Progression of Chronic Obstructive Pulmonary Disease after Multiple Episodes of an Occupational Inhalation Fever

Stephen N. Kales, MD, MPH
David C. Christiani, MD, MPH, MS

A carding machine operator in a synthetic fabric plant experienced marked symptomatic deterioration of obstructive pulmonary disease after multiple episodes of an occupational inhalation fever. Polytetrafluoroethylene was used in the industrial process and polymer fume fever is suspected as a cause of his febrile illnesses. A state industrial hygiene inspection revealed that major repairs had been performed on an air scrubber system in close proximity to the patient's work area after he had left the plant because of disability. We believe that this case provides further evidence that polymer fume fever is not always a benign, self-limited illness, especially when workers suffer multiple episodes and/or have underlying pulmonary disease.

The fume fever syndromes are caused by the inhalation of various metal fumes (metal fume fever) or the decomposition products of fluoropolymers such as polytetrafluoroethylene (PFTE) (PFF). Both are characterized by fever, chills, nausea, cough, often with leukocytosis and with spontaneous resolution after 24 to 48 hours, but unlike metal fume fever, tolerance to repeat exposure does not occur in PFF.[1] Although usually thought of as self-limited episodes, two case reports have questioned whether long-term pulmonary pathology might result from PFF.[2,3] Williams et al[2] described a woman who had suffered over 40 episodes of PFF. She died from an unrelated cerebral hemorrhage and at autopsy, moderate interstitial pulmonary fibrosis and mild honeycombing were found. Brubaker[3] reported the case of a young man with a severe episode of PFF and resultant pulmonary edema. Three weeks later he continued to complain of cough and chest pain, and pulmonary function testing showed moderately severe obstruction that was reversible and a depressed diffusing capacity. Two months after the PFF episode, he was without symptoms and his airway obstruction had resolved, but his diffusing capacity remained depressed.[3]

We report here a case of severe obstructive pulmonary disease after multiple episodes of an occupational inhalation fever where PFTE was used in the industrial process.

Case Report

A 45-year-old man was referred by his attorney for evaluation of severe

From the Harvard School of Public Health (Dr Kales, Dr Christiani) and the Harvard Medical School (Dr Kales), Cambridge, Massachusetts.

Address correspondence to: Stephen N. Kales, MD, MPH, Occupational Medicine, Department of Medicine, The Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139.

0096-1736/94/3601-0075$03.00/0

respiratory impairment and its relation to work in July of 1992. Before beginning work at a synthetic textile plant in January 1990, the patient denied any respiratory symptoms, but according to his pre-employment examination, he reported the use of an over-the-counter bronchodilator for occasional exertional dyspnea. He had quit smoking 6 years earlier (17 pack-years total). From January 1990 to March 1992 the patient operated a carding machine at a synthetic textile plant that at times required substantial physical exertion such as moving textile rolls. He worked in close proximity to a dryer, which heated the fabric along with various coating chemicals to high temperatures (reported to be 350 to 420°F assuming proper function). Potential exposures here included PFTE, formaldehyde, ammonia, phenol, and synthetic fibers. The dryer was exhaust ventilated by an air scrubber, but, according to the patient, it produced smoky fumes that caused cough, tearing, and a raw sensation in the throat. Fumes were often bad enough to cause the patient and co-workers to leave the building.

Two weeks after starting this job, he began to experience recurrent episodes of flu-like symptoms including fever, chills, nausea, and dry cough. The symptoms would increase as the work week went on, and got better on weekends. He began to miss work. In October 1990, after about 9 months on the job, he presented to his physician on a Friday with fever, chills, chest pain, productive cough, and malaise. Erythromycin was prescribed on an outpatient basis. A chest film showed hyperinflation and no infiltrates. A complete blood count returned with a leukocyte count of 20,000, and because the patient was still symptomatic the following Monday he was hospitalized. At that time, the white blood cell count had dropped to 9,700. An arterial blood gas on room air at rest was as follows: 7.38/38/70/93% sat. Empiric antibiotic treatment was given, but blood and sputum cultures demonstrated no pathogens. Pulmonary function tests (Table 1) revealed moderately severe obstructive disease, but no bronchodilator trial was given. The acute symptoms resolved, and the patient returned to work. However, he now developed dyspnea with even mild exertion.

TABLE 1
Serial Pulmonary Function Testing

	Prebronchodilator			
	October 1990	March 1992	July 1992	% Predicted
Spirometry				
FVC	3.06 l	2.26 l	2.75 l	67
FEV_1	1.46 l	0.98 l	0.99 l	29
FEV_1/FVC	48%	43%	36%	
	Postbronchodilator			
Spirometry				
FVC	–	2.95 l	3.29 l	80
FEV_1	–	1.29 l	1.37 l	40
FEV_1/FVC	–	44%	41%	
Lung volumes				
SVC	3.32 l	2.69 l	3.30 l	80
IC	2.20 l	2.11 l	2.36 l	86
ERV	1.12 l	0.58 l	0.94 l	69
FRC	3.59 l	4.12 l	3.53 l	109
RV	2.47 l	3.54 l	2.59 l	138
TLC	5.79 l	6.23 l	5.89 l	98
RV/TLC	43%	57%	44%	137
Lung diffusion				
DLCO(SB)	–	37.9	28.69	94

l, liters; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; SVC, slow vital capacity; IC, inspiratory capacity; ERV, expiratory reserve volume; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; DLCO, diffusing capacity for carbon monoxide; SB, single breath.

The patient continued to have recurrent episodes of a flu-like illness. Over the next 16 months, he had four more visits to his physician for bronchitic exacerbations and was treated with antibiotics. In February of 1992, the patient stopped working on the advice of his treating physician. One month later, he was rehospitalized with chest pain and diaphoresis. At that time, he complained of morning sputum production, chronic shortness of breath, and dyspnea on exertion. Electrocardiograms, cardiac enzymes, and cardiac stress test were normal. Pulmonary function tests showed severe obstruction with a significant bronchodilator response and normal diffusing capacity (Table 1). He was placed on disability leave from the company and has not returned since.

There was no family history of asthma, emphysema, nor other lung disease. Medications at the time of his initial consultation were Ventolin, Atrovent, Theophylline, and Azmacort. Examination was remarkable for mild shortness of breath at rest with a respiratory rate of 18 to 20, decreased breath sounds, and diffuse expiratory wheezing. Pulmonary function testing at our clinic again revealed severe obstruction with a significant bronchodilator response (Table 1). Pulse oximetry demonstrated an oxyhemoglobin saturation of 97 to 98% on room air. There was no desaturation with submaximal exercise (heart rate from 90 at rest to 120 with 3 minutes of walking). An α_1-antitrypsin level was 189 mg/dl (range, 93 to 224).

The patient was started on prednisone 60 mg/day and slowly tapered to 0 over 1 month; however, serial spirometry showed no significant improvement (forced expiratory volume in 1 second [FEV_1] of 1.32 liter and an FEV_1/forced vital capacity of 42% with combination bronchodilator treatment and after one month of systemic corticosteroids).

A Massachusetts Division of Occupational Hygiene inspection of the pa-

tient's workplace in August 1992 was significant in revealing that the company had done "major repair and renovation" to the dryer-air pollutant scrubber after our patient had left the workplace. These "renovations were widely reported to have significantly improved the capture of chemical contaminants . . ." and ". . . substantially improved air quality in the production area." Air sampling also revealed significant exposures to formaldehyde: 0.4 to 1.3 ppm (OSHA PEL 0.75 ppm), which were highest at the dryer guide arm platform.

Discussion

This patient gave a history of recurrent occupational fevers and respiratory symptoms and presented with markedly decreased pulmonary function and resultant severe functional limitations at a relatively young age. Although he denied prior respiratory symptoms to us in the context of a medicolegal evaluation, other medical records documented his pre-employment use of an over-the-counter bronchodilator. In fact, he probably had some degree of underlying obstructive pulmonary disease; however, he was able to carry out work tasks requiring significant exertion. Given his previous lack of functional impairment, it seems that he experienced a rapid, work-related decompensation during his 2 years of employment as a carding machine operator. This is supported by the 480 ml (33%) drop in FEV_1 over 17 months with subequent stabilization of the FEV_1 in the first 5 months after leaving the workplace. Attacks of PFF are suggested by the use of PFTE and his recurrent influenza-like episodes.

For PFF to occur, thermal decomposition of the fluoropolymers must occur by heating to temperatures over 572°F.[1] For this reason, most episodes have been described in smokers who have contaminated their cigarettes with fluoropolymers, which decompose when the tobacco burns at high temperatures.[1-5] Our patient had quit smoking years before entering this job, which means that if he had PFF, decomposition must have occurred by an alternative mechanism. The dryer was said to operate normally at temperatures up to 420°F, which would be insufficient to produce decomposition. However, we question whether the temperature was actually maintained at or about 420°F when the patient described the emission of smoky fumes from this unit; subsequently, the associated air scrubber was said to have undergone major repair and renovation. It is difficult to find an alternative explanation for his history. His other potential work exposures would not cause fever. Although influenza causes symptoms similar to PFF, it occurs only once a year and could not be expected to produce repetitive episodes limited to the period of employment.

The most dramatic aspect of the patient's course, however, is his resultant severe obstructive pulmonary disease. Although chronic obstructive disease has not been described as a sequela of multiple episodes of PFF, there are reports in the literature that support this possibility. Brubaker[3] reported a PFF case in which obstructive airways disease persisted several weeks after a single exposure. Kuntz and McCord[6] evaluated a woman after multiple episodes of PFF who had persistent dyspnea on exertion, mild airway obstruction, and a small increase in the functional residual capacity. There are also more recent reports of reactive airways dysfunction syndrome (RADS) after fume fever episodes. Sjogren et al[7] described two welders who developed febrile syndromes, mild decrements from baseline spirometry, and hyperreactivity to histamine bronchoprovocation after welding on a surface covered with a laquer that contained a chloropolymer. Spirometric values returned to normal over 1 year in the first welder who had six febrile episodes, and over 5 months in the second worker, who had five such episodes.[7] Langley[8] reported another case of RADS in a welder after fume fever. In this case, the exposure was welding over galvanized steel and brass pipe which he believed were covered by PFTE tape near the connection where he was brazing. There was a history consistent with one previous episode of metal fume fever 5 years earlier that was mild and did not require medical attention.[8] If several or even single attacks of fume fever can cause RADS, it is not unreasonable that multiple episodes of PFF over a short period of time could result in deterioration of chronic obstructive pulmonary disease such as that present in our patient. The normal diffusing capacity and severe obstruction with air trapping indicate that the main pathologic process is not emphysema, but large and small airways disease perhaps due to a chemically induced bronchiolitis.

It is also possible that persons with a smoking history are more severely affected by fume fever. Lewis and Kerby[9] found that 79% of smokers experienced symptoms of PFF during a period of exposure, compared to 33% of nonsmokers; however, this may be due to the cigarettes themselves serving as a vehicle for thermal decomposition of PFTE. Goldstein et al[10] reported on an inhalation exposure in six co-workers who sought attention in an emergency room with a syndrome consistent with fume fever due to the apparent pyrolysis of a chloropolymer. Three were nonsmokers and had a milder course and did not require hospitalization. The remaining three, described as "long-term heavy cigarette smokers," required hospital admission and developed moderate respiratory distress and hypoxia. Several weeks after the episode, pulmonary function testing in all three smokers showed mild obstruction, which was presumed to be due to tobacco use.[10] Our patient had reported the use of an over-the-counter bronchodilator for occasional exertional dyspnea and had a significant previous smoking history. Therefore, it is probable that he had significant pre-existing airways obstruction and hyperreactivity and that he was more susceptible to pulmonary toxicity on this basis. Unfortunately, pre-employment pulmonary function was not obtained, so that the extent of his baseline impairment is not clear.

Conclusions

We have reported a case of severe, fixed obstructive pulmonary disease

after multiple episodes of an occupational inhalation fever where PFTE was used in the industrial process. We believe that this case provides further evidence that PFF is not always a benign, self-limited illness and may result in permanent airways damage. More research on the long-term sequelae of fume fever syndromes is needed to clarify this possibility. In the meantime, it would be advisable for exposed workers to receive preplacement spirometry to establish a baseline. Workplace controls should ensure that fluoropolymers are not heated above temperatures that make decomposition possible, and strict no-smoking restrictions and hand-washing should be enforced to avoid the contamination of smoking materials.[1,4] We also agree with the recommendation that those who have had recurrent episodes of PFF or polymer-associated pulmonary edema should get long-term follow-up.[1,2]

Acknowledgments

We thank Salvatore Insogna, MSPH, of the Massachusetts Division of Occupational Hygiene for his inspection of the workplace.

This work was supported by the Occupational Safety and Health Educational Resource Center, National Institute for Occupational Safety and Health Grant Award 5 T15 OH07096 at the Harvard School of Public Health, and the Occupational Physician's Scholarship Fund of the American College of Occupational and Environmental Medicine. Also supported by National Institute for Environmental Health Sciences Grant Award E500002.

References

1. Rose CS. Inhalation fevers. In: Rom WN, ed. Environmental and Occupational Medicine, 2nd ed. Boston: Little, Brown and Company; 1992:373–380.
2. Williams N, Atkinson GW, Patchefsky AS. Polymer fume fever: not so benign. *J Occup Med.* 1974;16:519–522.
3. Brubaker RE. Pulmonary problems associated with the use of polytetrafluoroethylene. *J Occup Med.* 1977;19:693–695.
4. Albrecht WN, Bryant CJ. Polymer fume fever associated with smoking and use of a mold-release spray containing polytetrafluoroethylene. *J Occup Med.* 1987; 29:817–819.
5. Wegman DH, Peters JM. Polymer fume fever and cigarette smoking. *Ann Intern Med.* 1974;81:55–57.
6. Kuntz WD, McCord CP. Polymer fume fever. *J Occup Med.* 1974;16:480–482.
7. Sjogren B, Backstrom I, Fryk G, et al. Fever and respiratory symptoms after painting on welded steel. *Scand J Work Environ Health.* 1991;17:441–443.
8. Langley RL. Fume fever and reactive airways dysfunction syndrome in a welder. *South Med J.* 1991;84:1034–1036.
9. Lewis CE, Kerby GR. An epidemic of polymer fume fever. *JAMA.* 1965; 191:103–106.
10. Goldstein M, Weiss H, Wade K, Penek J, Andrews L, Brandt-Rauf P. An outbreak of fume fever in an electronics instrument testing laboratory. *J Occup Med.* 1987;29:746–749.

Hearing Aid

"Let me adjust my hearing aid. It could not accommodate the decibels of the Senator from Massachusetts. I can't match him in decibels, or Jezebels, or anything else apparently."

Senator Jesse Helms, after Senator Ted Kennedy made a loud and impassioned speech in favor of allowing foreigners with AIDS to have US residency.

From "Overheard." *Newsweek*, 1993;121:9, p 21