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Rapidly Progressive, Fixed Airway Obstructive Disease in Popcorn Workers: A New Occupational Pulmonary Illness?

[DEPARTMENTS: Letters to the Editor]

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To the Editor:

A number of former employees at a microwave popcorn packaging facility in Missouri presented in spring 2000 with severe pulmonary symptoms characterized by fixed airway obstruction. Most had well-preserved carbon monoxide diffusing capacity of the lungs. These patients had seen numerous other practitioners but for the first time were recognized as all working in the same facility and as having been potentially exposed to the same occupational environment. The characteristics of Popcorn Packers' Lung seemed to be due to an environmental exposure to a workplace toxin that causes a unique and previously unrecognized form of rapidly progressive obstructive lung disease. We report the clinical cases here to increase awareness of the occupational medical providers in the hope that additional cases will be classified, hazardous workplaces will be identified, and primary preventive intervention will take place.

The facility, located in Missouri, received raw corn and produced packaged popcorn. The process consisted of mixing salt, oil, and flavoring; combining this with the popcorn; and packing it in single-serving packages for use in microwave ovens. The flavoring consisted of various spices, and a butterlike flavor was provided by the chemical diacetyl. Depending on where the employee worked in the plant, exposure to the flavoring components could vary by more than an order of magnitude.

Case 1: A 46-year-old woman was employed at a popcorn facility for 18 months and was responsible for bagging popcorn. Approximately 16 months after employment, she began to develop shortness of breath and a cough. This progressed rapidly, and she was admitted to the hospital with acute asthma and diagnosed with bronchitis. She was a life-long nonsmoker and had no prior symptoms of asthma.

The patient's pulmonary function demonstrated a forced vital capacity of 45%; a forced expiratory volume in 1 second (FEV_1) of 25%; and a forced expiratory flow, midexpiratory phase, of 10% of predicted. Her carbon dioxide diffusing capacity was 80%, and her $alpha_1$-antitrypsin level was normal. She was evaluated at a referral medical center, where she was diagnosed with bronchiolitis obliterans on clinical presentation. An inspiratory computed tomographic scan of the

chest demonstrated interstitial changes. The patient was evaluated, accepted for a lung transplant at a transplant center, and is currently on 3 L of oxygen per hour.

Case 2: A 26-year-old man was employed at popcorn factory as an oil mixer. Thirteen months after employment, he noted onset of symptoms so abrupt that in 1 day he went from being asymptomatic to being unable to climb up a single flight of stairs to his workplace. He began to have wheezing and chest pressure. The patient was initially diagnosed with pneumonia. Previously, he had smoked a pack of cigarettes a day for 8 years and had stopped 3 years before working at the popcorn factory. In addition, he was nonasthmatic.

The patient was employed at the facility for a total of 18 months. Approximately 2 months after initial symptoms, pulmonary function studies demonstrated a forced vital capacity of 41%; FEV_1 of 18%; and forced expiratory flow, midexpiratory phase, of 5% of predicted. He had a carbon monoxide diffusing capacity of 102% of predicted. His pulmonary function values have remained at this level over the past 2 years.

An inspiratory computed tomographic scan of the chest demonstrated changes consistent with mild diffuse bronchiectasis bilaterally. A ventilation perfusion scan demonstrated diffuse lung disease, and a right heart catheterization was normal. He was treated with Cytoxan and prednisone without affect. Laboratory studies were negative for $alpha_1$-antitrypsin deficiency. The patient was evaluated at a lung transplant center and was placed on the lung transplant list.

Case 3: A 54-year-old nonasthmatic nonsmoker had worked for 4 years in another microwave popcorn packaging facility, where his duties included mixing flavorings with oil and salt. One week after beginning to use a new artificial butter flavoring, he developed blurred vision from corneal ulcerations and worsening of his mild chronic cough, which was productive of white sputum. Bibasilar rales were apparent on auscultation of the chest. Pulmonary function tests at diagnosis showed mild airway obstruction with no improvement after albuterol inhalation. The diffusing capacity for carbon monoxide was normal. A computed tomographic scan of thorax with inspiratory and expiratory views was suggestive of mild air trapping.

The popcorn processing plant then closed for 2 weeks. During this time, the patient was treated with prednisone, 40 mg per day, for 14 days. One week after the first clinic visit, he reported improvement in his cough and his FEV_1 had increased from 2.55 L at initial presentation to 3.02 L. After the plant reopened, he returned to mixing the previous butter flavoring. When he was reassessed 6 weeks after diagnosis, his FEV_1 had increased to 3.22 L, his cough had resolved, and his corneal ulcerations had healed.

In summary, this employee of a microwave popcorn plant, who had been routinely exposed to an artificial butter flavoring, developed acute worsening of his mild chronic cough and corneal ulcerations after using a new artificial butter flavoring product in his work. There was significant improvement in his lung function and eye symptoms after exposure to this product ended and after corticosteroid therapy. These observations suggest that cessation of exposure is important for the treatment of this syndrome. Corticosteroids may also play a role in the management of this clinical problem.

Summary: Evaluation of these exposures and four others initially demonstrated an unusual concentration of bronchiolitis obliterans–type symptoms in a small population. The longitudinal investigation is continuing under the aegis of the National Institute for Occupational Safety and Health (NIOSH). Recently, another case was diagnosed at a facility in northern Missouri where

butter flavoring is manufactured. Suspicion of the causal agent being the flavoring was focused in an animal study performed using rats exposed for 24 hours to the flavorings, which produced severe upper and lower airway changes in the animals. 1

Diacetyl (2,3-butanedione) is a commonly used food flavoring and also occurs naturally in butter, coffee, and bay oil. It forms the essential oil of butter and butter flavorings and has not previously been described as toxic when inhaled. 2 Diacetyl is not listed in the most commonly used occupational guide to workplace chemical hazards, the *NIOSH Pocket Guide to Chemical Hazards*. 3

Clearly, these early series of cases are of significance in inferring causality. The relative risk of a few former employees out of a total of approximately 400 is much higher than would be expected for the occurrence of bronchiolitis obliterans in the general population, which has been estimated to be between 1:40,000 and 1:100,000. 4 The effect seems to be seen only in the current and former employees of a popcorn packaging facility and not in the general population of the surrounding county. There was consistency of results of testing by different and independent investigators. Furthermore, a temporal and physical correspondence and a biologic plausibility exist by both analogy of other chemicals and preliminary animal tests. Therefore, the Hill Criteria are fulfilled. 5

We believe these cases represent a new and potentially lethal occupational pulmonary disease, Popcorn Packers' Workers' Lung. We would encourage all occupational health care providers to monitor employees who work in and around food flavorings by obtaining baseline and periodic values. Any eye, upper respiratory, and pulmonary symptoms among these workers require investigation. Unless exposure is stopped and therapy is initiated early on, the changes may be rapidly progressively and irreversible. Good industrial hygiene practices, including engineering projects to improve ventilation, provide personal protective equipment, and reduce exposure to the suspect agents should be urged. If any such cases are identified, the state public health department and NIOSH should be notified immediately.

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