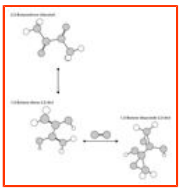
The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

◂ Previous Volume 347:1980-1982 December 12, 2002 Number 24 Next ▸

Bronchiolitis in Popcorn-Factory Workers

To the Editor: Kreiss et al. (Aug. 1 issue)[1] report a high incidence of bronchiolitis obliterans at a microwave-popcorn factory. The chemical diacetyl (2,3-butanedione) was singled out as a possible causal agent of this deadly condition and other medical problems found in workers in this plant. As a chemist, biochemist, and toxicologist, I would like to point out that 2,3-butanedione is in chemical equilibrium with 1,3-butane-diene-2,3-diol (Figure 1). This phenomenon, which is well known in organic chemistry, is called keto-enol tautomerism. This isomer is expected to be very reactive with oxygen both at room temperature and on heating. Thus, 1,3-butane-diepoxide-2,3-diol would be expected as a product. Although the parent compound is known to be reactive with arginine, the diepoxide is of particular interest, since butadiene diepoxide is a known human carcinogen. The appropriate government agencies must investigate and evaluate whether diacetyl should be banned from food products.



View larger version (13K):
[in this window]
[in a new window]

Figure 1. Chemicals 2,3-Butanedione and 1,3-Butane-Diene-2,3-Diol, and Their Expected Product, 1,3-Butane-Diepoxide-2,3-Diol.

Edward G. Ezrailson, Ph.D.
2308 West Settler's Way
The Woodlands, TX 77380
edez1@prodigy.net

THIS ARTICLE
- PDF
- PDA Full Text

TOOLS & SERVICES
- Add to Personal Archive
- Add to Citation Manager
- Notify a Friend
- E-mail When Cited

MORE INFORMATION
- Related Article by Schachter, E. N.
- Related Article by Kreiss, K.
- PubMed Citation

References

1. Kreiss K, Gomaa A, Kullman G, Fedan K, Simoes EJ, Enright PL. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. N Engl J Med 2002;347:330-338. [Free Full Text]

To the Editor: Kreiss and colleagues report frequent cases of bronchiolitis obliterans among workers in a popcorn plant that were attributed to the inhalation of the volatile ingredient diacetyl in the butter flavoring. Although this conclusion is in keeping with the toxic effects of diacetyl on the respiratory epithelium in animals, and although a dose–response relation (a decreasing forced expiratory volume in one second associated with increasing exposure to diacetyl) was established, it may not be the only causative agent. The workers who were affected the most were also exposed to the highest concentrations of other volatile compounds and respirable dust. Maize bran, glumes, and stigmas contain considerable amounts of tannins,[1] which are necessarily constituents of airborne particles. Inhaled tannins are considered to be an important causal factor in obstructive pulmonary diseases among workers exposed to dust of plant origin, such as those who work in cotton mills or grain elevators and those who work with herbal tea.[2] Therefore, tannins may be one of the substances implicated in the development of "popcorn worker's lung." This hypothesis is supported by the finding that clinical symptoms that follow the occupational inhalation of tannins are similar to those reported among popcorn workers. In addition, the lack of improvement in the symptoms with β_2-agonist bronchodilators is consistent with the inhibitory effect of tannin on adenylate cyclase in airway epithelial cells.[3]

Dirk Taubert, M.D., Ph.D.
Andreas Lazar, M.D.
Edgar Schömig, M.D.

Medical College of the University of Cologne
50931 Cologne, Germany
dirk.taubert@medizin.uni-koeln.de

References

1. Bradley PR, ed. British herbal compendium. Vol. 1. Bournemouth, England: British Herbal Medicine Association, 1992.
2. McL Niven R, Pickering CA. Byssinosis: a review. Thorax 1996;51:632-637. [Medline]
3. Cloutier MM, Guernsey L. Tannin inhibits adenylate cyclase in airway epithelial cells. Am J Physiol 1995;268:L851-L855.[Free Full Text]

To the Editor: In his editorial (Aug. 1 issue),[1] Schachter comments on occupational airway diseases but leaves out what I think is an important finding described in the accompanying article by Kreiss et al. As the occupational physician involved in this case, I noted that not only was an epidemic of bronchiolitis obliterans present, but the number of tobacco smokers involved was unusually small.[2] Only one of the initial eight patients was a smoker. Nonsmokers were overrepresented among patients as compared with the exposed population. In the study population described by Kreiss et al., the workers who never smoked had a rate of airway obstruction that was three times as high as that among the smokers, although all workers were affected. An understanding of the mechanism of this protection could lead to preventive interventions.

Allen J. Parmet, M.D., M.P.H.
Midwest Occupational Medicine
Kansas City, MO 64108
mommd@kc.rr.com

References

1. Schachter EN. Popcorn worker's lung. N Engl J Med 2002;347:360-361. [Free Full Text]
2. Parmet AJ, Von Essen S. Rapidly progressive, fixed airway obstructive disease in popcorn workers: a new occupational pulmonary illness? J Occup Environ Med 2002;44:216-218. [CrossRef][ISI][Medline]

The authors and a colleague reply:

To the Editor: We used diacetyl as an index of exposure to volatile organic chemicals in the popcorn plant because it was the predominant one found in plant air. However, identification of the causal agent or agents in the flavoring will rely on studies in animals in which individual constituents are tested; such studies are now under way. Diacetyl is a leading candidate for investigation of potential respiratory toxicity because alpha-dicarbonyl compounds react with functionally reactive arginine residues in proteins and with guanine and inhibit superoxide dismutase and glutathione reductase, which are involved in protection from oxidative stress. In addition to Dr. Ezrailson's concern about the properties of a derivative diepoxide, diacetyl itself has been nominated for studies by the National Toxicology Program (NTP) because of widespread human exposure, limited evidence of mutagenicity, and relations to carcinogens and mutagens in terms of structure and activity, as well as because diacetyl is representative of aliphatic alpha-diketones. (See the NTP Web site at http://ntp-server.niehs.nih.gov.floyd.lib.umn.edu)

We did not detect 1,3-butadiene-2,3-diol or 1,2;3,4-diepoxybutane-2,3-diol in any samples collected by thermal desorption tubes and analyzed with gas chromatography–mass spectrometry. However, we agree with Dr. Ezrailson that diacetyl would be present in equilibrium with its tautomers, as governed by the equilibrium constants for the conversions. Since diacetyl occurs naturally in butter and during the manufacture of alcoholic beverages, any proposed ban of diacetyl in food products raises issues of practicality.

As noted by Taubert and colleagues, other agents within the workplace may contribute to the clinical bronchiolitis obliterans seen in this workforce. Indeed, necrosis of the respiratory epithelium in the mainstem bronchus was more severe in rats exposed to butter-flavoring vapors than in rats exposed to diacetyl alone at a similar diacetyl concentration (unpublished data). We did not measure tannins. Workers managing the grain bins, presumably with greater exposure to organic dust, were in the low-risk group; mixers, who had almost no active contact with corn or its dusts, had the highest historical risk of fixed airway obstruction. The role of respirable salt dust in the airway damage found in microwave-popcorn production workers remains unclear. However, our observation that the same syndrome occurs in flavoring-production workers without exposure to grains or salt makes these agents less likely to be causal contributors.

Kathleen Kreiss, M.D.
Ann Hubbs, D.V.M., Ph.D.
Gregory Kullman, Ph.D.
National Institute for Occupational Safety and Health
Morgantown, WV 26505
kkreiss@cdc.gov

The editorialist replies:

To the Editor: Dr. Parmet points out an interesting but unexplained observation of his study and that by Kreiss et al. In his original study, nonsmoking workers accounted for the majority of index cases of bronchiolitis; among the workers studied by Kreiss et al., those who had never smoked had unusually high rates of airway obstruction. This latter finding is not particularly unusual, since a high prevalence of disease among nonsmokers is frequently used to confirm the presence of a true occupational or environmental effect.[1] What Parmet focuses on is the fact that although the frequency of airway obstruction in smoking workers in this cohort is increased (prevalence ratio, 1.6), it is not increased to the same extent as that among nonsmoking workers (prevalence ratio, 10.8). In occupational airway disease, the effect of the pollutant tends to be more pronounced among smokers, because the injury is frequently additive. Possible explanations for the lack of such an additive effect in this setting include a healthy-worker effect, by which sicker smoking workers would leave the industry at an early date, before the onset of bronchiolitis, and the possibility that cigarette smoking alters the deposition of inhaled particles[2] in such a way as to decrease the amount of other pollutants arriving in smaller airways. Further speculation is possible, but the primary public health message raised by these studies remains clear: injury to the airway in industries dealing with organic pollutants such as those associated with the manufacturing of microwave popcorn may be frequent, disabling, and occasionally life-threatening.

E. Neil Schachter, M.D.
Mount Sinai School of Medicine
New York, NY 10029

References

1. Beck GJ, Maunder LR, Schachter EN. Cotton dust and smoking effects on lung function in cotton textile workers. Am J Epidemiol 1984;119:33-43. [Free Full Text]
2. Lippmann M, Yeates DB, Albert RE. Deposition, retention, and clearance of inhaled particles. Br J Ind Med 1980;37:337-362. [ISI][Medline]