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Editorials: Popcorn worker's lung

E Neil Schachter. **The New England Journal of Medicine**. Boston: Aug 1, 2002. Vol. 347, Iss. 5; pg. 360, 2 pgs

Abstract (Summary)
Predominant involvement of the small airways, such as the bronchioles, is infrequently reported in occupational airway disease but may lead to serious consequences. Bronchiolitis obliterans is one disease with such involvement, initiated by damage to the epithelium of the small conducting airways and progressing to inflammation of these airways and frequently of the adjacent alveolar tissue; the clinical consequence of this injury and inflammation is irreversible airway obstruction.

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Full Text (1440 words)

OCCUPATIONAL airway diseases are common workplace injuries that include occupational asthma, bronchitis, reactive airways dysfunction syndrome, and byssinosis (an airway disease affecting textile workers). The population prevalence of these syndromes is not known with certainty, but some studies suggest that as many as 15 percent of adult patients with asthma have airway disease attributable to workplace conditions.1 Within different industries, the prevalence of these syndromes varies from sporadic to frequent (10 percent or greater). The mechanisms of these injuries may involve immune sensitization, but often the disease mechanisms are unknown and are presumed to involve nonallergic, irritant-mediated responses to inhaled agents.2 In such responses, the relations between the concentrations of agents to which workers are exposed and the severity of illness - so-called close-- response relations - can frequently be established.

Clinically, many of these illnesses are difficult to distinguish from their nonoccupational, sporadic counterparts. Often, epidemiologic investigations or specific challenge testing is required to establish an association between the workplace and the findings. In many industries, such as some of those that process textiles and food products, the prevalence of respiratory symptoms among employees is several times that in nonexposed populations, presumably because of the presence of subclinical disease.3,4 For some workers, such as those in the textile industry, early reversible symptoms have been linked to the gradual onset of nonreversible disease, such as chronic obstructive pulmonary disease similar to that found in some patients who smoke cigarettes.5

Predominant involvement of the small airways, such as the bronchioles, is infrequently reported in occupational airway disease but may lead to serious

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consequences. Bronchiolitis obliterans is one disease with such involvement, initiated by damage to the epithelium of the small conducting airways and progressing to inflammation of these airways and frequently of the adjacent alveolar tissue; the clinical consequence of this injury and inflammation is irreversible airway obstruction. In the occupational setting, the clinical syndrome of bronchiolitis has been associated with the presence of irritant gases, notably oxides of nitrogen but also chlorine, phosgene, ozone, hydrogen sulfide, and sulfur dioxide as well as organic and inorganic dusts. Among silo workers, exposure to high concentrations of oxides of nitrogen (higher than 50 parts per million) is paradoxically well tolerated during the first few hours of exposure, with relatively few symptoms. Unlike water-soluble irritant gases, which rapidly dissolve on the mucous membranes of the upper airway, oxides of nitrogen hydrolyze slowly into acids, which penetrate to the lower airways. Here, they produce an intense inflammatory reaction. Lower respiratory symptoms become apparent only 3 to 24 hours after the beginning of the exposure. The most common symptoms include cough, dyspnea, and fever. Occasionally, a worker who is exposed to very high levels of oxides of nitrogen may have acute respiratory failure as a result of noncardiogenic pulmonary edema and may die before resuscitation can be performed. For those who survive the acute illness, symptoms may recur in three to six weeks, with respiratory insufficiency developing slowly. Histologic examination reveals bronchiolitis obliterans with marked intraluminal proliferation of fibrous tissue.6

A number of investigators have reported sporadic cases of bronchiolitis obliterans among workers in unrelated industries that have not previously been associated with this disease, including nylon-flock workers,7 workers who spray prints onto textiles (with polyamide-amine [Acramin FWN, Bayer] dyes),8 battery workers (who are exposed to thionyl chloride fumes),9 and workers in the food-flavoring industry.10 Most of these cases have involved the identification of a few affected workers, followed in some instances by a concerted effort on the part of regional or national organizations to discover additional cases.

In this issue of the journal, Kreiss et al.11 investigate the clustering of cases of bronchiolitis obliterans in a microwave-popcorn packaging plant. As reported earher this year,12 in May 2000 a physician specializing in occupational medicine described fixed obstructive lung disease in eight former employees of this microwave-popcorn plant, all of whom had been employed there between 1992 and 2000. Symptoms in all eight were compatible with descriptions of bronchiolitis obliterans developing in workers in other industries. Four of the eight had worked in the mixing room, and the other four had worked in the microwave-popcorn packaging area. Of the 425 people who had been employed at the plant between 1992 and 2000, only 13 had worked in the mixing room, suggesting that the incidence of disease in this group was very high. Air sampling in the plant detected many volatile organic compounds, but diacetyl, a ketone with butter-flavor characteristics, was singled out as a likely cause of the disease, given its very high concentration in the mixing room. Subsequent toxicity studies in rats have supported this association.13 The current investigation was a cross-sectional evaluation of 117 current workers in the plant. Unlike previous studies of occupational bronchiolitis,7-10 this investigation concentrated on the frequency of subclinical findings in the plant. The authors found that the prevalence of respiratory symptoms and of findings of obstruction on spirometry among the current workers was about three times that in the general population. Moreover, there was a strong exposure-response relation between cumulative diacetyl exposure and the frequency and extent of airway obstruction.

The implications of these quantitative studies can best be understood in the context of the questions they answer and, perhaps more important, the questions they suggest. Clearly, work in the mixing room of this microwave-popcorn plant conferred a high risk of this rare, severe lung disease. In a more subtle finding, subclinical disease, corresponding to symptoms and lung-function abnormalities not of a degree sufficient to cause respiratory impairment, was seen to be clearly associated with the gradient of

the irritant presumed responsible for the overt bronchiolitis obliterans. If these symptoms represent subclinical, smoldering bronchiolitis obliterans, many more workers in this industry may be at risk, particularly for a slowly developing but progressive form of chronic obstructive pulmonary disease. Respiratory findings with similar prevalences have been widely reported in many dusty industries, none of which to date have been associated with bronchiolitis obliterans.3,4 If injuries of this nature are more common in industries that produce organic dust and fumes, then more widespread control measures are needed to prevent the possibility of chronic disease.

Certainly, for those at high risk in the microwave-- popcorn industry, immediate controls are required. For workers with early respiratory symptoms and lungfunction abnormalities, studies to characterize airway injury by bronchoalveolar lavage and possibly lung biopsy are warranted and would clarify the implications of the dose-response relations established in the current study. More generally, workers in other industries that produce similar irritant dusts, fumes, or gases need to be evaluated for small-airway disease that could result in serious impairment such as that seen in workers in the microwave-popcorn plant. As for the health effect of microwave-popcorn products in the general population, there are no findings to date to suggest that consumers are at any risk.

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