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# Evaluation of Flavorings-Related Lung Disease Risk at Six Microwave Popcorn Plants

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## Learning Objectives

- Explain how the concentration of diacetyl, an airborne butter-flavoring chemical, relates to the specific type of work performed by employees at plants producing microwave popcorn.
- Relate the level and duration of exposure to butter-flavoring chemicals such as diacetyl, as well as smoking history, to respiratory tract symptoms, airway dysfunction, and lung biopsy findings of bronchiolitis.
- Describe practical measures that may decrease exposure to butter-flavoring chemicals and forestall or prevent the development of respiratory tract disease.

## Abstract

***Objective:*** *After investigating fixed airways obstruction in butter flavoring-exposed workers at a microwave popcorn plant, we sought to further characterize lung disease risk from airborne butter-flavoring chemicals.* ***Methods:*** *We analyzed data from medical and environmental surveys at six microwave popcorn plants (including the index plant).* ***Results:*** *Respiratory symptom and airways obstruction prevalences were higher in oil and flavorings mixers with longer work histories and in packaging-area workers near nonisolated tanks of oil and flavorings. Workers were affected at five plants, one with mixing-area exposure to diacetyl (a butter-flavoring chemical with known respiratory toxicity potential) as low as 0.02 ppm.* ***Conclusions:*** *Microwave popcorn workers at many plants are at risk for flavoring-related lung disease. Peak exposures may be hazardous even when ventilation maintains low average exposures. Respiratory protection and engineering controls are necessary to protect workers.* (J Occup Environ Med. *2006;48:149–157*)

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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Since August 2000, National Institute for Occupational Safety and Health (NIOSH) staff have investigated the occurrence of fixed obstructive lung disease consistent with constrictive bronchiolitis obliterans in microwave popcorn workers exposed to airborne butter-flavoring chemicals. A NIOSH cross-sectional medical and environmental survey at plant A (the index plant) revealed an elevated prevalence of obstructive lung disease that was associated with cumulative exposure to diacetyl, the predominant butter-flavoring chemical in the air of the plant.[1,2] In experiments conducted at NIOSH, rats exposed to vapors from a butter flavoring used at this plant developed severe injury of their airway epithelium.[3] Rats developed similar airway damage (although less extensive) with inhalation of vapors of pure diacetyl.[4] These findings implicated butter-flavoring chemicals as a likely etiologic agent for obstructive lung disease in the workers at the index plant. Similar lung disease has also occurred in workers at flavoring-manufacturing plants.[5,6]

We performed medical and environmental surveys at five additional microwave popcorn plants to determine if other workers were at risk and to characterize exposures, controls, and work practices in different plants. In this article, we present our findings from cross-sectional evaluations at all six plants (including the index plant) and discuss the implications for prevention of lung disease and other health effects in workers exposed to butter flavorings.

## Materials and Methods

### Selection of Plants

Under federal regulations (42 CFR 85),[7] NIOSH staff can conduct a workplace health hazard evaluation after receiving a request from company management, three current workers, or a labor union that represents the workers. Additionally, state health departments can request NIOSH technical assistance with a workplace evaluation. Of the six plant evaluations, two were requested by management, two by state health departments, and two by workers. Three of the plants, each with more than 100 workers, were owned by three of the five largest producers of microwave popcorn in the United States.

### Medical Survey

At each facility, we invited all current workers to participate. After obtaining written informed consent from participants, NIOSH interviewers administered a questionnaire to collect information on symptoms, medical diagnoses, smoking history, work history, and work-related exposures. We used questions adapted from the American Thoracic Society standardized respiratory symptom questionnaire[8] to assess shortness of breath on exertion (when hurrying on level ground or walking up a slight hill, hereafter referred to as "SOB 1"; when walking with people your own age on level ground, hereafter referred to as "SOB 2"), chronic cough (usual cough on most days for 3 consecutive months or more during the year), and wheezing (apart from colds). A positive smoking history was defined as having smoked at least 20 packs of cigarettes in a lifetime or at least one cigarette a day for 1 year.

Using a dry rolling-seal spirometer interfaced to a computer, NIOSH technicians performed spirometry tests following American Thoracic Society guidelines[9] with results compared with spirometry reference values generated from the Third National Health and Nutrition Examination Survey (NHANES III).[10] We defined airways obstruction as a forced expiratory volume in the first second of exhalation ($FEV_1$) and an $FEV_1$/forced vital capacity (FVC) ratio that were both below the lower limit of normal. We administered a bronchodilator to differentiate reversible obstruction, defined as an increase in the $FEV_1$ of at least 12% and 200 mL, from fixed obstruction.

We aggregated the medical survey data from all six plants and used SAS software (SAS version 9.1, 2002–2003; SAS Institute, Inc., Cary, NC) for statistical analyses. We compared medical survey findings in ever-mixers (workers who reported having mixed oil and flavorings for at least 1 day) with findings in all other workers. We also compared findings in packaging-area workers (who had never worked as mixers) in two sets of plants—those with isolated heated tanks of oil and flavorings and those with nonisolated tanks—and compared findings in maintenance workers with those of workers who had never worked in maintenance, mixing, or packaging. $\chi^2$ and Fisher exact tests were used to analyze categorical data, and Student $t$ test was used to analyze continuous data. We considered $P$ values of 0.05 or less to represent differences that were unlikely due to chance.

Some workers who reported undergoing medical evaluations by personal physicians due to respiratory symptoms that began after they started work in microwave popcorn production gave consent for us to review their medical records. We specifically looked for findings of fixed obstruction on spirometry, normal diffusing capacity, and evidence of air trapping on chest computed tomography (CT) scans, because the presence of these findings is consistent with bronchiolitis obliterans. We also reviewed available lung biopsy reports if biopsies had been performed.

### Environmental Survey

We characterized the production process at each plant in terms of the number of production lines and number of heated tanks of flavorings and oil-flavoring mixtures, exposure controls (ie, general dilution and local exhaust ventilation, isolation of oil and flavoring-mixing processes), temperatures of the contents in heated tanks, and use of respirators by flavoring-exposed workers. As an indicator of exposure to butter-flavoring chemicals, we measured full-shift time-weighted average (TWA) air concentrations of diacetyl in several areas of each plant with sorbent tubes and gas chromatography according to NIOSH Method 2557.[11] At most plants, we also obtained personal exposure measurements for diacetyl with sampling equipment located on the worker. At one plant, we used a Gasmet DX-4010 Fourier Transform Infrared (FTIR) Gas Analyzer (Temet Instruments Oy, Helsinki, Finland) to measure real-time concentrations of diacetyl in a worker's breathing zone while he handled open containers of butter flavorings.

## Results

### General Production Process and Plant Characteristics

Plants varied widely in terms of plant size and number of workers, but the basic production process was similar. In each plant, one to three workers per work shift (ie, mixers) measured butter flavorings (liquids, pastes, and powders) in open containers such as 5-gallon buckets and poured the flavoring into heated soybean oil in large (eg, 500-gallon) heated mixing tanks, most of which had loose-fitting lids. Although visible plumes of vapors were often apparent when tank lids were opened, only one mixer at one plant reported consistent use of a respirator with organic vapor cartridges during mixing tasks. Mixers also added salt and coloring to the oil and flavoring mixture, which was then transferred by pipes to nearby packaging lines to be combined with kernel popcorn in microwaveable bags. Workers on the packaging lines operated the packaging machines and facilitated the placement of the finished product into cartons and boxes. In most plants, quality-control (QC) workers popped product in microwave ovens that were usually located in a separate QC laboratory. Other workers were located in warehouse and office areas. In separate areas of some plants, workers also packaged plain kernel popcorn in plastic bags without oil or flavorings.

The number of different butter flavorings used ranged from two in one of the smaller plants to more than 20 in the largest plant. Two small plants had one or two mixing tanks and one packaging line. One medium-sized plant had one mixing tank, three holding tanks for oil and flavorings, and three packaging lines. Three large plants had five or more tanks and seven or more packaging lines. In some plants, flavoring-mixing activities, and tanks were located in a separate room adjacent to the packaging area. In other plants, some or all tanks of heated oil and flavoring were located in the same room as, and in close proximity to, the packaging lines.

**TABLE 1**
Mixing-Area and Packaging-Area Diacetyl Air Concentrations at Six Microwave Popcorn Plants

| | Diacetyl Air Concentration Mean (range; ppm)* | | | |
|---|---|---|---|---|
| | Mixing Area | | Packaging Area | |
| Plant | Area | Personal | Area | Personal |
| A (index) | 37.8 (1.3–97.9) ($n$ = 12) | | 1.9 (0.3–6.8) ($n$ = 22) | |
| B | 0.6 (0.4–1.0) ($n$ = 3) | 0.6 (0.4–0.7) ($n$ = 2) | 0.7 (0.4–1.2) ($n$ = 9) | 0.5 (0.2–1.0) ($n$ = 8) |
| C | 0.4 (0.02–0.9) ($n$ = 2) | 0.03 (0.01–0.04) ($n$ = 2) | 0.03 (0.01–0.05) ($n$ = 4) | 0.02 (0.01–0.04) ($n$ = 7) |
| D | 0.2 (ND–0.6) ($n$ = 3) | 0.02 (ND–0.05) ($n$ = 5) | 0.004 (ND–0.03) ($n$ = 13) | 0.002 (ND–0.009) ($n$ = 12) |
| E | 0.6 (0.3–0.9) ($n$ = 2) | 0.4 ($n$ = 1) | 0.3 (0.2–0.4) ($n$ = 2) | 0.6 (0.3–1.2) ($n$ = 3) |
| F | 1.2 (0.5–2.7) ($n$ = 6) | 1.0 (0.2–2.0) ($n$ = 7) | 0.02 (LOQ–0.03) ($n$ = 18 | 0.02 (LOQ–0.03) ($n$ = 24) |

* Parts per million parts air by volume.
ND indicates below limit of detection for the sampling method (0.001 ppm); 0.0005 used for calculation of mean; LOQ, below minimum quantifiable concentrations for the sampling method (approximately 0.01 ppm); 0.005 used for calculation of mean.

## Diacetyl Exposures

Compared with the index plant, mean diacetyl air concentrations in the mixing areas at the other five plants were generally one to two orders of magnitude lower (Table 1). In four of these five other plants, the highest TWA diacetyl air concentration measured with area sampling in mixing areas was between 0.6 and 1.0 parts per million (ppm) compared with 98 ppm at the index plant. In plant F, the highest TWA diacetyl air concentration measured with area sampling in the mixing room was 2.7 ppm, just slightly above the lowest mixing-room TWA diacetyl air concentration in the index plant.

Of note, two of the three heated tanks in the mixing room of the index plant contained heated liquid flavorings only (ie, flavoring not yet mixed into soybean oil). None of the other plants used heated tanks to hold only butter flavoring. Plant D, the only plant that had both local exhaust ventilation of tanks and general dilution ventilation with outside air, had the lowest mixing area mean diacetyl air concentration. However, plants C and E, without either of these types of ventilation, had only slightly higher mean diacetyl air concentrations. In general, the mixing areas differed with regard to several characteristics simultaneously (eg, size of area, ventilation, number of tanks, tank temperatures, and numbers and types of butter flavorings used) such that the relative importance of any particular characteristic to measured diacetyl air concentrations could not be determined.

Real-time monitoring in a mixer's breathing zone at plant D revealed peak diacetyl air concentrations of over 80 ppm over several minutes while he poured liquid butter flavorings into tanks of heated oil (Fig. 1).

In five of the six plants, packaging areas had lower mean diacetyl air concentrations than mixing areas. Compared with the index plant, mean diacetyl air concentrations in the packaging areas of all other plants were much lower (Table 1). The lowest TWA diacetyl air concentration measured with area sampling in the packaging areas of plants B through F ranged from below the limit of detection (0.001 ppm) in plant D to 0.4 ppm in plant B. The highest TWA diacetyl air concentration measured with area sampling ranged from 0.03 ppm in plants D and F to 1.2 ppm in plant B (compared with 6.8 ppm in the index plant). Packaging area mean diacetyl air concentrations were much lower in plants where all tanks of heated oil and butter flavorings were in a room separate from the packaging area (range 0.004–0.03 ppm measured with area sampling in plants C, D, and F) compared with plants where some or all tanks were located adjacent to packaging lines (range 0.3–1.9 ppm measured with area sampling in plants A, B, and E). NIOSH air sampling at plant F occurred after the company had made recent ventilation changes to render air pressure negative in the mixing room relative to the packaging area. On a prelimi-

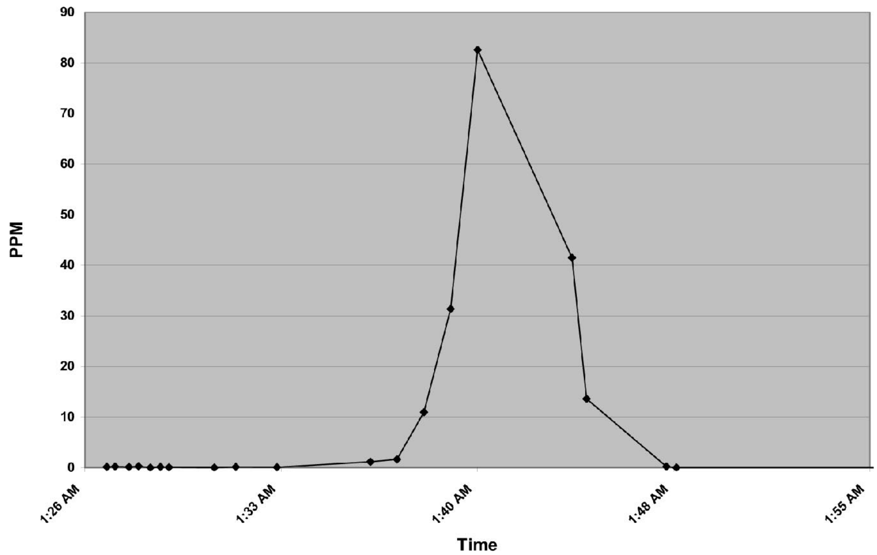


**Fig. 1.** Fourier Transform Infrared real-time diacetyl air concentrations at plant D. The diacetyl peak occurred when a mixer poured several 5-gallon containers of liquid butter flavoring into a heated tank of oil.

nary visit to this plant before the ventilation changes, NIOSH had determined that the mixing room had positive air pressure relative to the packaging area. This finding, and reports from several workers that the door to the mixing room was often left open, suggests that packaging area diacetyl air concentrations at plant F were probably higher in the past than those we measured. For an analysis of medical survey findings in packaging-area workers, we grouped plant F with plants A, B, and E ("nonisolated" or inadequately isolated tanks) and plant C with Plant D ("isolated tanks").

## Survey Participation and Worker Characteristics

Of 708 current workers, 537 (76%) participated in our surveys (Table 2). The mean age of participants was 39 years. Slightly more than half of participants were male, and most were white. Sixty-three percent were current or former smokers.

## Medical Records Review

In addition to the four known affected mixers and four known affected packaging-line workers among former workers of the index plant (plant A), medical records documented that an additional worker at plant A with past mixing experience,[12] mixers at plants B, D, and F (one at each plant), and three packaging-line workers at plant E had fixed airways obstruction, normal diffusing capacity, and evidence of air trapping on chest CT scans. The three largest plants (plants A, D, and F, each with over 100 workers) had mixers with these findings. Plant B (less than 10 workers) was one of two smaller facilities where a mixer also had these findings.[13] Of the lung biopsy reports we reviewed, two of three workers biopsied from plant A and three of six workers biopsied from plant E had findings consistent with constrictive bronchiolitis obliterans.

## Medical Survey Findings in Mixers

Eighty-six workers across all six plants reported having mixed oil and butter flavorings for at least 1 day. Compared with workers with no history of work as mixers (ie, never-mixers), these ever-mixers had higher prevalences of all respiratory symptoms with statistically significant excesses for SOB 2, chronic cough, and wheezing (Table 3). The mean percent predicted $FEV_1$ was 89% in ever-mixers and 94% in never-mixers (statistically significant, $P = 0.02$). The prevalence of smoking was similar in the two groups (56% vs 64%). Stratifying by smoking status, ever-mixers had higher symptom prevalences and lower mean percent predicted $FEV_1$ than never-mixers, with several comparisons achieving statistical significance (Fig. 2). Mean percent predicted $FEV_1$ values were 91 (ever-mixers) and 93 (never-mixers) among ever-smokers and 87 (ever-mixers) and 96 (never-mixers) among never-smokers. Although the overall prevalence of airways obstruction was similar in ever- and never-mixers (approximately 11%), ever-mixers had a higher prevalence than never-mixers among never-smokers (15.8% vs 6.9%), although this difference was not statistically significant. Nine of 10 ever-mixers with obstruction had a bronchodilator administered; eight of the nine (89%) had fixed obstruction.

Of the 86 ever-mixers, 26 had worked as mixers for more than 12 months and 45 had worked as mixers for 12 months or less. (For 15, length of time as a mixer was unknown.) Compared with ever-mixers with 12 months or less of mixing experience, ever-mixers with more than 12 months of mixing experience had higher prevalences of all respiratory symptoms and airways obstruction; the difference for SOB 1 was statistically significant, whereas the differences for airways obstruction and SOB 2 were borderline significant (Table 4). The mean percent predicted $FEV_1$ was 82% in ever-mixers with more than 12 months of mixing experience and 95% in those with 12 months or less of mixing experience (statistically significant, $P = 0.004$). Both ever- and never-smokers with more than 12 months of mixing experience had higher prevalences of all respiratory symptoms and airways obstruction and a lower percent predicted $FEV_1$ than ever- and never-smokers with 12 months or less

**TABLE 2**
Characteristics of Survey Participants at Six Microwave Popcorn Plants

| Plant | Workers | Survey Participants n (%) | Age (years) Mean (range) | Male (%) | White (%) | Smokers Current (%) | Smokers Former (%) | Smokers Never (%) |
|---|---|---|---|---|---|---|---|---|
| A (index) | 135 | 123 (91) | 37 (18–67) | 47 | 91 | 41 | 15 | 44 |
| B | 6 | 5 (83) | 60 (53–76) | 40 | 100 | 40 | 20 | 40 |
| C | 13 | 11 (85) | 37 (23–62) | 9 | 100 | 0 | 9 | 91 |
| D | 193 | 157 (81) | 43 (18–71) | 55 | 78 | 37 | 17 | 46 |
| E | 48 | 35 (73) | 49 (25–64) | 46 | 97 | 40 | 40 | 20 |
| F | 313 | 206 (66) | 36 (18–67) | 69 | 92 | 61 | 11 | 28 |
| All plants | 708 | 537 (76) | 39 (18–76) | 57 | 88 | 47 | 16 | 37 |

**TABLE 3**
Mean Percent Predicted Forced Expiratory Volume in One Second ($FEV_1$) and Prevalences of airways obstruction and Respiratory Symptoms in Workers Who Mixed Oil and Butter Flavoring Compared With Workers Who Never Performed This Task

| | Ever-Mixers | Never-Mixers | *P* Value |
|---|---|---|---|
| Mean percent predicted $FEV_1$ | 89.4 | 94.2 | 0.02 |
| Obstruction on spirometry, n (%) | 10* (11.6) | 47† (10.7) | 0.8 |
| Shortness of breath on exertion (SOB 1), n (%) | 33 (39.3) | 134 (30.7) | 0.12 |
| Shortness of breath on exertion (SOB 2), n (%) | 15 (17.9) | 43 (9.8) | 0.03 |
| Chronic cough, n (%) | 21 (24.7) | 55 (12.5) | 0.003 |
| Wheezing, n (%) | 36 (42.4) | 98 (22.2) | <0.0001 |

*Nine of 10 had a bronchodilator (BD) administered; eight of nine (89%) did not respond to BD.

†Forty of 47 had a BD administered; 31 of 40 (78%) did not respond to BD.

SOB 1 indicates shortness of breath when hurrying on level ground or walking up a slight hill; SOB 2, shortness of breath when walking with people your own age on level ground.

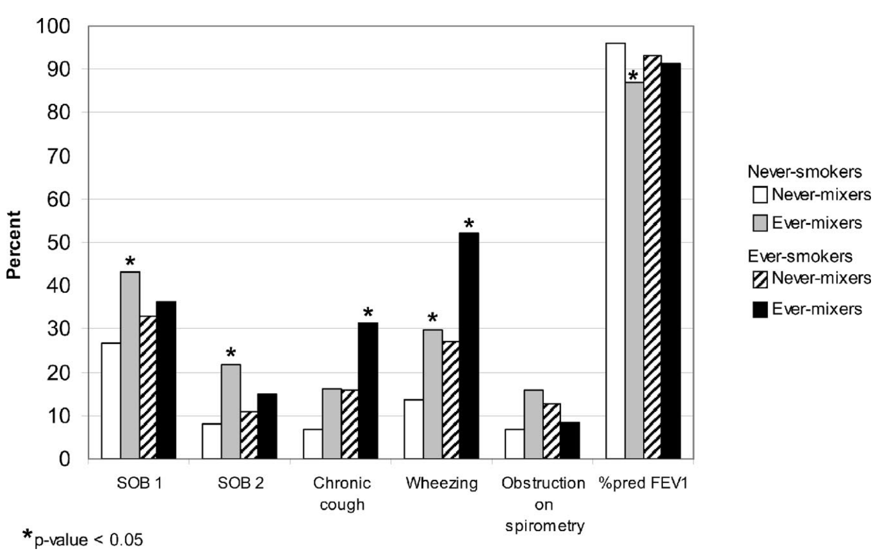


**Fig. 2.** Prevalences of respiratory symptoms and airways obstruction and mean percent predicted forced expiratory volume in 1 second in ever-mixers compared with never-mixers by smoking status. (Asterisk denotes $P < 0.05$ for comparison within smoking category.)

experience as mixers (Fig. 3). The differences for SOB 1 among never-smokers and in mean percent predicted $FEV_1$ among ever-smokers were statistically significant.

To determine if data from the index plant were responsible for the excess rates of obstruction and respiratory symptoms in the aggregate data, we repeated our analyses after excluding the data from the index plant. The prevalences of respiratory symptoms were still higher in ever-mixers compared with never-mixers; the excess for wheezing was statistically significant (38.3% vs 19.5%; $P = 0.001$) and for chronic cough was borderline significant (18.3% vs 10.3%; $P = 0.07$). Mean percent predicted $FEV_1$ was 90% in ever-mixers and 95% in never-mixers (statistically significant, $P = 0.02$). Mean percent predicted $FEV_1$ was 79.7% in ever-mixers with more than 12 months of mixing experience and 95% in those with 12 months or less of mixing experience (statistically significant, $P = 0.005$). Those with more time as mixers also had higher prevalences of all respiratory symptoms and airways obstruction but only the excess for SOB 1 was statically significant (57.9% vs 22%; $P = 0.006$).

## Medical Survey Findings in Packaging-Area Workers

Compared with packaging-area workers in plants with isolated tanks, packaging-area workers in plants with nonisolated or inadequately iso-

**TABLE 4**
Mean Percent Predicted Forced Expiratory Volume in One Second ($FEV_1$) and Prevalences of Airways obstruction and Respiratory Symptoms in Workers Who Mixed Oil and Butter Flavoring for More Than 12 Months Compared With Workers Who Did This Task for 12 Months or Less Time

| | Mixer >12 Mo | Mixer <12 Mo | *P* Value |
|---|---|---|---|
| | (*n* = 26) | (*n* = 45) | |
| Mean percent predicted $FEV_1$ | 82.1 | 95.0 | 0.004 |
| Obstruction on spirometry, n (%) | 5* (19.2) | 2† (4.4) | 0.09 |
| Shortness of breath on exertion (SOB 1), n (%) | 13 (54.2) | 11 (24.4) | 0.01 |
| Shortness of breath on exertion (SOB 2), n (%) | 6 (25.0) | 3 (6.7) | 0.06 |
| Chronic cough, n (%) | 7 (28.0) | 8 (17.8) | 0.32 |
| Wheezing, n (%) | 13 (52.0) | 17 (37.8) | 0.25 |

*Five of five had a bronchodilator (BD) administered; four of five (80%) did not respond to BD.

†Two of two had a BD administered; two of two (100%) did not respond to BD.

SOB 1 indicates shortness of breath when hurrying on level ground or walking up a slight hill; SOB 2, shortness of breath when walking with people your own age on level ground.

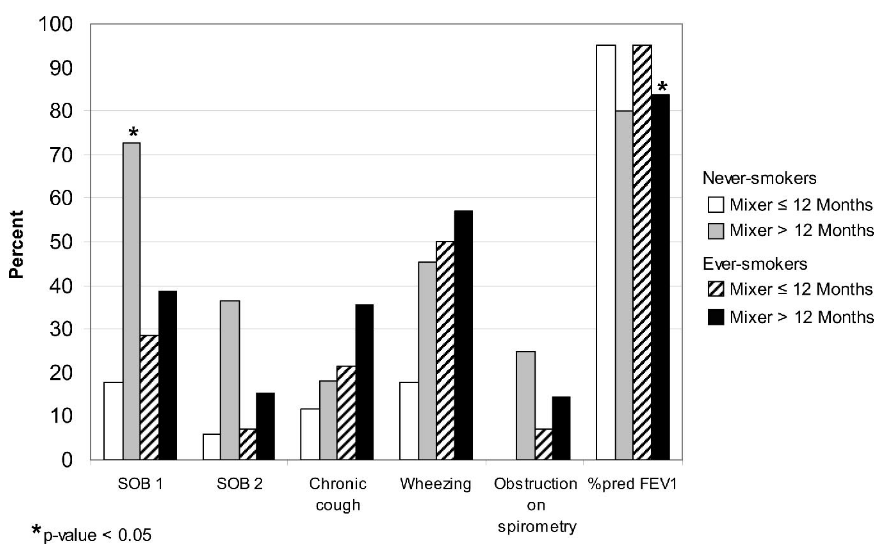


**Fig. 3.** Prevalences of respiratory symptoms and airways obstruction and mean percent predicted forced expiratory volume in 1 second in mixers with 12 or fewer months of mixing experience compared with mixers with more than 12 months mixing experience by smoking status.

lated tanks had higher prevalences of all respiratory symptoms and airways obstruction; the excess for wheezing was statistically significant ($P = 0.001$), and for airways obstruction, it was borderline significant ($P = 0.06$) (Table 5). Mean percent predicted $FEV_1$ was lower in packaging-area workers who worked near nonisolated tanks (93.7% vs 96.4%), but this difference was not statistically significant. Of 27 packaging-area workers with airways obstruction in plants with nonisolated or inadequately isolated tanks, 23 had a bronchodilator administered; 21 of 23 (91%) had fixed obstruction. The percentage of ever-smoker packaging-area workers was higher in plants with nonisolated or inadequately isolated tanks than in plants with isolated tanks (73% vs 45%). However, after stratifying by smoking status, both ever- and never-smoker packaging-area workers in plants with nonisolated or inadequately isolated tanks had higher prevalences of airways obstruction and most respiratory symptoms than ever- and never-smoker packaging-area workers in plants with isolated tanks (Fig. 4). The excesses for SOB 1 and wheezing among never-smokers were statistically significant.

After excluding data from the index plant from the analysis, packaging-area workers in plants with nonisolated or inadequately isolated tanks still had higher prevalences of airways obstruction (11.5% vs 5.5%; not statistically significant) and wheezing (25% vs 10.7%; statistically significant, $P = 0.01$), whereas the prevalences of other respiratory symptoms were similar in both groups.

## Medical Survey Findings in Other Workers

*Quality Control.* For plants A, D, and F, Table 6 provides data on the number of bags popped by QC workers per day, diacetyl air concentrations in the QC laboratory, and spirometry results in QC workers. The other plants popped fewer bags and/or did not have workers that did QC work exclusively. Five of six QC workers tested (85%) had airways obstruction at plant A, which clearly had the highest QC laboratory mean diacetyl air concentration (0.6 ppm). No other plant had high rates of obstruction in QC workers.

*Maintenance.* Thirty-seven workers reported having worked in maintenance but never as a mixer or packaging-area worker. Compared with 138 workers with no history of work in maintenance, mixing, or in the packaging area, maintenance workers had higher prevalences of all respiratory symptoms with statistically significant excesses for SOB 2 (18.9% vs 5.8%; $P = 0.01$) and wheezing (32.4% vs 15.3%; $P = 0.02$) and a borderline significant excess for SOB 1 (37.8% vs 23.4%; $P = 0.08$). Mean percent predicted $FEV_1$ was lower in maintenance

**TABLE 5**

Mean Percent Predicted Forced Expiratory Volume in One Second ($FEV_1$) and Prevalences of Obstruction and Respiratory Symptoms Among Packaging-Area Workers in Plants with Nonisolated or Inadequately Isolated Tanks of Heated Oil and Butter flavoring (Plants A, B, E, and F) Compared With Packaging-Area Workers in Plants With Isolated Tanks (Plants C and D)

| | Packaging-Area Workers in Plants With Nonisolated Tanks (*n* = 195) | Packaging-Area Workers in Plants With Isolated Tanks (*n* = 75) | *P* Value |
|---|---|---|---|
| Mean percent predicted $FEV_1$ | 93.7 | 96.4 | 0.26 |
| Obstruction on spirometry, n (%) | 27* (14.0) | 4† (5.5) | 0.06 |
| Shortness of breath on exertion (SOB 1), n (%) | 68 (36.2) | 20 (26.7) | 0.14 |
| Shortness of breath on exertion (SOB 2), n (%) | 23 (12.2) | 5 (6.7) | 0.19 |
| Chronic cough, n (%) | 31 (16.2) | 8 (10.8) | 0.27 |
| Wheezing, n (%) | 57 (29.7) | 8 (10.7) | 0.001 |

*Twenty-three of 27 had a bronchodilator (BD) administered; 21 of 23 (91%) did not respond to BD.

†Four of four had a BD administered; two of four (50%) did not respond to BD.

SOB 1 indicates shortness of breath when hurrying on level ground or walking up a slight hill; SOB 2, shortness of breath when walking with people your own age on level ground.

workers (91.6% vs 94.3%), but this difference was not statistically significant and prevalence of airways obstruction was similar in both groups (8.1% vs 9.5%). After excluding data from the index plant from this analysis, maintenance workers still had excess wheezing that was statistically significant (34.5% vs 16%; $P = 0.02$). However, the prevalences of other respiratory symptoms were now similar in both groups, mean percent predicted $FEV_1$ was also similar (approximately 94%), and prevalence of airways obstruction was lower in maintenance workers (3.5% vs 8%).

## Discussion

The investigation of severe fixed obstructive lung disease in workers of a microwave popcorn plant in 2000 identified inhalation exposure to butter-flavoring chemicals as the likely cause.[1,2] The results of animal studies showing severe airway epithelial injury after a 6-hour inhalation exposure to a butter flavoring used at this plant, and similar injury after a 6-hour inhalation exposure to pure diacetyl, provided additional support for this conclusion.[3,4]

Our analyses of aggregated data from medical and environmental surveys at the index plant and five additional microwave popcorn plants indicate an apparent widespread risk for occupational lung disease from exposure to butter-flavoring chemicals in this industry. In five of six plants, mixers and/or packaging-area workers with onset of respiratory symptoms after starting work had undergone medical evaluations that revealed fixed airways obstruction and other findings consistent with bronchiolitis obliterans. Our findings from medical surveys of current workers at these plants are consistent with the medical evaluations, indicating risk to mixers who combine butter flavorings with heated oil and to packaging-area workers who work near inadequately isolated tanks of heated oil and flavorings.

Our analyses highlight the high potential for lung disease in mixers of oil and butter flavorings. Mixers at four of six plants had medical findings consistent with bronchiolitis obliterans, and mixers with more than 12 months' mixing experience had the highest respiratory symptom and airways obstruction prevalences and the lowest mean percent predicted $FEV_1$ in our analyses of the data from surveys of current workers. At plant D, one of the four plants where a mixer had developed lung disease, the mean TWA diacetyl air concentration measured with area sampling in the mixing room was only 0.2 ppm compared with 37.8 ppm at the index plant. However, peak exposures measured at plant D during open handling of butter flavorings were much higher. These findings suggest that even when ventilation maintains low-average exposures, mixers are still at risk from

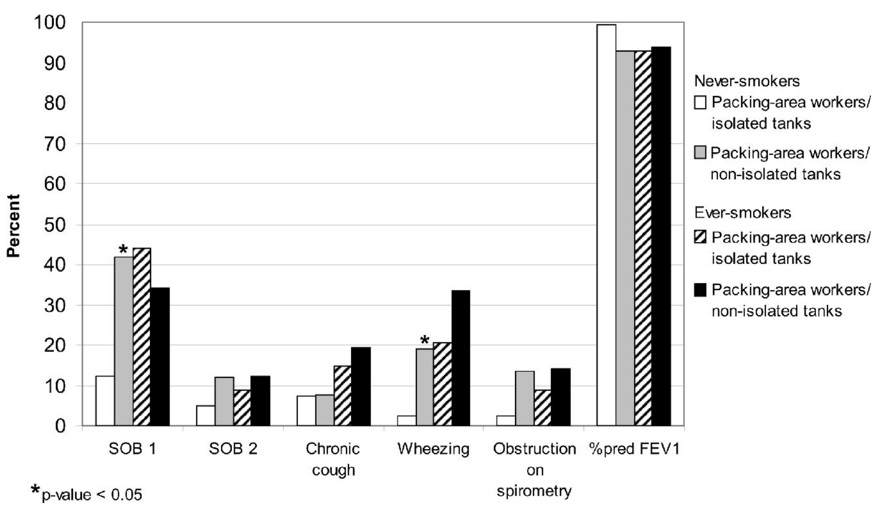


**Fig. 4.** Prevalences of respiratory symptoms and airways obstruction and mean percent predicted forced expiratory volume in 1 second in packaging-area workers in plants with isolated tanks compared with packaging-area workers in plants with nonisolated tanks by smoking status.

**TABLE 6.**
Number of Bags of Microwave Popcorn Popped in Microwave Ovens per Quality Control (QC) Worker, QC Laboratory Diacetyl Air Concentrations, and Proportion of QC Workers With Airways Obstruction at Plants A, D, and F

| Plant | Number of Bags Popped Per QC Worker | Diacetyl Air Concentration Mean (range; ppm)* | Proportion of QC Workers With Obstruction |
|---|---|---|---|
| A (index) | ~100 per 8-hr work shift | 0.6 (0.3–0.9) | 5 of 6 |
| D | ~75 per 8-hr work shift | <0.001 | 0 of 3 |
| F | ~130 per 12-hr work shift† | 0.02 (<0.01–0.03) | 1 of 11 |

* Parts per million parts air by volume.
† At plant F, workers only performed this task 3 to 4 days per week for 1 of every 3 weeks.

brief, intense exposures associated with open handling of butter flavorings or opening lids to check on tanks of heated oil and flavorings.

Packaging-area workers near nonisolated tanks that contain heated oil and flavorings are likely at risk from higher average concentrations of flavoring chemicals in the air or from intermittent peak exposures when mixers add butter flavorings to tanks or lift tank lids to check on the contents. Of the three plants where tanks were isolated, plant C had the highest packaging area mean TWA diacetyl air concentration (0.03 ppm from area sampling). This was still an order of magnitude *lower* than the lowest mean TWA diacetyl air concentration in the packaging area at plants where tanks were not isolated (0.3 ppm from area sampling at plant E).

The high prevalence of airways obstruction in QC workers at plant A implies that this job can pose risk when many dozens of bags are popped daily without adequate control of exposures. In plants that performed QC popping of product, air concentrations of diacetyl in the QC laboratory were as low as, or lower than, the air concentrations in the packaging area in the same plant. However, the much higher temperatures that occur in microwave popping (compared with the temperatures in heated tanks) increase the volatilization of other chemicals. Because of this, QC workers' exposures may be substantially different from those of other production workers, and diacetyl air concentrations alone may not be a satisfactory predictor of risk for these workers. In addition, QC workers, like mixers, experience intermittent peak exposures that may increase their risk although their average exposures are much lower.

Because our analyses were conducted on data from cross-sectional medical surveys of current workers, it is possible that the prevalences of respiratory symptoms and airways obstruction in mixers and in packaging-area workers who worked near inadequately isolated tanks might have been higher if our survey had included former workers, some of whom may have left employment due to respiratory illness (a healthy worker effect). Given the fact that mixers comprised a small percentage of the workforce at all plants, including former workers might possibly have resulted in larger numbers of ever-mixers and led to additional findings of statistical significance in our analyses. During the initial cross-sectional survey at the index plant, we invited former workers to participate. However, despite our efforts to notify former workers about the planned survey through phone calls, mailed notifications, and media advertisements, many could not be located. Of an estimated 425 former workers who worked at plant A between 1992 and 2000, only 161 (approximately 38%) participated in our survey. Because of this low participation and the possibility that this was not a representative sample of former workers, we did not include this group in our analyses and did not attempt systematic surveys of former workers at other plants.

At this time, insufficient data exist on which to base workplace exposure standards or recommended exposure limits for butter flavorings. Because the risk for occupational lung disease may be partly due to short-term peak exposures, an exposure limit based on an 8-hour TWA may not be sufficient to protect workers. Moreover, because flavorings are complex mixtures of many chemicals, most of which have not been evaluated with respect to inhalation toxicity, focusing solely on diacetyl air concentrations may not be adequate to assess risk in different plants using a variety of different flavorings. Few flavoring chemicals have an Occupational Safety and Health Administration (OSHA)-permissible exposure limit (PEL) or a NIOSH-recommended exposure limit (REL).[14] The lowest mean TWA diacetyl air concentrations that we measured in mixing areas (0.02 ppm personal exposure and 0.2 ppm area air concentration) were at a plant with an affected mixer (plant D); therefore, it would seem prudent to maintain worker exposures to diacetyl below these levels.

Because entirely safe levels of occupational exposure to butter-flavoring chemicals are not known, it is important to limit worker exposures as much as possible. The most reliable way to do this will require microwave popcorn companies to re-engineer their production processes to closed systems that eliminate the need for workers to handle flavorings in open containers and to open the lids of heated tanks to check on their contents. Until this is accomplished, all flavoring handling and mixing activities, and all tanks of heated oil and flavorings, should be isolated in a room under negative air pressure and with ventilation separate from the rest of the plant. In addition, all tanks should have local exhaust ventilation. Any worker entering the mixing room should wear, at all times, a NIOSH-approved air-purifying respirator with organic vapor cartridges and particulate filters or a more protective respirator (such as a supplied-air respirator). Respirator use must be part of a formal, written respiratory protection program that adheres to the requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134). Respirators should only be considered a short-term solution because they may allow intermittent exposures through improper use, improper fit, or respirator malfunction. Encapsulated powdered flavorings that release less flavoring-related vapors into the air may be a safer alternative to liquid and paste flavorings. However, workers may be at risk from any respirable dust generated during the handling of these powders, so workers should use respirators during open handling of powdered flavorings as well as during the handling of liquids and pastes. Because some flavoring chemicals, including diacetyl, are known irritants, skin and eye exposure should be limited with appropriate work clothes, gloves, and eye protection. Microwave ovens used by QC workers should have local exhaust ventilation, and bags of product should be allowed to cool before being opened. Because flavoring-related decreased lung function can occur before the onset of symptoms, relying solely on self-reporting of respiratory symptoms by workers as a way to identify early lung disease is insufficient to prevent clinically significant irreversible lung disease.[1] Therefore, regularly scheduled medical monitoring with spirometry for workers who enter the mixing room or perform QC popping of product in microwave ovens is essential for early detection of declines in lung function that may indicate flavoring-related lung disease.

Workers exposed to butter-flavoring chemicals in the manufacture of other food products besides microwave popcorn may also be at risk for occupational lung disease. Clinicians should consider this possibility if they are evaluating respiratory symptoms or impairment in patients with a history of work in food production or in flavoring-manufacturing plants. Diagnosis of lung disease that is possibly flavoring-related in such workers should prompt further evaluation of the affected worker's workplace and coworkers to identify ongoing risks, if any, so that disease in other workers can be prevented.

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