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Work-Related Asthma from Exposure to Cardboard and Paper Product Dust

Multiple studies have been conducted concerning respiratory disease among workers in the paper milling and pulp industries. Workers in these facilities can be exposed to multiple potential respiratory toxins, including hydrogen sulfide, sulfur dioxide, chlorine, chlorine dioxide, and terpenes (Toren et al, 1996). Studies have found an increased prevalence of asthma and obstructive changes on spirometry associated with acute exposures to chlorine and ozone used to bleach the paper (Mehta et al, 2005). Additional studies have associated increased levels of paper dust exposure with increased obstructive changes among workers at Swedish paper mills (Anderson et al, 2019), increased mortality from asthma and COPD among 7,880 workers from three Swedish soft paper mills (Toren et al, 2020), and an increase in obstructive changes and respiratory symptoms among workers in four Ethiopian paper mills (Tafese et al, 2024 and 2025). Soft paper mills, which produce products such as toilet paper, tissue, and napkins, are more dusty than other types of paper mills, and the products sometimes contain additives and softeners such as talc and kaolinite.

Although paper and pulp mill workers are not only exposed to paper dust but also the multiple irritants listed above, the studies controlling for these irritant exposures found that levels of paper dusts $>5 \text{ mg/m}^3$ were associated with obstructive pulmonary function changes and respiratory symptoms. In the United States, there is no specific occupational standard for paper dust set by the Occupational Safety and Health Administration (OSHA), but rather paper dust is regulated as a nuisance dust with allowable total permissible exposure limit (PEL) of 15 mg/m^3 . This level is high enough that there would be visible dust in the air. In Great Britain, the Workplace Exposure Limit (WEL) for cellulose dust is 10 mg/m^3 and 4 mg/m^3 for the respirable fraction. Paper dust may cause the development of respiratory symptoms through diverse mechanisms; irritant-driven respiratory dysfunction, sensitizer mediated reaction, and endotoxin mediated reaction, particularly if the paper becomes wet.

Studies of respiratory disease/symptoms to paper dust in a non- paper/pulp mill work setting are limited. A population-based study of asthma among adults in Finland found a significant increased risk of adult-onset asthma to paper dust in office settings (adjusted odds ratio = 1.97; 95% confidence interval, 1.25-3.10) (Jaakkola, and Jaakkola, 2007). There is a case report of work-related asthma to cellulose documented by specific inhalation challenge of a 37-year-old male machine operator in a South African sanitary pad manufacturer (Knight et al, 2018). Cellulose is a polysaccharide with glucose units. It is the chief constituent of plant/wood fibers and paper. Cotton is the purest natural form of cellulose. The machine operator had a two-year history of a tight chest, wheeze, hoarse voice, blocked nose, and itchy eyes that were related to work and improved off work. He had no personal or family history of asthma. He was an ex-smoker, quitting six years prior. His medication decreased, his lung function improved, and his symptoms were reduced after being moved to a non-exposure area. The cellulose was bleached chlorine-free paper made from pine tree species. He did peak flow monitoring for 18 workdays, and 24 non-workdays. He had a greater than 20% variability consistent with asthma and a pattern consistent with work-related asthma. He had negative IgE to common environmental allergens, pine, xylanase, and mold. With specific inhalation challenge testing, he had a 39% decline in FEV1 with exposure to cellulose and no decrease after exposure to lactose. The cellulose was derived from pine. The authors considered the possibility that a contaminant in the cellulose was the causative agent, but no detectable soluble protein could be extracted from the cellulose, the cellulose was dry and no endotoxin or mycotoxin was considered likely in the cellulose and no immunological reaction could be elicited with the cellulose extract.

What has been reported in Michigan?

Michigan has an important paper production industry. In 2023, there were 190 paper and 67 cardboard manufacturing companies in Michigan employing 8,523 and 3,974 workers, respectively (US. BLS). Despite the number of companies and employees who work in paper manufacturing, no individuals with work-related asthma have been identified from a Michigan pulp or paper mill.

From 1988-2022, seven cases of work-related asthma from exposure to cardboard dust and one from exposure to paper dust have been reported in Michigan. Five of the cases were new-onset asthma, and all were exposed to cardboard dust. The remaining three cases were work-aggravated asthma. At the time of the development of their respiratory symptoms, four worked in a manufacturing industry and were exposed to cardboard dust in the process of shipping or receiving manufactured goods in cardboard boxes, two worked in a cardboard box manufacturing facility, one worked at a cardboard recycling facility, and one was exposed to paper dust at a post office. Four were men and four were women. Ages ranged from 20 to 60. The average latency from the first workplace exposure to paper or cardboard dust to the onset of their breathing problems was 7.4 years, ranging from zero to 26 years. Seven of the eight individuals presented to an emergency department at least once due to their workplace exposure, and two were each hospitalized twice.

Case Example:

A worker in their late 30's developed chest tightness and shortness of breath at work 17 years after beginning to work as an inspector checking parts in an auto parts manufacturer. They worked in the warehouse and were exposed to cardboard dust. They never worked in an production area. They were treated with a steroid inhaler and bronchodilator. Their symptoms improved on the weekends and vacations. They also improved after they began treatment with the steroid inhaler. They went to the emergency department on three occasions for respiratory symptoms. They had a personal and family history of allergies. They smoked up to 10 cigarettes a day for 20 years. Spirometry was normal.

The eight cases identified over the 34-year observation period suggest that workplace exposure to cardboard or paper dust can lead to acute and chronic respiratory symptoms causing workers' respiratory morbidity. Because we know that work-related asthma is widely underdiagnosed and underreported (Reilly et al, 2019), we expect the actual impact of cardboard and paper-induced breathing problems to be greater than what has been identified.

Even though paper dust is a known respiratory irritant, different categories of paper products have rarely been studied as distinct entities. Reports in Michigan suggest that cardboard exposure may disproportionately contribute to work-related asthma among workers exposed to paper dust of any type. Globally, 407 million metric tons of paper were manufactured in 2014, over half of which was used in packaging. Global consumption of cardboard and paper has grown 75% between 1990 and 2022. Paper consists of nearly pure cellulose, an insoluble branched polysaccharide. Trace amounts of hemicelluloses, lignans, minerals, and other polymers survive the pulping process. However, in unbleached paper products such as cardboard, the lignin content may be as high as 2-5%, versus <0.5% in bleached paper products such as copy paper or hygienic paper. No studies have been identified which explore the pathophysiologic impact of inhaled lignin.

Animal studies have found pure cellulose dust to be bio persistent in the lungs for at least one year, causing a granulomatous reaction and mild interstitial fibrosis (Muhle et al, 1997), that mice exposed to cellulose nanocrystals had significant lung damage including elevated neutrophils and eosinophils on bronchoalveolar lavage (Yanamala et al 2014), and increased macrophages, lymphocytes, myeloperoxidase, interleukins of numerous types, G-CSF, peribronchial and perivascular inflammation, and increased airway responsiveness to methacholine challenge, all of which were worse in females (Shredova et al, 2016). The wide range of manufactured cellulose products in use today, from traditional brown paper bags to engineered oil-resistant paper food containers, and their diverse array of additives and contaminants equates to the possibility of different substance exposures for workers throughout many different industries.

Other respiratory conditions that have been reported with exposure to cardboard and paper dust: an abstract of a case report of eosinophilic pneumonia in a worker in cardboard manufacturing (Lipatov et al, 2016); an increased incidence of intestinal cancer in soft paper mill workers (Toren et al 2023); and an outbreak of hypersensitivity pneumonitis linked to water spray and corrugated cardboard (Woodward, 1988) have been identified.

Workers in the recycling industry may also have an increased likelihood of developing sensitizer-induced asthma from immunogenic microorganisms and endotoxins emanating from contaminated, moist wastepaper (Poole and Basu, 2018). One of the eight Michigan reports was of a worker who developed asthma while working at a cardboard recycling facility, though the exact recycling process at this plant and subsequent mode of exposure were unknown.

Inhalable cellulose powder has been proposed as a treatment of allergic rhinitis by creating a gel-like diffusion barrier over the nasal mucosa. Identical technology has also been explored for use as an excipient for nasally insufflated medications. While this technique was safe and effective in short-term studies of the upper respiratory tract, the long-term effects of pulmonary inhaled cellulose have not been studied.

We are extremely interested in any patients you suspect that have respiratory disease from cardboard or paper products. Dr. Kenneth Rosenman can be reached at rosenman@msu.edu or via 1 800-466-7805 for anyone who has a patient with possible lung disease from cardboard/paper products.

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