful medical evaluation permits the clinician to distinguish ODTS from other disease processes. Inhalation of endotoxin is the most likely cause of ODTS in people exposed to swine confinement barns. There is growing evidence that a history of ODTS is a predisposing factor for chronic bronchitis, although this association has not yet been confirmed in persons who work in swine confinement barns. Studies of larger groups of persons who work in swine confinement buildings will be needed to determine whether experiencing ODTS symptoms is a risk factor for the airway disease that is a common problem in this population.

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