An Epidemic of Polymer-Fume Fever

Charles E. Lewis, MD, and Gerald R. Kerby, MD

An "epidemic" of polymer-fume fever involved 36 of 61 employees in one industry over a 90-day period. All of those involved demonstrated the classic history of an influenza-like syndrome, with fever and chills occuring several hours after exposure to the products of pyrolysis of polytetrafluoroethylene (Teflon). The majority of cases resulted from the smoking of cigarettes which were contaminated with a fine dust of this material. A study of pulmonary function of all workers involved demonstrated changes that could be accounted for only on the basis of smoking habits. Three persons experienced changes in pulmonary function consistant with mild obstruction of the airways, in association with the onset of symptoms. While no serious consequences were observed, the effects of these illnesses upon the health and productivity of the group could have been prevented.

Within ten years after the first description of the properties of polymers of tetrafluoroethylene (Teflon, Fluon) the first account of their effects on man appeared in the medical literature. In 1951, Harris described four cases of "polymer-fume fever."[1] The signs, symptoms, and natural history of this malady were similar to those of "metal-fume fever," which was described by Thackrah in 1831. In the interval since 1951, there have been several reports of illness resulting from exposure to the products of pyrolysis when these polymers are heated to temperatures in excess of 300 C.[2,3] Also, false reports of fatal illnesses resulting from such exposures have appeared in the medical literature.[4]

During a 90-day period in the summer of 1964, an "epidemic" of polymer-fume fever occurred in a large industrial plant. Thirty-six out of 61 workers in a single department were affected. This study reports an epidemiologic investigation of this outbreak, as well as the results of pulmonary-function studies performed on the men in this environment.

Process and Events Preceding Investigation

The department involved manufactured small, light-weight sub-assemblies which required metal bonding, using epoxy resins. These parts were assembled on a "tool" or assembly block. The unit then was autoclaved at increased pressure and temperature to cure the resin. A parting compound was applied to the tool or assembly unit to permit separation of the sub-assembly from the tool after autoclaving. This process was originally carried out in a large, open space and had not been attended by any medical difficulties.

For editorial comment see page 406.

In April 1964 the sub-assembly operation was moved to a balcony location in the same general plant area. On May 13 it became necessary to enclose and air-condition the area to improve the environmental conditions for a more efficient assembly of the unit. During the same week, a different parting compound was substitued for the original silicone-base material.

Approximately 40 of the men in this department work on a day or an evening shift in the subassembly enclosed area (A). The other personnel in the department (25 men) are employed on the balcony, which is an open area (B) in the same general plant. These men handle the "tools" or assembly blocks and prepare them for reuse after they come from the autoclave.

Symptoms of polymer-fume fever first appeared among the group in area A as early as May 14 (the day after the air conditioning was installed). Symptoms also appeared in the group working in the same department, but outside the enclosed air conditioning (area B) during May. The symptoms noted by the workers in area B were milder than in those in area A.

Methods

A history form was used to collect data from all employees working in areas A and B. All members of group A and those with complaints of polymer-

Table 1.—Frequency of Various Complaints Among 36 Workers With Symptoms of Polymer-Fume Fever

Complaint	No.	% of Total of 61 Workers
Tightness of chest	31	51
Malaise	30	49
Shortness of breath	26	43
Headache	24	39
Cough	22	36
Chills	22	36
Temperature, 100-104 F (37.8-40 C)	20	33
Sore throat	6	10
Sputum	1	1.6

From the departments of preventive medicine and medicine, University of Kansas Medical School, Kansas City, Kan.

Reprint requests to Department of Preventive Medicine, University of Kansas Medical Center, Rainbow Blvd at 39th St, Kansas City, Kan. 66103 (Dr. Lewis).

Table 2.—Relationship of Smoking to Symptoms of Polymer-Fume Fever

	Symptoms	No Symptoms	Total
Group A			
Smoke	14	6	20
Do not smoke	7	13	20
Totals	21	19	40
Group B			
Smoke	13	1	14
Do not smoke	2	5	7
Totals	15	6	21
Both Groups			
Smoke	27	7	34
Do not smoke	9	18	27
Totals	36	25	61

fume fever symptoms in group B were subjected to ventilatory-function studies. Forced expiratory capacity (FEC), forced expiratory volume in one second (FEV_1), and maximum midexpiratory flow rate between 25% and 75% of the forced expiratory capacity (MMF) were measured on a 6-liter recording vitalometer, using the best of two or more efforts. The peak-flow rate (PFR) was measured with a peak-flow meter as the best of three efforts. Histories and spirometric measurements were done at the beginning of the day shift (between 7 and 9 AM), and were repeated at the end of the shift (between 2 and 3:30 PM). The same procedure was followed for the second, or evening, shift. Special attention was paid to eliciting any past history of hay fever, asthma, or other respiratory disease, and a quantitative estimate of smoking was made.

Results

In area A symptoms developed in 12 workers during May; two became symptomatic in June, five in July, and one in August. In area B, the onset of symptoms was as follows: six in May, two in June, six in July, and one in August.

Table 1 demonstrates the frequency with which various symptoms were observed in the 61 employees interviewed. Symptoms developed in 59% of the group, or 36 workers. The most frequent complaint was a tightness of the chest, which was described with some difficulty by many of the workers. Descriptions such as "difficult to get a breath" and "a sort of squeezing feeling" were among the most common given. General malaise and fatigue, particularly involving the lower extremities, were the next most common complaints. Only one sixth of those who were symptomatic claimed to have irritation of the throat, and only one worker had a cough productive of sputum.

Table 3.—Physical Measurements in Area A

Temperature	72 F
Relative humidity	62%-50%
Room volume	21,600 cu ft
Fresh air changes	5.5/hour
Total air changes	20/hour

A characteristic history of the illness was recorded. With two exceptions, the workers noticed symptoms after being at work four to five hours, and usually immediately after the afternoon smoke break. Chills and fever occurred approximately 12 hours after the onset of exposure and approximately 5 to 6 hours after the onset of the first symptoms. Attacks occurred at least once per week in most workers. Some stated that some symptoms developed every day at work in area A or B.

Table 2 presents data on the relationship of symptoms and smoking habits. Among those with symptoms, only nine of the 36 persons did not smoke. Among those without symptoms, seven gave a positive history of smoking. Of this group, two had worked in the area only four days; one worked only outside areas A and B; one was in area A only two minutes every second or third day; and one spent three days per week doing a time-and-motion study in areas A and B.

Table 3 gives data regarding ventilation and physical measurements of the environment in area A.

The results of the spirometric studies are demonstrated in Tables 4-7. FEC, MMF, and PFR are expressed as percentage of predicted normal for age, or age and height, according to standard tables.[5-7] FEV_1 is expressed as a percent of FEC. There was a general reduction of all of these values in the group of smokers as contrasted to the nonsmokers. Since these two groups are almost identical to those with symptoms of polymer-fume fever and those without, there are very few data available for use in separating the effects of smoking and the effects of environmental exposure. However, Table 6 shows the means of the two small

Table 4.—Mean Values of Pulmonary Function Studies*

		Baseline†								Following Exposure†							
Group	No.	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD
All subjects	47	93	18.2	86.7	12.2	87.5	25.1	94.3	14.5	94.2	14.9	86.8	9.0	86.5	26.3	95.2	16.6
Subjects with respiratory symptoms	24	90.1	20.3	85.3	15.6	87.1	28.7	90.7	14.6	90.3	13.6	87.0	9.6	79.0	20.3	90.2	20.9
Subjects without respiratory symptoms	23	96.0	15.9	88.1	8.5	87.9	21.7	98.0	14.1	98.4	15.9	86.5	16.1	94.7	30	100.6	13.5
t value		1.11		0.75		0.11		1.75		1.98		0.13		2.05		1.95	
Probability		<0.3		<0.5		>0.5		<0.1		<0.1		>0.5		<0.05		<0.1	

* t tests for all four function tests—before vs after exposure showed $P>0.05$.
† Forced expiratory capacity, FEC; forced expiratory volume in 1 second, FEV_1; maximum midexpiratory flow rate between 25% and 75% of the forced expiratory capacity, MMF; peak-flow rate, PFR; and standard deviation, SD.

Table 5.—Mean Values of Pulmonary Function Studies*

		Baseline†								Following Exposure†							
Group	No.	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD
Smokers	29	90.4	14.6	86.9	3.1	86.9	31.5	91.0	15	91.3	14.5	86.9	2.5	82.8	23.7	90.7	18.2
Nonsmokers	18	97.1	22.3	86.2	16.2	88.4	9.5	99.6	12.4	98.6	15.4	86.5	11.7	92.2	29	102.1	11.7
t value		1.24		0.18		0.19		2.04		1.59		0.14		1.16		2.31	
Probability		<0.3		>0.5		>0.5		<0.05		<0.2		>0.5		<0.3		<0.05	

* t tests for all four function tests—before vs after exposure showed $P>0.05$.
† Forced expiratory capacity, FEC; forced expiratory volume in 1 second, FEV_1; maximum midexpiratory flow rate between 25% and 75% of the forced expiratory capacity, MMF; peak-flow rate, PFR; and standard deviation, SD.

groups—those with symptoms who do *not* smoke, and those who do not have symptoms and who *do* smoke. These suggest that the difference may be attributed completely to the effects of cigarette smoking.

As indicated in the tables, there was no significant change in the results of the tests of function at the beginning and at the end of the work shift. This was true in both groups—smokers and nonsmokers.

As demonstrated in Table 7, only three patients showed a significant change in their pulmonary-function studies during the course of the day at work. One of these gave a history of asthma; one had a history of hay fever. The changes noted during the day in these individuals are suggestive of the development of obstructive changes in the airways. One of these men had some improvement in pulmonary function after the inhalation of isoproterenol.

Comment

This "epidemic" of polymer-fume fever illustrates very well the interaction of agent, host, and environment in the causation of illness. The present outbreak would seem to be explained according to the following sequence of events: The new parting compound was a telomere of polytetrafluoroethylene with a molecular weight of 3,700-5,000, which existed as a fine dust on the tools. Cigarettes became indirectly contaminated with small particles of this material which had been deposited on the workers' hands. Inhalation of the products of pyrolysis of polytetrafluoroethylene produced the syndrome in those who smoked contaminated cigarettes. The occurrence of symptoms in a few men who did not smoke would seem to be related to the fact that a small hot-air gun was used in the application of the epoxy resin in the subassembly. This gun has a heating element that reaches a temperature of 750 F. In all probability, the air currents generated by this gun resulted in dispersion of the particles of polymer, which subsequently reached the heating element. With two possible sources of thermal degradation of the polymer—the heating element of the hot-air gun and the cigarettes—it would seem that an adequate supply of pyrolysis products of the polymer was available.

The epidemic pursued a rather lengthy course because of two factors: (1) management had confidence in the innocuous properties of the new parting compound, and (2) changes in ventilation had been associated with the onset. As complaints of symptoms began to accumulate, the ventilation was changed so that in area A, air-conditioners brought in 25% outside air rather than providing 100% recirculated air. This change in ventilation seemed to reduce the severity of symptoms, but it did not completely eliminate them. The spread of the complaints of symptoms in area B was also somewhat baffling initially. The increase in ventilation would have decreased somewhat the ambient-air concentration of these products of pyrolysis. This would not have helped those who were smoking contaminated cigarettes.

In retrospect, the history given by these employees was classical for polymer-fume fever. It is rather interesting that seven men specifically identified the new parting compound as the agent which they felt was causing the problem. This is significant with regard to the Oslerian aphorism about "listening to the patient."

In 1955, Sherwood reported seven cases of polymer-fume fever and related it to a history of smoking in the workers.[8] In the literature there have appeared second-hand reports of deaths resulting from inhalation of the pyrolysis products of polymers of tetrafluoroethylene. These have proved to be difficult to exterminate and have had at least one rebirth in the past two years. There

Table 6.—Mean Values of Pulmonary Function Studies

		Baseline*								Following Exposure*							
Group	No.	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD	FEC, % Predicted Normal	SD	FEV_1, % FEC	SD	MMF, % Predicted Normal	SD	PFR, % Predicted Normal	SD
Nonsmokers with symptoms	4	91.6	14.5	85.0	4.4	87.3	5.5	99.6	2.5	94.2	10.6	84.2	2.2	86.0	5.4	100	5.6
Smokers without symptoms	6	91.1	12.7	92.6	4.9	93.0	25.3	94.5	14.9	93.0	8.1	91.2	3.0	104.8	23.0	93.4	12.4

* Forced expiratory capacity, FEC; forced expiratory volume in 1 second, FEV_1; maximum midexpiratory flow rate between 25% and 75% of the forced expiratory capacity, MMF; peak-flow rate, PFR; and standard deviation, SD.

Table7.—Patients Demonstrating Significant Reduction in Pulmonary Function During and After 8-Hour Exposure

	Patient 1	Patient 2	Patient 3
*FEC—before	3.5 liters	3.4 liters	4.4 liters
after	3.1 liters	3.3 liters	4.4 liters
FEV_1—before	2.3 liters	3.4 liters	4.0 liters
after	2.1 liters	2.6 liters	3.8 liters
MMF—before	2.2 liters/sec	2.8 liters/sec	5.5 liters/sec
after	1.9 liters/sec	2.7 liters/sec	3.7 liters/sec
PFR—before	480 liters/min	250 liters/min	680 liters/min
after	310 liters/min	220 liters/min	720 liters/min

* Forced expiratory capacity, FEC; forced expiratory volume in 1 second, FEV_1; maximum midexpiratory flow rate between 25% and 75% of the forced expiratory capacity, MMF; peak-flow rate, PFR; and standard deviation, SD.

seems to be little doubt that teflon itself has rather remarkable properties, including a physiologic inertness. However, when heated to above 300 C, the products of its thermal degradation are capable of producing a short-lived "influenza-like syndrome" in almost all those inhaling these by-products.

Numerous studies have attempted to characterize these breakdown products. They consist of higher-chain fluorocarbons, the most toxic of which is isooctofluorobutylene.[9]

Capodaglio studied four cases of polymer-fume fever and stated that three of four showed abnormal pulmonary function for six weeks to six months after exposure.[10] Data derived in this study would indicate that changes in respiratory functions which occur while at work are minimal and consistent with mild obstructive disease in the airway. Gandevia studied the pulmonary function of workers exposed to toluene di-isocyanate (TDI) vapor.[11] A decrease of 180 cc in FEV_1 on successive days was noted and said to be significant. One half of all the subjects (all smokers) showed an increased sensitivity to inhalation of histamine aerosol.

The decrease in pulmonary function in the group with symptoms of polymer-fume fever is consistent with differences noted between smoking and nonsmoking populations, as reported in previous studies.[12-15]

One of the most severely affected workers was on two occasions admitted to a hospital, with severe respiratory distress and x-ray findings suggestive of pulmonary edema. This patient's symptoms and x-ray changes responded rapidly to corticotropin (ACTH). Such a case was recently reported.[16]

The mechanism by which pyrolysis products produce fever is not known. Cavagna et al,[17] and Pernis et al[18] have showed a degranulation of polymorphonuclear leukocytes after their exposure to teflon. They suggest that release of endogenous pyrogen is the mechanism for the production of the syndrome.

It is apparent from this study that, despite adequate warning in the manufacture's brochure, and reports in the medical literature, polymer-fume fever may not be recognized. It is also apparent that workers handling the dust of such polymers cannot smoke in the work area. A past history of hay fever, asthma, or other pulmonary disease also is probably sufficient cause to exclude such a worker from exposure to these materials. While the disease process is short and self-limited, it can significantly reduce the operational effectiveness of a department, as well as produce unnecessary illness in man. Sufficient knowledge is available to classify this as a preventable disease.

Generic and Trade Names of Drug

Corticotropin (ACTH)—*Acth, Acthar, Corticotropin.*

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