III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Fluorocarbon polymers are made from substituted polyethylene monomers of the general formula (XCF-XCF)n, where X can be H, F, Cl, CF3, or CF3-CF2-CF2-O [1]. Copolymers, made from two monomers with as little as 10% of the comonomer, and terpolymers, made from three monomers, are additional forms of fluorocarbon polymers [1]. Fluorocarbon telomers are fluorocarbon polymers of low-molecular-weight produced by chemical reactions that limit the degree of polymerization [2].

Some important commercial fluorocarbon polymers are listed, along with the monomers used in their preparation, in Table III-1 [1].

The preparation of unsaturated fluorocarbon monomers from saturated fluorinated hydrocarbons is normally carried out in closed systems. These processes present a potential hazard because such toxic byproducts as perfluoroisobutylene (PFIB) may be formed [3]. Fluorocarbon polymers are prepared from the monomers by conventional free-radical polymerization techniques, but the preparation of each polymer requires different formulation procedures involving a variety of redox catalyst systems [1].

The replacement of hydrogen by fluorine in polyolefin polymers results in many important properties: chemical inertness, low coefficient of friction (nonstick properties), excellent dielectric properties (insulation), good performance over a wide temperature range, low flammability, low moisture absorption, and weatherability [1].

TABLE III-1

PRINCIPAL COMMERCIALLY USED FLUOROCARBON POLYMERS

Polymer		Monomer	Comonomer
Abbreviation	Name		
PTFE	Polytetrafluoroethylene	Tetrafluoro-ethylene	-
FEP	Fluorinated ethylene-propylene	"	Hexafluoro-propylene
PCTFE	Polychlorotrifluoroethylene	Chlorotri-fluoroethylene	-
CTFE-VF2	Poly(chlorotrifluoroethylene-vinylidene fluoride)	"	Vinylidene fluoride
ETFE	Poly(ethylene-tetrafluoroethylene)	Tetrafluoro-ethylene	Ethylene
E-CTFE	Poly(ethylene-chlorotrifluoroethylene)	Chlorotri-fluoroethylene	"
PVF	Polyvinyl fluoride	Vinyl fluoride	-
PVF2	Polyvinylidene fluoride	Vinylidene fluoride	-
PFA	Perfluoroalkoxy	Tetrafluoro-ethylene	Perfluoropropyl vinyl ether
CTFE-VC	Poly(chlorotrifluoroethylene-vinyl chloride)	Chlorotri-fluoroethylene	Vinyl chloride
VF2-HFP	Poly(vinylidene fluoride-hexafluoropropylene)	Vinylidene fluoride	Hexafluoro-propylene
VF2-HFP-TFE	Poly(vinylidene fluoride-hexafluoropropylene-tetrafluoroethylene)	"	Hexafluoro-propylene, tetrafluoro-ethylene

Fluorocarbon polymers are produced in the following forms: granular resins (for molded parts and sheets and for extruding thick-walled tubing and rods); fine powders made by coagulating dispersions (for extruding thin sections); aqueous dispersions (for coatings, fiber impregnation, and preparation of fibers); elastomers; fibers; lubricant powders; and waxes, oils, and greases [1]. Table X-1 [4] lists the uses of fluorocarbon polymers.

Fluorocarbon polymers, with the exception of PTFE, can be processed by conventional melt processing techniques [1]. The better melt-flow characteristics of non-PTFE fluorocarbon polymers allows the use of techniques such as injection molding, screw extrusion, and vacuum forming [1].

Because of its high viscosity at temperatures greater than its crystalline melting point (327 C), PTFE must be processed by techniques similar to those used for processing powdered metals or ceramics (eg, compression molding or ram extrusion) [1]. The heat treatments necessary for processing fluorocarbon polymers may result in the generation of toxic decomposition products [4,5].

Total estimated production of fluorocarbon polymers in 1974 was approximately 27 million pounds, 67% of which was PTFE. Other fluorocarbon polymers, including fluorocarbon elastomers, accounted for the remaining 9 million pounds [1]. NIOSH estimates that 5,000 workers are exposed to the decomposition products of fluorocarbon polymers.

Identification of Decomposition Products

The decomposition products of fluorocarbon polymers depend not only on the chemical composition of the intact polymers but also on the conditions under which they are decomposed. The temperature to which the polymer is subjected, the atmosphere in which decomposition occurs, and the material of the vessel used can alter the kinds and quantities of the decomposition products formed.

The studies that discuss the identities of the products of pyrolysis of fluorocarbon polymers that have been found [4,6-33] give the following general picture of the pyrolysis products: at temperatures that produce just softening or melting of the polymer, the monomer tends to be the principal pyrolysis product. This is true for PTFE up to a temperature of about 500 C. At the same time, however, perfluoropropene, other perfluoro compounds containing four or five carbon atoms, and a particulate, waxy fume are generated. For PTFE, the principal pyrolysis product within the range of temperatures from 500 to 800 C becomes carbonyl fluoride. This compound hydrolyzes readily to hydrogen fluoride and carbon dioxide, so that, in the presence of moist air, these may appear to be the principal pyrolysis products in this temperature range. At temperatures above 800 C, the principal pyrolysis products of PTFE are tetrafluoromethane, hydrofluoric acid, and carbon dioxide. If pyrolysis occurs in the presence of glass, silicon tetrafluoride may be formed by reaction between the silicon in the glass and hydrofluoric acid.

Pyrolysis of PTFE in a vacuum at 360-700 C has yielded almost 100% of its monomer, tetrafluoroethylene [16,17,26]. Zapp et al [19] reported that a fine dust or sublimate was produced at temperatures above 200 C. Harris

[10] reported the evolution of a mineral acid when PTFE was pyrolyzed at 140-325 C. Adams [22] found that hydrogen fluoride was released when PTFE was heated above 300 C. Waritz and Kwon [7] found that hydrolyzable fluoride was evolved from PTFE heated at 400 C and suggested that this was carbonyl fluoride or hydrogen fluoride. Zapp et al [19] reported that carbonyl fluoride was not detected by the method of analysis used when PTFE was decomposed at 300-550 C.

Other pyrolysis products of PTFE that have been identified include: octafluorocyclobutane (OFCB) at 300-360 C and at 500-550 C [19], perfluoroisobutylene (PFIB) at 380-400 C [19], at 475-480 C [7], and at 500-550 C [19], tetrafluoroethylene (TFE) at 450-480 C [7] and at 500-550 C [19], hexafluoropropylene (HFP) at 450-480 C [7] and at 500-550 C [19], hexafluoroethane (HFE) at 300-360 C [19], an unidentified five-carbon olefin at 500-550 C [19], and a higher-boiling residue consisting of a complex mixture of perfluoroolefins at 500-550 C [19].

Silicon tetrafluoride has been formed from the pyrolysis of PTFE at temperatures ranging from 300 to 650 C [8,19] and was probably produced by the reaction of hydrogen fluoride with silicon dioxide from the glass vessel. Table X-2 summarizes these results.

Several investigators [7,9,19] have indicated that particulate material or sublimate, with particle size ranging from 0.2 μm to 0.5 μm, was evolved when PTFE was decomposed. Some authors speculated that this particulate material contained absorbed hydrogen fluoride [19], acidic carboxyl groups [13], or oxygen difluoride [9].

Errede [21] advanced a hypothetical mechanism, shown in Figure III-1, to explain the formation of the various decomposition products of PTFE that

have been identified. The first step is a random homolytic chain cleavage that requires heat and probably does not require oxygen.

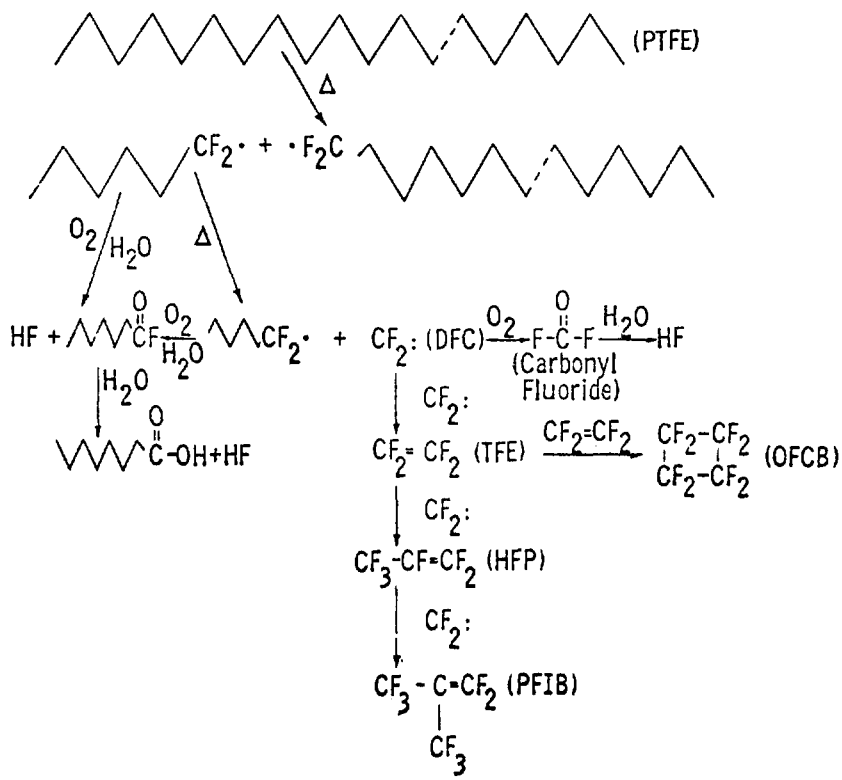

Figure III-1 - POSSIBLE MECHANISM FOR THE DECOMPOSITION OF PTFE After Errede [21] from Waritz and Kwon [7]

The short chain represents the primary particle. Difluorocarbene (DFC) would tend to form preferentially. Combination of two DFC moieties would form TFE, and one TFE could combine with one DFC moiety to form HFP. Although theoretical, Errede's hypothesis [21] does account for the formation of the pyrolysis products of PTFE that have been identified.

Further evidence of the multiplicity of the pyrolysis products was obtained by mass spectrometric analysis [8,13]. Typical mass spectra of the products of PTFE pyrolysis in air [8] and of the particles so obtained were reported by Coleman et al [13] and are shown in Tables X-3 and X-4.

The decomposition products of other fluorocarbon polymers have not been so intensively studied as those of PTFE. Polychlorotrifluoroethylene (PCTFE) heated at 347-418 C in a vacuum yielded 27% of the monomer, chlorotrifluoroethylene [32]. Birnbaum et al [14] found that pyrolysis of PCTFE in air at 375 C and at 400 C produced hydrolyzable fluoride, which they thought was carbonyl fluoride. No carbonyl chloride (phosgene) was found. The authors speculated that fluorocarbonylchloride (COFCl) and chlorodifluoroacetylchloride (CF2ClCOCl) had been evolved and presented evidence for the formation of a variety of fluorinated, chlorinated compounds with up to three carbon atoms. The authors also found a particulate with a mean particle size of 0.5 μm.

When a copolymer of vinylidene fluoride (VF2) and hexafluoropropylene (HFP) and a terpolymer of VF2, HFP, and TFE decomposed at 550 C and 800 C, carbon monoxide and carbon dioxide were produced [6]. Clayton [23] has suggested that decomposition of VF2-HFP, VF2-HFP-TFE, and polyvinyl fluoride would produce hydrogen fluoride, but he gave no experimental data to support this theory. Clayton [23] also suggested that the decomposition of fluorinated ethylene propylene (FEP), a copolymer of TFE and HFP, would produce HFP; again, no experimental data were given. Madorsky et al [26] reported that pyrolysis of polyvinyl fluoride and polyvinylidene fluoride in a vacuum at 372-500 C produced hydrogen fluoride and a waxlike material consisting of chain fragments of low volatility.

Effects on Humans

As early as 1951, Harris [10] described two cases of an influenza-like syndrome in workers who had been experimenting with PTFE for an unspecified period. The first worker, 29 years old, was exposed to fumes emitted from PTFE heated in an extruder with a malfunctioning thermostat. Although the extrusion process was normally carried out at 350 C, the machine in this instance overheated to about 450-500 C. While manually feeding PTFE powder into the extruder, the worker noticed a distinctive odor emanating from the point where the polymer rods emerged from the extruder, and he experienced chest discomfort. That evening, the worker experienced what he considered to be an attack of influenza and contacted his physician. The patient described a recurrent symptom cycle of subjective elevation in temperature, culminating in violent shivering accompanied by perspiration, and then a subjective drop in temperature. Physical examination revealed a temperature of 101 F and no other clinical abnormalities.

The next morning, the patient felt better but was fatigued and noted a slight tickling sensation in his throat. A physical examination showed that he was pale, had a temperature of 98.8 F, a pulse rate of 80/minute, a blood pressure of 140/75 mmHg, and a trace of albumin in the urine. The patient felt well enough to resume work within 36 hours after exposure, but the albuminuria persisted. Harris [10] noted that physical examination at a hospital 2 weeks postexposure confirmed that the albuminuria was postural in origin. At this time, a random urine sample contained 1.4 ppm of fluoride, which the author concluded was of no significance. The worker had previously had less severe attacks with similar symptoms, which

generally began several hours after he left work. The worker also indicated that he had occasionally experienced milder symptoms after disintegrating PTFE powder without heating, but the author expressed doubt that these symptoms were related to exposure to cold PTFE. Harris did not indicate whether this man smoked. After local exhaust ventilation was installed in the work area, the worker was reported to have suffered no further ill effects.

The second worker described by Harris [10] became ill on two occasions while removing PTFE from an oven in which it had been heated to 450 C and then allowed to cool to an unspecified temperature. On the first occasion, the 25-year-old patient complained of aching limbs and general malaise. Examination revealed a temperature of 99.8 F, pulse rate of 100, and blood pressure of 125/75 mmHg. There was no shivering, although the patient had experienced shivering attacks at home after work 4 months earlier. Recovery was complete within 24 hours. On the second occasion, the worker experienced chest discomfort on breathing deeply. He subsequently had an attack of shivering. Examination showed no clinical abnormalities, and his temperature was normal. Administration of oxygen relieved the symptoms. He returned to work 2 days later. The worker had had asthma attacks for many years, although he had been symptom-free for 18 months prior to this incident. Harris noted that the exhaust ventilation system on the oven was subsequently found to be inadequate and that, once that situation was remedied, no further attacks occurred. He called the illness of these workers polymer fume fever, which he proposed was caused by inhalation of fume from heated PTFE, and noted the similarity of this syndrome to metal fume fever.

Harris [10] also noted that the two cases he had diagnosed as polymer fume fever were similar to two cases of illness in PTFE workers described to him by HF Gilbert in a personal communication. The first worker heated PTFE in an oven at an unspecified temperature and manipulated the polymer on a hot roller of unspecified temperature. No work history was given. He experienced a gradual onset of symptoms that corresponded closely with those Harris reported in his patients, but shivering was not reported. The worker had a temperature of 101.6 F, a pulse rate of 100/minute, a respiration rate of 36/minute, and a few scattered rales in the chest. X-ray examination revealed "definite evidence of congestion, particularly of the right lobe." Treatment consisted of bed rest, and the patient recovered within 24 hours. There was no mention of a followup X-ray examination.

The second worker, who was engaged in forming sheets of polymer on heated roller mills, developed "an attack of the shakes" of rapid, but otherwise undescribed, onset. This second man's work history was also not reported. Physical examination revealed a few moist rales in both lung bases, and the patient was treated with oxygen and complete rest. His temperature rose to 103.2 F, and his pulse rate was 120/minute. He also had a leukocytosis of more than twice the normal count. Recovery was complete within 24 hours. Harris concluded that the similarity of symptoms, comparative lack of physical signs, usually gradual onset of illness several hours after exposure, and rapid recovery in the cases presented were characteristic of polymer fume fever as he defined it.

Because the symptoms so closely resembled those seen in metal fume fever, Harris [10] analyzed PTFE ash and the sublimate evolved from PTFE

heated at 400 C for various metals. The sensitivity of the method of analysis was not reported. From these studies, Harris concluded that the concentrations of metals in the ash and the sublimate could not explain their findings, so that a toxic fume from heated PTFE seemed to be the responsible agent in polymer fume fever from PTFE.

In 1967, Bruton [34] described two cases of illness in aviation employees whose work involved contact with a neoprene door seal that had been sprayed with an aerosol of an unspecified fluorocarbon telomer. Smoking was not permitted in the hangar; however, toward the end of his shift, the first worker had smoked a cigarette in an office where smoking was allowed. Approximately 30 minutes later, he experienced shivering and chills, which lasted for about 6 hours, but no other effects. The second worker had been handling the polymer spray for approximately 1 year and had become ill once before when he failed to wash his hands before smoking after working with the aerosol. On this occasion, he started to smoke a cigarette during his break and realized by the taste that it was contaminated. He extinguished the cigarette immediately, but, within 30 minutes, he began to shiver and developed a headache and muscular aches, but no respiratory effects. Recovery was complete within 24 hours.

Bruton [34] believed that the polymer-treated surface had contaminated the cigarettes. To demonstrate the possibility of hand contamination, he conducted an informal experiment in which the aerosol was sprayed onto a clean aluminum surface according to the manufacturer's instructions. When he wiped the surface with his finger, a line across the sprayed surface and a faint white dust on his finger were visible. The author suggested that handling of objects treated with aerosols of

fluorocarbon telomers represented a hazard to smokers because of the possibility of contamination of smoking materials. He noted that workers should be required to wash their hands before smoking to avoid contaminating smoking materials. Although Bruton diagnosed this syndrome as polymer fume fever, he did not disprove the possibility that the respiratory symptoms were due to other causes. He was correct in assuming that the temperature of the cigarette was sufficient to cause pyrolysis of the fluorocarbon telomer, however, since the temperature of the burning zone of cigarettes has been shown to range from 854 to 913 C [35].

In 1964, Nuttall et al [36] reported an incident of in-flight illness that affected 35 passengers, including 2 flight surgeons and 4 of 5 crew members, on a C54 aircraft. The total flight time was 165 minutes, and the authors mentioned a flight altitude of 9,500 feet. The auxiliary power unit (APU) of the aircraft was located in the rear compartment, which "freely communicated" with the main passenger cabin. The crew compartment door was closed. After the passengers and crew members boarded the plane, the APU was started; fume and odor levels within the main cabin were reported to have been "normal." Takeoff was delayed because of magneto trouble, and the passengers debarked after the APU had run for approximately an hour. A few had mild symptoms of respiratory irritation, and some became nauseated when they smoked. About 1.5 hours later, the passengers reboarded the aircraft and the APU was restarted. The plane took off 45 minutes later and the APU was turned off. Within 1 hour of takeoff, most of the passengers and two of the crew members had chest discomfort and general malaise, including chills, nausea, and respiratory distress in some. One passenger vomited and collapsed and was found 5-10

minutes later in a cyanotic state with a weak and rapid pulse. A second passenger had severe respiratory distress and moderate collapse. Six passengers were incapacitated, and five were given oxygen. The heating system was suspected of being a source of toxic fumes and was turned off. Although a fusilage hatch was opened to provide ventilation, some passengers continued to complain. On arrival, three passengers required hospitalization, and everyone aboard the plane except one co-pilot had experienced effects, which persisted after the plane landed.

To characterize the illness, Nuttall et al [36] interviewed and gave questionnaires to all crew members and passengers. The answers to the questionnaire revealed a toxic reaction pattern similar to that of influenza, with onset of symptoms occurring within 2-6 hours after exposure to the unidentified agent. Typical symptoms were chest discomfort, difficulty in breathing deeply, chills, muscular aches, fever, dull headache, and general malaise. Respiratory symptoms were not present in all cases, and nausea and aversion to cigarettes was often reported. The number of smokers aboard the plane was unspecified, and it was not stated whether smoking was permitted during the flight. Recovery was complete within 24 hours in most cases, including those of the three hospitalized patients. The authors noted that examination of these three patients showed elevated temperatures, increased white blood cell counts with a shift to the left (indicative of an increased proportion of young cells), and rapid pulse rates. They emphasized the similarity of the reported symptoms to those of metal or polymer fume fever, characterizing 50% of the cases as "typical" examples of this syndrome. The questionnaire data indicated that 6 cases were severe, 12 were moderate, and 9 were mild.

Although 12 of those aboard the flight did not complete questionnaires because they could not be located, the flight surgeons who had interviewed everyone on the plane at the time of the incident reported that they also had been affected to some extent.

Nuttall and coworkers [36] conducted an extensive investigation to determine the cause of the illness. Air samples were collected in the grounded aircraft and analyzed for total metals and zinc with negative results. The four who collected samples developed a typical fume fever reaction. Six volunteers were exposed to fumes from the APU for 40 minutes. All six developed symptoms similar to those of the affected passengers and crew members 1-3 hours after exposure. All had elevated temperatures and elevated white blood cell counts, with polymorphonuclear leukocytosis and a shift to the left. A trip made by the same plane 2 days later, after a new APU had been installed, was uneventful.

The tape used to wrap the exhaust manifolds of the old APU was subjected to a variety of tests [36]. Five volunteers were exposed to fumes emitted from the APU before the manifold was wrapped with tape. No symptoms were reported after 35 minutes of exposure. Next, the APU exhaust manifolds were wrapped with an unspecified amount of asbestos tape salvaged from the old wrappings of the manifold, and used APU oil was placed on the wrapping. In this instance, two of six subjects exposed for 35 minutes reported symptoms, and small quantities of uncharacterized fumes were observed around the wrappings. Carbon monoxide levels were below 50 ppm in both these runs. The authors noted elevated temperatures and mild leukocytoses in the two affected subjects, but suggested that the reported effects were questionable. This second run was repeated, whereupon two of

the six subjects exposed for 35 minutes developed mildly elevated temperatures and leukocytosis. Subsequent exposure of four subjects to oil fumes alone for 40 minutes failed to produce symptoms. Nuttall et al [36] concluded that the asbestos tape was the source of toxic fumes, although the oil might have been a modifying agent. New asbestos tape of the same type that had been used to wrap the manifolds of the APU was analyzed with an infrared spectrometer. This examination revealed the presence of PTFE, a finding that was later confirmed by the manufacturer.

In a final experiment, one subject was exposed to fumes emitted from an unspecified amount of the tape pyrolyzed in a platinum dish at 800-1,000 F. The subject developed mild respiratory symptoms, fever, and leukocytosis after one 35-minute exposure in a closed room. The authors concluded that the illness suffered by the passengers and crew of the aircraft was polymer fume fever caused by exposure to fume of PTFE pyrolysis products from the asbestos tape. They noted that early tests of the used tape failed to reveal fluoride, but suggested that this may have occurred because the tape had been used sufficiently to remove the fluorocarbon polymer filler. They also suggested that the symptoms observed in the severely affected passengers were caused by more than PTFE fumes alone, citing as possible additional factors hypoxia, hyperventilation, apprehension, and the general psychologic state of the individuals involved. The role of pyrolysis products of the oil was left undetermined. Although the authors failed to report the temperature of the APU, the thermal decomposition products of PTFE seemed likely to have been the cause of the toxic reaction aboard the aircraft.

In 1967, Barnes and Jones [37] gave the results of an investigation of an outbreak of respiratory illness affecting 4 of 19 workers at a factory that made abrasive wheels. The affected workers were male press operators, aged 20-32 years, whose employment histories were not given. Their work involved placing by hand a mixture of phenol-formaldehyde resin, furfural, abrasive grain, a small amount of hexamethylenetetramine, and, occasionally, a rectifying oil containing cresylic acid on cold presses in a tray. The wheels thus formed were removed from the press room and placed in batches in an oven heated to 177 C for curing. The investigators noted that the factory consisted of one large shed and that the press room was not physically closed off from the area where the mixture was made. The press room was mechanically ventilated by recirculated, cooled air, and the mixing area was air-conditioned.

In describing these four case histories, Barnes and Jones [37] noted that these workers were moderate to heavy smokers who smoked on the job. All four had suffered recurrent bouts of illness over a 2- to 4-month period and had experienced respiratory distress characterized as either tightness of the chest or difficulty in breathing deeply. Typical symptoms of these attacks included uncontrollable shivering lasting 1-2 hours in two workers, pain in the retrosternal area in one worker, sore throat in one worker, and severe headache in one worker. Physical examinations at the time of the plant visit revealed scattered rhonchi in the chest of one worker, congested throat and congested soft palate in a second worker who had not complained of a sore throat, congested pharynx in a third, and no signs in a fourth worker who had been transferred to the packing room 2 weeks earlier. The authors discovered during their investigation of the

plant that the use of powdered PTFE as a mold-release agent had been initiated approximately 3 months earlier. They noted that, although the pressing and curing processes were carried out at temperatures below 300 C, all the affected workers handled the PTFE-treated plates and all smoked while working. They further stated that PTFE powder was detected on the hands of the press operators and that there was ample opportunity for the skin to become contaminated in the plant. Smoking on the job was then prohibited. The authors reported that, according to the plant manager, there had been no recurrence of symptoms during the 2 months after the reported illnesses and the prohibition of smoking in the work area. Although the decomposition products of PTFE may have been the cause of the illness, some of the typical polymer fume fever symptoms were not present.

In 1974, Wegman and Peters [38] reported the investigation of a similar outbreak of influenza-like illness in workers in a textile mill that produced imitation crushed velvet. The fabric was made of nylon and rayon, and the final stage of its production was a flocking process that consisted of the addition of a liquid fluorocarbon polymer to the material, with subsequent dipping, rolling, and squeezing of the mixture, curing at 150-155 C, mechanical crushing and steaming at 135 C, and final static elimination. In an initial interview, the plant manager revealed that a number of workers involved in the flocking process had reported symptoms of weakness, muscle aches, fever, chills, and shortness of breath.

The authors [38] interviewed and examined all workers in the flocking division, 10 men and 3 women, ranging in age from 19 to 61 years. Those complaining of symptoms had been employed in this division for from 2 months to 6 years. Seven of these workers, six men and one woman,

described symptoms of cough, muscular aching or weakness, fever, and chills. Four of these seven workers also had experienced shortness of breath. All had suffered repeated bouts of illness, three of the seven workers having experienced as many as six attacks during an unspecified period of time. In several instances, symptoms were of such severity that affected workers had to leave the plant. Onset of symptoms was generally gradual and illness persisted for 6-72 hours, most workers reporting recovery within 24 hours. Of the six workers who did not report such attacks, one nonsmoking man had experienced headache on five occasions and possibly some coughing; a second had had an isolated bout of cough, fever, and chills, which the authors attributed to a common cold. One woman who did not report typical attacks had an unspecified number of attacks of coughing, fever, chills, and shortness of breath, but these were of rapid onset and short duration. One of the six men experienced severe weakness, chest discomfort, and shortness of breath on one occasion. The affected workers experienced symptoms only when they worked in the area where the fluorocarbon polymer-treated material was cured.

The authors [38] considered four materials as possible causes of the symptoms: ammonia, formaldehyde, nylon, and the fluorocarbon polymer. Analysis of the air of the workplace found air concentrations of less than 50 ppm of ammonia and less than 1 ppm of formaldehyde. The nylon was reported to be of nonrespirable size. The authors maintained that exposure could not have resulted from the flocking process itself, since the maximum temperatures at which the fluorocarbon was applied and cured were at or below 165 C. However, the authors noted that all seven workers who had "typical" symptoms of polymer fume fever were cigarette smokers, and that

all but two of the other workers experiencing symptoms were also smokers. They observed that workers engaged in applying the polymer to the material had frequent hand contact with both liquid and cured polymer and that they often smoked during breaks without first washing their hands. The authors concluded that the source of the illness was polymer fume generated by the smoking of PTFE-contaminated tobacco. No further symptoms were reported after smoking in the work area was prohibited and the workers were instructed to wash their hands before smoking or eating.

In 1973, Evans [39] reported a case of respiratory illness in a 49-year-old man who had been using an oxyacetylene torch to dismantle a metal table used to hold PTFE-coated molds. The molds had been sprayed with S-143, a dispersion of TFE telomer in unspecified fluorocarbon solvents. About 1 hour after he began to use his torch on the table, the worker became too ill to continue the work. He reported to the company medical office complaining of a sore throat, dry cough, and difficulty in breathing. Although the patient had a history of smoking two packs of cigarettes a day for an unspecified number of years, he reported that he had not smoked while in the molding area. He had an oral temperature of 100.6 F, slight dyspnea, and basal rales in both lungs. A chest X-ray was taken, and the patient was administered oxygen through a nasal catheter for approximately 1 hour and then sent home. He arrived at work the next morning feeling tired but otherwise comfortable. The author noted that the chest X-ray taken on the day of exposure was consistent with a diagnosis of pulmonary edema. Subsequent X-rays taken 1 and 7 days later revealed progressive resolution of the edema.

The author [39] measured the rise in temperature during cutting of a cast iron pipe with an oxyacetylene torch and found a maximum temperature of 740 C within 1/16 inch of the flame. She concluded that the temperature of the metal table had been in excess of 300 C long enough to allow PTFE to decompose, but she did not report what distance separated the area of the table sprayed with PTFE from that to which the oxyacetylene flame was applied. She diagnosed the patient's illness as pulmonary edema resulting from inhalation of toxic fluoride fumes from PTFE. Possible effects of the acetylene used in the cutting torch were not discussed. It was not stated whether the worker used protective devices or wore protective clothing during the cutting operation, or whether he may have had any direct contact with the spray or the sprayed molds. Although the author diagnosed the pulmonary edema as being the result of exposure to PTFE fumes, the evidence presented is not conclusive.

In 1964, Robbins and Ware [40] reported a case of pulmonary illness in a 38-year-old welder in a sheet-metal factory. Although PTFE was not normally used in the plant, the patient had been working on a special order that involved welding thin steel channels fitted with PTFE blocks to the sides of a drawer. The welder worked in a 50- x 100- x 15-foot room with four other men, who remained unaffected. The authors did not state whether the workplace was ventilated. On the day before his illness, the patient had cut and drilled 24 blocks of 5/8-inch PTFE, and he had smoked during this process with no ill effects. While tack welding the steel channels to the drawers, he observed a blue flame and smokey vapor emanating from the work. The patient reported that the PTFE blocks were blackened, apparently charred from the heat of the welding arc. He wore a welding hood with no

protective mask and inadvertently inhaled some of the fumes when he lifted his hood to examine the work. The patient described the vapor as being very irritating and acrid. He continued welding and, approximately 3 hours later, experienced dizziness and mild headache. Shortly thereafter the patient became nauseated and had chills, weakness, coughing, tightness of the chest, and shortness of breath. He left work and reported to the hospital. Physical examination revealed an elevated temperature of 103 F, a pulse rate of 120/minute, respirations of 30/minute, diffuse moist rales in both lungs, and signs of dyspnea. An electrocardiogram indicated sinus tachycardia. A chest X-ray showed diffuse bilateral infiltration of the lungs. The patient was treated with bed rest, oxygen, and 1,000,000 units of penicillin daily. His respiratory symptoms and signs and fever subsided within 72 hours, at which time a chest X-ray showed complete resolution of the edema, and he returned to work. The authors diagnosed the illness as pulmonary edema caused by PTFE fume. The flame and the charring of the PTFE indicated that the polymer had reached a temperature of at least 575 C, its approximate ignition point [5].

In 1975, Blandford et al [41] described a case of nonoccupational respiratory illness in a man who had inhaled fumes from a PTFE-coated pan that had contained only water and had boiled dry when left unattended on an electric stove. When he removed the pan from the stove, the man noticed that the fumes "took his breath." No smoke was visible. Five cockatiels kept caged in an adjoining room died within 30 minutes after the incident. The patient's wife, who was in the same room as the birds during the incident, was unaffected. About 60 minutes postexposure, the patient experienced shortness of breath and a paroxysm of coughing when he tried to

smoke a cigarette. About 80 minutes after the incident, the man's symptoms included shivering, dizziness, and nausea. He felt cold and noted a painful tightening of the chest. The next day, on awakening after 8 hours of sleep, he had a severe headache, which subsided during the morning. The tightness of the chest persisted for the remainder of the day. The subsequent recovery was complete and uneventful, although the patient had difficulty remembering events following the death of his birds and felt that the fumes had affected his level of consciousness. The authors noted that this was an unusually clearcut case of polymer fume fever, because there had been no smoke and the pan had contained only water. The data as reported by the authors demonstrated that PTFE produced toxic decomposition products that were more lethal to birds than to humans.

In 1967, Clayton [23] published the results of investigations conducted by Kligman for the Haskell Laboratory for Toxicology and Industrial Medicine to determine the effects on humans of smoking cigarettes contaminated with known amounts of a TFE fluorocarbon telomer. The sex, age, medical and employment histories, and smoking histories of the subjects were not reported, and the author did not specify whether the same or different subjects were exposed at the various dose levels.

The first experiment evaluated the effects of smoking a cigarette to which 0.05, 0.10, 0.20, or 0.40 mg of a TFE fluorocarbon telomer had been added. Ten volunteers smoked one cigarette apiece with each of the added amounts of telomer. Results indicated that 0.40 mg telomer in each cigarette was necessary to cause an increase in body temperature and pulse rate. No symptoms were reported at the lower levels, although average maximum pulse rates were slightly elevated at an unspecified interval after

smoking. At the 0.40 mg dose level, the author reported that 9 of 10 subjects had what he considered to be typical symptoms of polymer fume fever, with cough as the first symptom in 6 subjects. The symptoms reported by the nine affected subjects were headache, muscular aches, chills, malaise, sluggishness, excessive perspiration, and weakness. Onset of symptoms occurred 1-3.5 hours after smoking, with a mean latency period of 2 hours. From 2.5 to 5.5 hours after the volunteers smoked, the average temperature of the nine affected volunteers increased to 100.5 F from a mean preexposure value of 98.1. From 2.5 to 4.5 hours after they smoked, the average pulse rate of the nine affected volunteers increased from 75 to 99. Recovery time averaged approximately 9 hours, with a range of 5-11 hours, but the author did not define the criteria for recovery. The author noted that complaints of coughing and other symptoms generally occurred before increases in temperature and pulse rate were detected. The subject who did not have full-blown symptoms of polymer fume fever had a slight increase in body temperature and pulse rate, a slight headache, and an occasional cough. The measurements from this man were not used to calculate the average values because he was not considered to have had a typical effect from inhaling polymer fume.

In the second experiment [23], 10 volunteers each smoked 6-10 cigarettes. Each cigarette contained 0.05 mg of added TFE telomer. Two subjects had no signs or symptoms of polymer fume fever after smoking 10 contaminated cigarettes. Four other subjects, who also smoked 10 cigarettes, experienced mild attacks in which the primary, and often the only, symptom was headache. In addition, one of the mildly affected subjects reported slight stomach and chest pains, and another subject

reported having a dry mouth. In the four mildly affected subjects, average temperatures increased from 97.9 to 99.0 F, and average pulse rates increased from 66 to 96 after smoking.

The other four subjects expressed well-defined symptoms of polymer fume fever after smoking six to eight cigarettes; the first symptom to appear was chills. Other symptoms were the same as those of subjects in the first experiment, except that coughing was not reported by any of the subjects. Clear symptoms first appeared 3-5 hours (average 3.8) after the subjects smoked. Five to 6 hours after smoking, average temperatures of these four subjects increased from 98.3 to 101.4 F. From 1 to 9.5 hours (average 5.4) after smoking, the average pulse rate of the four affected subjects increased from 87 to 111. Recovery time in the subjects with well-defined attacks was 7.5-12.5 hours (average 9.8), but the author did not explain the criteria for recovery. The cumulative amount of added telomer necessary to elicit signs and symptoms of illness in these four patients was 0.30-0.40 mg.

Clayton [23] noted that the cumulative amount of telomer (0.30-0.40 mg) needed to produce well-defined symptoms in four subjects coincided with the amount of telomer (0.40 mg) needed to produce symptoms in subjects who smoked one cigarette. The sequence of events was similar in subjects given both single and cumulative exposures, but the signs and symptoms differed. Six of 10 subjects complained about a cough in the first experiment but none of the 4 subjects in the second experiment complained of cough. Clayton suggested that subjects receiving single large exposures to fluorocarbon telomer had an initial respiratory tract irritation that was not experienced by subjects receiving cumulative exposures because the

latter were subjected to irritant substances at lower concentrations. The same amount of telomer, however, produced fever in both experiments. Clayton concluded that there is no obligatory sequence of effects in polymer fume fever and that the absence of cough does not preclude a diagnosis of this illness. He emphasized that the total clinical picture should be considered by anyone contemplating a diagnosis of polymer fume fever, and that objective measurements such as temperature, pulse rate, and white blood cell counts should be relied on as indices of illness; however, he did not report white blood cell counts. The interval between the smoking of cigarettes was also not specified, and any individual differences in the subjects that might have explained their differing reactions were not discussed. Nevertheless, these experiments indicate that smoking cigarettes contaminated with a TFE-telomer can result in a syndrome commonly referred to as polymer fume fever.

In 1965, Makulova [42] reported five cases of perfluoroisobutylene (PFIB) poisoning in two male and three female laboratory workers. A 34-year-old woman had worked with this compound for approximately 2.5 years with no previous ill effects. The ages and employment histories of the other patients were not specified. Four of the five workers reported that exposure to PFIB lasted less than 1 minute, during which time they inhaled two to five times. All patients described symptoms of coughing, difficulty in breathing, and chest pains immediately after exposure. These symptoms became progressively more severe, and by 6-8 hours after exposure, all patients had developed headaches and other symptoms and had begun to expectorate sputum.

Makulova [42] noted no respiratory tract or ocular mucous membrane irritation. Physical examination revealed pallor, dark circles under the eyes, cold sweating of the hands and torso, cyanosis of the lips, nose, and ear tips, rapid and shallow superficial breathing (40-60 respirations/minute), a rapid pulse of 100-140, and muted heart sounds in all patients. Blood-pressure readings ranged from 130/90 to 110/80 mmHg. Unspecified cardiac changes were reported to have occurred in the electrocardiograms of three patients. Moist rales were noted in the lungs of one and dry crepitant rales in those of the other patients. All had temperatures ranging from 99 to 100.4 F for 2-25 hours after exposure. Chest X-rays of all patients showed significant pulmonary changes that came on rapidly 4-6 hours postexposure and became fully developed approximately 48 hours postexposure. In four patients, these changes consisted of bilateral, confluent pulmonary edema, especially in the middle lobes, with emphysematous lateral borders and segments above the diaphragm. In the other patient, multiple clearly defined small foci of intense opacity were found.

The author [42] noted that treatment was largely symptomatic and consisted of calcium chloride, ascorbic acid, glucose, unspecified cardiac medication, and oxygen administration to combat the pulmonary edema. Penicillin or streptomycin in combination with sulfonamides was given during the first few hours postexposure. Symptomatic improvement was noted in some patients within 4-6 days postexposure, and complete resolution of breathing difficulties and pulmonary rales occurred 7-10 days after exposure. At 10-13 days postexposure, pulmonary damage observed in X-rays had been resolved, and leukocytosis and eosinopenia improved 15-20 days

postexposure. Three patients were discharged from the clinic in good health 13-23 days after exposure, and a followup 2 years later revealed no complications. One patient developed exudative pleurisy and remained in the clinic for more than 2 months.

The fifth patient, the 34-year-old woman, died 2 days after exposure. Makulova [42] described the last patient's history and illness in detail, noting that she had suffered from influenzal pneumonia 2 months before poisoning. She was unable to give any information on the duration or degree of her exposure to PFIB on the day she became ill. Her symptoms were similar to those already described, and clinical findings were similar to those for the other patients. She was admitted to the clinic with a diagnosis of bilateral confluent focal pneumonia and pulmonary insufficiency, and she was treated with penicillin, streptomycin, intravenous glucose, oxygen, camphor injections 4 times a day, and strophanthin. On the 2nd day after exposure, she was bled. The attempted therapy failed to produce any improvement, and the patient died approximately 55 hours postexposure. Autopsy confirmed the diagnosis of pneumonia and pulmonary edema and revealed hemorrhage into the left adrenal and hyperemia of the internal organs. The author concluded that death was caused by exposure to PFIB but did not discuss the role of the patient's previous pneumonia or any possibly deleterious effects of her treatment regimen, most notably the bloodletting. Makulova suggested that PFIB belongs to that class of asphyxiants that induces toxic pulmonary edema in the absence of upper respiratory tract and conjunctival irritation, and that serious illness and complications can result from exposure to this compound.

In 1972, Burns et al [43] reported a tumor that occurred at the site of a PTFE-Dacron vascular graft. The patient was a 31-year-old man with a 3-week-old, rapidly growing mass on his left thigh. A laceration of his left superficial femoral artery 10.5 years before had caused a loss of distal pulses. The injury was repaired with a PTFE-Dacron prosthetic graft. Circulation was restored and his recovery at that time was uneventful. The patient had remained largely asymptomatic until he noticed the mass in the area of injury. Physical examination revealed a firm, nontender, nonpulsating, 8- x 10-cm mass palpable in the front of the left thigh. Subsequent biopsy of the tumor was performed, yielding a specimen that resembled a malignant vascular tumor. The authors noted that they had considerable difficulty in arriving at a diagnosis, although they tentatively classified the tumor as an angiosarcoma. The tumor and the superficial femoral artery and vein were removed with subsequent vein ligation and artery reconstruction from a segment of saphenous vein taken from the opposite thigh. The patient recovered uneventfully, and there was no evidence of recurrence approximately a year after the operation.

The specimen consisted of a segment of the prosthesis, adjacent blood vessels, and surrounding tissues. The PTFE-Dacron graft was surrounded by a circumscribed grayish-white tumor that had invaded adjacent subcutaneous and muscular tissues. The authors noted that, although the tumor did not invade the femoral artery, it constricted and encircled more than half its length, including the graft. The tumor was lobulated and contained scattered, slit-like spaces, gelatinous areas, and hemorrhagic foci. An additional small, firm nodule was attached to the junction of the PTFE-Dacron graft with the artery.

Fixed specimens of the tumor and associated tissues were examined by light and electron microscopy [43]. Light microscopy revealed that the tumor was composed of bundles of large, elongated, spindle-shaped cells with processes and moderately pleomorphic, vesiculated or hyperchromatic nuclei. Only rare, atypical mitotic figures were present. There was no organized vascular pattern in the tumor; pools of blood cells were surrounded by fibroblasts only. The authors noted that the fibroblasts accounted for the apparent vascularization described after the examination of the specimen taken for biopsy. Electron microscopy revealed that the tumor was composed of well-differentiated fibroblasts that were associated with amorphous or hyalinized collagen rather than with normally fibrinous collagen. The nodule removed from the junction of the graft and blood vessel was composed of bundles of proliferated nerve-sheath cells among typical collagenous and fibroblastic cellular elements.

On the basis of these findings, the tentative diagnosis of angiosarcoma was changed to one of an unusual form of fibrosarcoma, and the authors [43] suggested that the pools of red blood cells represented a hemorrhagic phenomenon unique to this type of tumor. They stated that it was impossible to be sure that the malignancy was induced by the graft. They cited the similarity of the tumor to those produced in animals by embedded plastics, including PTFE [44,45], as a factor in their conclusion that the sarcoma might have arisen in response to implantation of the graft. However, the authors did not discuss the role of Dacron in the development of the fibrosarcoma.

Epidemiologic Studies

Although no thorough epidemiologic studies on workplace populations exposed to the decomposition products of fluorocarbon polymers have been found, some investigators have assessed the occurrence of polymer fume fever in employees of PTFE processing plants.

In 1974, Polakoff et al [46] questioned workers and measured PTFE dust concentrations in a small fabricating plant. Air was sampled by drawing 2 liters/minute through a Millipore AA filter (pore size 0.8 μm). Sampling times ranged from 40 to 117 minutes. Filters were placed in open-faced holders attached to the worker's lapel or collar. General area samples were taken in various locations in the plant. Filters were weighed before and after the survey to obtain the weight of the dust, which was expressed as mg/cu m. PTFE was identified by a mass spectrometer.

PTFE dust concentrations ranged from 0 to 2.4 mg/cu m in breathing-zone samples taken in the blow-mold area, and those in general area samples from the same area ranged from 0 to 3.2 mg/cu m [46]. PTFE dust concentrations in breathing-zone samples were 0.4-5.5 mg/cu m in a room where gaskets were produced, 0.2-2.9 mg/cu m in the machine shop, and 2.5-2.9 mg/cu m in a sample for a worker who operated the ring-grinding machines.

A questionnaire was completed by 77 workers (about 75% of the workers in the plant) [46]. Sixty of the production workers (86%) said that they had experienced polymer fume fever at some time in the past, but only 50% had experienced polymer fume fever during the past year. Fourteen percent of the workers stated that they had had more than three episodes in the preceding year. Only 10% of those who had experienced polymer fume fever

had sought medical assistance. None of the samples exceeded the federal standard for respirable nuisance dust (5 mg/cu m [15 Mppcf]), but the authors noted that this fact did not preclude the possibility that some workers can suffer adverse effects at lower concentrations. The authors recommended improvements in housekeeping and the prohibition of smoking in the work area. It should be noted that at the time of sampling there were no reported cases of polymer fume fever. Therefore, no conclusions regarding the possible adverse effects of the PTFE dust concentrations can be drawn from this study.

In 1955, Sherwood [47], as a member of an industrial hygiene team, studied the atmospheric concentrations of fluorine compounds in a PTFE-fabricating works where fever believed to have been induced by fume from a tetrafluoroethylene polymer was thought to have affected seven men, aged 25-48. Six of the men smoked while they were working, and the nonsmoker worked at the ovens. All the men occasionally complained of dry throats, usually before an attack of fever. Chest X-rays taken during the acute phase of two of the attacks revealed no abnormalities. One worker had conjunctival congestion. During an acute attack of fever, a urine sample was taken from a man who had been experimenting with a new machine for sintering granular polymer. The sample contained a fluorine concentration of 5 mg/liter. The author concluded that this worker had absorbed fluorine from the factory atmosphere.

In the fabrication techniques studied by Sherwood [47], the polymer was pressed into a mold or "pre-form" and sintered at 350-380 C to form a finished product or a material suitable for machining to final specifications. Variations of this technique included prebaking before

molding, repressing after sintering, and extrusion. Machining was carried out on standard metal-working machines, and waste was recovered for reuse. Tape was produced by veneering followed by a heat treatment, which is known as tensilating.

Air samples were collected by drawing air through filter papers and bubblers containing a dilute alkali solution that separated solids from gases [47]. Fluoride was then determined by the method of Willard and Winter [48]. In addition to samples taken for chemical analysis, samples for microscopic examination were taken with a thermal precipitator before and after improvements in local exhaust ventilation [47].

Before improvements in environmental conditions were made, air samples contained concentrations of fluorine-containing compounds as high as 3.5 mg/cu m (expressed as PTFE). After improvements in the factory, the concentrations of PTFE in the workplace air were 0.2-0.4 mg/cu m. Before improvements, a general examination showed a very fine, highly refractive fume and a few large particles, which the author thought to be PTFE in the process of disintegrating into a fume. After factory improvements, dust counts were on the order of 1,000 particles/cc less than 0.5 μm in diameter, 15 particles/cc with diameters between 0.5 and 1.0 μm, and 1 particle/cc with a diameter of more than 1 μm.

Despite the reduction in concentrations of airborne fluorine compounds, Sherwood [47] reported that occasional cases of polymer fume fever still occurred and speculated that the most likely cause was smoking tobacco contaminated with PTFE. Sherwood calculated that, when a single 1-mm particle of PTFE is burned on a cigarette, the quantity of fumes inhaled is equivalent to that which would result from breathing PTFE at a

concentration of 0.4 mg/cu m for 8 hours. Sherwood recommended banning smoking and providing exhaust ventilation and thermostatic oven controls wherever PTFE is fabricated.

Sherwood [47] did not discuss the pertinence of calculating the fluoride determined as PTFE, even though the method of Willard and Winter [48] is a method of fluoride analysis. In addition, Sherwood [47] did not specify which areas were sampled and did not discuss the possibility that some fluorine compounds would not be detected by the method of Willard and Winter [48].

In 1963, Adams [22] conducted an investigation to determine the cause of polymer fume fever in employees in a plant where PTFE was processed. Altogether, 30 wage and 8 staff employees were interviewed by a medical officer. An investigation of the plant was also conducted. Of the 30 wage employees, 14 had experienced symptoms of polymer fume fever in the 2 months previous to the interview. A total of 32 incidents of polymer fume fever were reported by these 14 workers. Only employees working in the finishing room had been affected. Of the 18 men who worked in the finishing room, 12 who were smokers accounted for 30 incidents and 2 nonsmokers accounted for the other 2 attacks. A detailed investigation showed that 6 men who rolled their own cigarettes had had 21 of the attacks of polymer fume fever. Of the eight staff employees, only one, a pipe smoker, had had an attack of polymer fume fever.

In the finishing room, PTFE was dried, sifted, and packed [22]. In an unspecified drying operation, a small amount of PTFE was occasionally heated beyond the normal drying temperatures. Air samples were taken by an unidentified method at points close to the drying ovens and the ovens where

the polymer was further heated when required. Adams found concentrations of hydrogen chloride as high as 35 ppm on occasions when PTFE was heated only to normal drying temperatures. When oven temperatures exceeded 300 C, the author found up to 6 ppm of hydrogen fluoride. Although acetic acid is usually used to coagulate PTFE latex, it is possible that hydrogen chloride was used and that residues of this acid provided the HCl. HCl boils at 110 C whereas something like 250 C is required to liberate HF from PTFE.

Adams [22] concluded that the majority of incidents of polymer fume fever resulted from the smoking of PTFE-contaminated tobacco. He noted that precautions must be taken to prevent particles of polymer from lodging beneath nails, in hair, or on clothing. Adams did not report the method of analysis used to detect hydrogen fluoride. That the hydrogen chloride in the vicinity of the drying ovens came from PTFE per se is highly unlikely because this polymer contains no chlorine atoms.

Animal Toxicity

A list of compounds that have been identified as pyrolysis products of fluorine-containing polymers, as stated previously in the section on Identification of Decomposition Products, includes carbon monoxide, carbon dioxide, hydrofluoric acid, carbon tetrafluoride (fluoromethane), carbonyl fluoride, silicon tetrafluoride, tetrafluoroethylene, hexafluoroethane, chlorotrifluoroethylene, hexafluoropropene or hexafluorocyclopropane, perfluoroisobutylene, and octafluorocyclobutane. Coleman et al [8,13] have presented mass spectra for a number of other compounds present in the pyrolysis products of PTFE; Birnbaum et al [14] found mass spectrographic evidence of the existence of several other compounds among the pyrolysis

products of PCTFE. None of these compounds represented by mass spectra has been identified conclusively.

In addition to the various molecular species mentioned in the preceding paragraph, there is the particulate material that may be the principal cause of polymer fume fever [49]. Harris [10] had found in 1957 that heating PTFE at temperatures above 300 C produced the deposition of a solid material within his exposure chamber and also liberated an acid into the air of the chamber. Four rats exposed to such atmospheres developed congested or hemorrhagic lungs and pulmonary edema. Harris concluded that PTFE heated to 300 C or more produced a sublimate or an acid that induced pulmonary edema and killed rats thereby.

In 1968, Waritz and Kwon [7] and Birnbaum et al [14] suggested that the particulate material may carry adsorbed toxic materials (perhaps hydrofluoric acid, carbonyl fluoride, octafluoroisobutene, or chlorotrifluoroethylene) into the alveoli, the latter group of researchers [14] having found that the mean particle size of this material was 0.5 μm and that 99% of the particles had diameters of less than 2 μm. These dimensions place the polymer fume in the category of inhalable dusts. Waritz and Kwon [7] found that removal of the particulate material by filtration of the fume from pyrolyzing PTFE removed the toxicity of the fume without reducing appreciably its content of hydrolyzable fluoride, tetrafluoroethylene, hexafluoropropene, or octafluoroisobutene. The postulated carrier function of the particulate material may be, therefore, an important factor in the toxicity of the pyrolysis products of fluorinated polymers.

Of the fluorinated compounds listed above as identified products of pyrolysis of fluorinated polymers, some information on the biologic actions of all but hexafluorocyclopropane has been found. Machle and Kitzmiller [50] exposed five rabbits, three guinea pigs, and two rhesus monkeys to a mean analytic concentration of 15.2 mg/cu m of hydrofluoric acid for 6-7 hours/day, 5 days/week, for 10 weeks. Two guinea pigs died, but the other animals survived the series of exposures and seemed to be in good health until they were killed about 240 days after the last exposure. These animals were found to have elevated concentrations of fluorine in their tissues, especially bones, lungs, and teeth [51]. Their lungs, livers, and kidneys contained evidence of further damage by the exposures [50] despite survival of the animals without obvious deleterious effects. The concentration of hydrofluoric acid used cannot be considered, therefore, to be a safe one for the species tested. Higher concentrations of hydrogen fluoride caused more evident damage, graded in severity in rough accord with the concentration at which the animals were exposed [52]. A concentration of 24.5 mg/cu m killed 0/3 rabbits and 0/3 guinea pigs exposed to it for seven 6-hour days; one rabbit had considerable damage in its liver and kidneys and early fibrosis in addition to emphysema in its lungs. At the other extreme of the range of concentrations of hydrogen fluoride used in this paper, exposure at concentrations of 1,000 to 1,500 mg/cu m killed some animals exposed for only 5 minutes.

Darmer et al [53] performed short-term (1-hour) exposures of mice, rats, and monkeys to hydrofluoric acid with 14-day observation periods after the exposures, determining the LC50 of the compound for each species under these conditions. For mice, rats, and monkeys, respectively, the

approximate lethal concentrations were 410, 1,044, and 1,452 mg/cu m.

Clayton [54] reported that a mixture of 90% tetrafluoromethane and 10% air (about 3,240,000 mg/cu m of tetrafluoromethane) was the approximate LC50 for rats exposed to it during a 15-minute period. When guinea pigs were exposed later to the same substance during a 2-hour period, a concentration of 20% killed none of 12 animals [23].

Carbonyl fluoride was found to be less toxic to adult rats than to juvenile ones [55], the 14-day LC50 for 1-hour exposures being 945 and 1,215 mg/cu m for 8-week-old and 24-week-old rats, respectively.

Silicon tetrafluoride had a 14-day LC50 for the rat in a 1-hour exposure of 3,924 mg/cu m [55].

Zhemerdey [56] reported that inhalation of TFE monomer in concentrations of 4.0 and 2.5 volumes% (163,600 and 102,250 mg/cu m) produced minimal mortality in rabbits and rats, respectively. Hyperemia of the liver, hemorrhage in spleen and lungs, dystrophic changes in the epithelium of the renal tubules, atelectasis and emphysema in the lungs, and desquamation of the bronchial epithelium were the principal changes attributed to the monomer. Clayton [54,57] reported that the LC50 for the rat exposed to tetrafluoroethylene for 4 hours was 163,600 mg/cu m.

For CTFE, the LC50 for rabbits and white rats exposed for 2 hours was reported to be 24,000 mg/cu m [58]. The "absolutnaya smertelyenya kontsentratsiya," meaning probably the LC100, was said to be 26,400 mg/cu m for the rabbit and 36,000 mg/cu m for the white rat. No actual data on the numbers of deaths after exposure at any concentration were provided.

Clayton, in a series of papers [23,54,57] all probably referring to a single estimation of the inhalation toxicity of CTFE, has reported that the

LC50 for the rat exposed for 4 hours was 1,000 ppm (4,770 mg/cu m).

More recently, Hood et al [59] have exposed rats, guinea pigs, rabbits, and dogs to chlorotrifluoroethylene at concentrations of 300 ppm (1,431 mg/cu m) for 4 hours/day, 5 days/week, for a total of 18 exposures. One of 10 male guinea pigs died after the sixth exposure. One of 10 male rabbits died after 4 exposures and another after 5. None of 10 rats of each sex and none of 3 dogs died. The guinea pigs and rabbits, even those that died, had no signs of specific anatomic injury. Transient granulocytic leukopenia, with occasional atypical cells, appeared in the dogs during the first 2 or 3 days of each week of exposure. The only pathologic change found in the dogs was a mild encephalopathy without observable neurologic abnormality.

Kochanov [58] exposed rabbits and rats for prolonged periods to CTFE (for 4-6 hours/day, 6 days/week, for up to 130 exposures) at concentrations of 1,200-2,400 mg/cu m. Control animals were handled and maintained in the same way as the experimental ones. Congestion of the liver, the spleen, and the kidneys and hypochromic anemia and leukopenia were the principal pathologic changes reported in these animals. During the series of exposures, the exposed rats either lost weight or lagged behind the control animals in gaining weight. Oxygen consumption by the exposed rats was stated to have decreased less during the experiment than that by the control animals. During passive orientation in a vertical position (using the spine as the axis), the heartbeat of the experimental rabbits was said to have increased more than that of the control animals; the increase was stated to have become progressively larger throughout exposure in the exposed rabbits. The exposed animals also were said to have recovered from

the orthostatic tachycardia more slowly than the control animals. These observations suggest that exposure to CTFE altered the properties of the sympathetic nervous system, including possibly such centers in the brain stem as the bulbar vasomotor mechanisms. The exposed rats were reported to have undergone a significant decrease in the ability to summate subthreshold stimuli (presumably applied to the motor nerve of some unidentified effector).

Hood et al [59] exposed rats of both sexes, male guinea pigs, male rabbits, and dogs for 6 hours/day, 5 days/week, for 14 months to CTFE at concentrations starting at 15 ppm (about 71.6 mg/cu m) and increasing progressively, at irregular intervals of time, to 30, 50, 100, and 150 ppm (715.5 mg/cu m). These exposures produced no significant pathologic effects in rabbits and guinea pigs but produced severe tubular necrosis in rats. Two of four exposed dogs began to exhibit signs of neurologic disturbances after 27 and 64 exposures, respectively, at 150 ppm. These consisted of stiffness and weakness of the legs and unsteadiness in standing. One of two other dogs that were added to the exposed group at the beginning of exposure at 100 ppm (477 mg/cu m) died after 56 exposures at that concentration followed by 54 exposures at 150 ppm. The second of these dogs was reported to have become very irritable at this same time. Degenerative changes in the central and peripheral portions of the somatic nervous system were found, most severe in samples of nerve tissue from the dog that had exhibited the most marked neurologic signs (temporary prostration at the end of each period of exposure, ataxia, and difficulty in swallowing). This dog was found to have atrophy of the muscles of the hindlegs.

Clayton [54] reported that a mixture of 80% hexafluoroethane with 20% oxygen (about 4,515,000 mg/cu m of hexafluoroethane) was an approximate lethal concentration for the rat exposed to it for 4 hours.

Two different laboratories have reported data on the inhalation toxicity of hexafluoropropene. One reported that, with a 4-hour exposure of the rat, the LC50 for hexafluoropropene was 18,404 mg/cu m [54]. The other reported that the same duration of exposure of the rat gave an LC50 value of 17,177 mg/cu m [60].

Perfluoroisobutylene (PFIB) has been used in two different experiments that yield limits within which the LC50 value for 6-hour exposures may lie [54]. Exposure to air containing 0.3 ppm (2.5 mg/cu m) of PFIB killed 0/2 rats. Exposure at 0.5 ppm (about 4.1 mg/cu m) killed both rats put into that concentration. A 4-hour exposure at 0.76 ppm (about 6.2 mg/cu m) was lethal for rats [57]. The last experiment yielded the same Ct product as the second.

Octafluorocyclobutane appears to be one of the least toxic compounds examined. Ninety daily 6-hour exposures of mice, rats, rabbits, and dogs to air containing 10% of this compound had no observable effect on the animals [54,61]. Exposure of rats for a single 4-hour period to octafluorocyclobutane at concentrations of up to 80% had no apparent effect on the animals [54].

The data in these paragraphs allow arrangement of the compounds on which information is available in a hierarchy of decreasing toxicity, albeit with some uncertainty. There is little doubt that perfluoro-isobutylene is the most toxic compound and that octafluorocyclobutane and hexafluoroethane are the least toxic. The ranking of inhalation toxicity

for the rat, based largely on single exposures, that NIOSH has derived from the information stated above is as follows, going from the most toxic to the least: perfluoroisobutylene, hydrofluoric acid, carbonyl fluoride, silicon tetrafluoride, chlorotrifluoroethylene, hexafluoropropene, tetrafluoroethylene, tetrafluoromethane, hexafluoroethane, and octafluorocyclobutane.

In addition to the information summarized above on the breakdown products of PTFE and PCTFE, the results of studies of the toxicities of several fluorinated derivatives of methane and ethane, including vinyl fluoride and vinylidene fluoride, have been reported [62]. These two monomers have been used for the preparation of both homopolymers and copolymers [63]. Lester and Greenberg [62] reported that neither vinyl fluoride nor vinylidene fluoride was anesthetic or lethal to rats after 30-minute exposures at concentrations of 80%. Rats exposed at this concentration of vinyl fluoride for 12.5 hours or of vinylidene fluoride for 19 hours were judged at necropsy to have suffered no adverse effects from their exposures. Du Pont [62] has stated that exposures of rats to vinyl fluoride at a concentration of 100,000 ppm (188,100 mg/cu m) for 7 hours/day, 5 days/week, for a total of 30 exposures, had no effect on observable functions or behavior, rate of weight gain, weights of individual organs, and gross and microscopic anatomy. No similar information for vinylidene fluoride was provided.

The other general approach to assessing the toxicity of the pyrolysis products of fluorinated polymers, ie, exposing experimental animals to mixed decomposition products of polymers heated to various temperatures, has been used by a number of investigators. In 1955, Zapp et al [19]

pointed out that the intact PTFE polymer is nearly inert but that products of its thermal decomposition are not. Polymer fume fever has been recognized to be a consequence of exposure to heated PTFE since its description in 1951 by Harris [10]. Studies of the toxicity of the pyrolysis products of PTFE had been started at the Haskell Laboratory in 1943, but polymer fume fever had not been reproduced in experimental animals. Lethal activity had been demonstrated, however [19].

Strips of PTFE subjected to temperatures of 200 and 250 C in a stream of air passing into an exposure chamber containing 2 rats caused no deaths of the rats after a 6-hour exposure [19]. Similar exposures to air passing over strips of PTFE heated to 300 and 350 C did result in the death of rats, the higher temperature having a more marked effect with "Teflon 6," described as a low-molecular-weight polymer, than with "Teflon 1," a high-molecular-weight polymer.

Clayton et al [64] reported that, when "Teflon 1" and "Teflon 6" were subjected to temperatures of 300, 325, and 350 C in tubes of either glass or stainless steel, the materials heated in glass tubes yielded more toxic pyrolysis products than those heated in the stainless steel tubes. The differences were most marked for "Teflon 6" at 300 C and for "Teflon 1" at 350 C. Samples of "Teflon 6" that yielded comparatively large amounts of particulate material were more toxic than those that yielded less. Filtration of the pyrolysis products with a filter having a pore size of 0.45 μm lowered the mortality of rats exposed to the pyrolysis products from 43/48 to 7/48.

"Teflon 6" manufactured before 1958 was reported [57] to yield toxic breakdown products at 350 C, whereas "Teflon 6" manufactured "currently"

(1959 and thereafter) yielded pyrolysis products of approximately equal toxicity only when the temperature was raised to 425 C.

Cavagna et al [49] reported they had been able to produce attacks of fever in rabbits subjected to inhalation of aerosolized 20% acetic acid, in an undisclosed concentration in the inspired air, for 10 minutes, followed 16 hours later by exposure for 30 minutes to an atmosphere containing 10-12 mg/cu m of hydrogen fluoride and 1.0-1.7 billion particles/cu m with diameters greater than 0.7 μm, which had been generated by heating PTFE in a tube furnace at 400-500 C. Seven of 11 rabbits had temperature increases of 0.5-1.5 C. These appeared after a latency period of about 5 hours, during which a decrease in body temperature, leukopenia, and cough and rhinorrhea were observed. The fever lasted 6-7 hours and coincided approximately in onset, but not in duration, with leukocytosis. Exposures of naive rabbits to fumes from heated PTFE produced initial hypothermia and irritation of the respiratory tract but no fever.

Similar results were obtained by iv injections of 3-4 mg of particles collected by condensing the fumes from heated PTFE in a sterile Drechsel bottle. These particles were washed with apyrogenic water and suspended in isotonic saline for injection. After injection of these particles, the fever appeared within 20-40 minutes and the duration was 3-4 hours. The fever had about the same relation to leukopenia and leukocytosis as in the inhalation exposures. Injections of suspensions of particles on successive days failed to produce fever after five to eight repetitions. The resistant rabbits still responded with fever to injections of endotoxin from E. coli. It is possible that the apparent resistance of the rabbits to the repeated injections may have been related to aging of the particles,

as reported in Blagodarnaya's paper [65], discussed below. The paper of Cavagna et al [49] does not indicate whether the particulate material was prepared fresh daily or was prepared once and used for the entire series of injections. In vitro exposure of granulocytes from rabbit blood to the particulate material resulted in both phagocytosis of the particles and degranulation of the cells. The authors suggested that the extrusion of granules from the cells released an endogenous pyrogen into the plasma, with subsequent derangement of heat-balancing mechanisms.

Waritz and Kwon [7] found that filtration of the products of pyrolysis of "Teflon 5" at 450 C in air reduced the mortality of rats exposed to the pyrolysis products from 6/6 to 0/6 but did not reduce the concentrations of hydrolyzable fluoride, tetrafluoroethylene, hexafluoropropene, and perfluoroisobutylene in the exposure chamber. The authors also reported that traces of PFIB were produced when PTFE was pyrolyzed at 475 C and that pyrolysis at 480 C produced 5 ppm of PFIB. Accordingly, they proposed that the principal toxic component in the pyrolysate from PTFE is a particulate material that may have other toxicants adsorbed on it. Waritz and Kwon showed also that their results agree with Errede's hypothesis [21] of the mechanism for degradation of PTFE and with the demonstration by Scheel et al [55] that carbonyl fluoride is the product of oxidation of the backbone of the polymer at about 550 C.

Blagodarnaya [65] subjected PTFE to pyrolysis at 550 C, collecting the particles produced. Some of this powder was used at once, another aliquot was washed with water to remove the gaseous products of decomposition, and a third portion was stored for 6 months before being used. These three samples of powder were compared with a powder produced

by grinding PTFE that had not been pyrolyzed and with powdered chalk. The powders were administered to rabbits by iv injection of 1-1.5 mg/kg in suspension in sterile, apyrogenic saline. Control rabbits received only saline. Only the unwashed pyrolyzed particles produced a febrile reaction in the rabbits. This was preceded by leukopenia, which was frequently succeeded by leukocytosis. A similar response was induced in rabbits by inhalation exposure to the unwashed pyrolyzed particles at a concentration of 122.8 mg/cu m for 2.5 hours.

The succession of leukopenia, pyrexia, and leukocytosis reported by Blagodarnaya [65] in the rabbits exposed to unwashed pyrolyzed particles from PTFE is reminiscent of the febrile response to gram-positive bacteria injected iv into rabbits [66]. The failure of washed pyrolyzed particles to produce fever in these experiments indicates that the response is not to particulate agents alone. The presumption is that some water-soluble and volatile component of pyrolyzed PTFE adsorbed on the surfaces of the particulate material render the particles capable of interacting with the leukocytes of the blood and releasing the leukocytic pyrogen as suggested by Cavagna et al [49]. Some further study of the pyrogenic process after exposure to pyrolyzed fluorocarbon polymers seems desirable.

Treon et al [67] compared the toxicities of the pyrolysis products of PTFE and of two polymers of PCTFE differing in extent of polymerization, so that one (FL) was a liquid and the other (KF) was a solid. The liquid polymer (FL) was dropped into an Inconel tube heated by an electric current through resistance wire wound around the tube. The solid polymers (PTFE and KF) were prepared as strips which were inserted into the cold Inconel tube. The tube was then raised to the planned temperature as rapidly as

possible. Air or nitrogen (PTFE only) was passed through the furnace at a rate of 31.8 liters/minute and into the 800 liter exposure chamber. PTFE was pyrolyzed at temperatures of 375-878 C. FL was pyrolyzed at either 371 or 482 C, whereas KF was heated to temperatures of 803-813 C.

Groups of five mice, six rats, four guinea pigs, four rabbits, one cat, and one dog (PTFE only) were exposed in the chamber to various concentrations of pyrolysis products (graded by the rate at which the polymer was fed into the furnace) and for different spans of time [67]. The exposures to pyrolysis products of PTFE lasted for 30-180 minutes, most being less than 60 minutes in duration. Exposures to the pyrolysis products of FL were for 2, 7, or 24 hours, whereas those to the pyrolysis products of KF were for 32-34 minutes.

Dogs, mice, and rabbits were the most resistant species to PTFE pyrolyzed at temperatures of 739-813 C in the presence of air. When PTFE was pyrolyzed at temperatures of 811-878 in nitrogen, rabbits, guinea pigs, and rats were more resistant than mice. Cats and dogs were not used in these last tests. When the temperature of pyrolysis was 491-527 C in the presence of air, rats and rabbits were more resistant to a lethal effect than mice and guinea pigs. Cats and dogs were not included in these studies either. Pyrolysis of PTFE in the presence of air yielded pyrolysis products of greater toxicity than those produced in nitrogen. Lowering the temperature of the pyrolysis apparatus from 739-813 to 491-527 C decreased the toxicity of the pyrolysis products to rats, rabbits, and mice, but slightly increased the toxicity to guinea pigs.

Cats and rats were the most resistant species to the lethal effect of the pyrolysis products of FL heated at 482 C [67]. When the pyrolysis

temperature of this polymer was lowered to 371 C, no animals were killed during exposures of 2 or 7 hours. Mice, cats, and rabbits were more resistant to the lethal action of the pyrolysis products of KF than were guinea pigs and rats.

When PTFE was pyrolyzed in the presence of nitrogen, pyrolysis at a rate of 1.99 g/hour produced no fatalities in any of the four species exposed [67]. When PTFE was pyrolyzed in air, pyrolysis at a rate of 2.60 g/hour at 506 C produced death of only 1/6 rats, 1/4 rabbits, 0/5 mice, and 0/4 guinea pigs after an exposure of 36 minutes. Pyrolysis at a rate of 1.67 g/hour at 805 C produced death of 3/6 rats, 2/4 rabbits, 2/5 mice, and 0/4 guinea pigs after an exposure of 33 minutes.

Pyrolysis of FL at 482 C at rates of 3.18 g/hour or 1.02 g/hour killed no animals after exposures of 2 and 7 hours, respectively [67]. Pyrolysis of KF at 805 C at a rate of 0.88 g/hour killed no mice, rats, guinea pigs or rabbits after an exposure of 34 minutes [67].

The Treon et al [67] data are difficult to interpret in a comparative way because of the various conditions of pyrolysis and exposure of the experimental animals. A higher temperature of pyrolysis seems generally to produce more toxic pyrolysis products. The observations that species sensitivity to the pyrolysis products of the three polymers varies not only with the polymer but also with the conditions of pyrolysis indicate that, under similiar conditions, the two polymers of PCTFE probably yield different pyrolytic products, despite their monomeric identity, and that a single polymer yields different products under different conditions of pyrolysis. Pyrolysis in the presence of an inert gas seems to be less hazardous than that in the presence of air. The pyrolysis products from FL

may be less hazardous than those from either PTFE or KF, but this conclusion cannot be supported satisfactorily by the data provided. Good comparative data would be useful. Zapp [68] gave a little further information about the pyrolysis of PCTFE, finding that it, like PTFE, undergoes degradation when exposed to a temperature of 300 C but not when exposed to one of 250 C.

Birnbaum et al [14] exposed rats to the products of pyrolysis of PCTFE heated to temperatures of either 375 C or 400 C, determining the rate at which a rod of PCTFE had to be fed into a pipe heated to the desired temperature in an electric furnace to maintain an LC50 of pyrolysis products within an exposure chamber fed with air passed through the furnace at a rate of 4 liters/minute. The exposure periods were either 1 or 3 hours. One-hour exposures at 375 C did not result in sufficient mortality to yield valid estimates of the LC50 at the highest rate of feed of the PCTFE rod into the heated tube. The 3-hour exposure to the products of pyrolysis at this temperature yielded an estimate that 31.5 g/hr of the polymer had to be subjected to pyrolysis to maintain an LC50 of the pyrolysis products within the chamber. Exposure for 1 hour at the higher temperature of pyrolysis (400 C) yielded an estimate that 23.5 g/hr of the polymer had to be pyrolyzed at this temperature to maintain an LC50 of the pyrolysis products within the chamber. The particles in the pyrolysis products ranged in diameter from about 0.15 to 3.0 μm, 85% of the particles being less than 1 μm in diameter and 99% less than 2 μm. Infrared and mass spectrometers were used to obtain some idea of the molecular species present in the exposure atmosphere; these two techniques indicated the

presence of perhaps as many as 13 different materials in the pyrolysis products.

Comparatively little information about pyrolysis products of fluorocarbon polymers other than PTFE and PCTFE has been found. Clayton [57] reported studies of the inhalation toxicities of two samples of a copolymer of vinylidene fluoride and hexafluoropropylene for the rat. One sample heated to 300 C killed 2/4 rats exposed to the products for 4 hours; the products from the same polymer heated to 350 C killed 4/4 rats during a 1-hour exposure. The products of the second sample heated to 350 C killed 0/2 rats exposed for 4 hours; the products of the same sample of polymer heated to 375 C killed 4/4 rats after a 4-hour exposure. The pyrolysis products gave an acid reaction with an indicator paper and produced irritation of nose and eyes, severe respiratory impairment, and acute pulmonary edema in rats that died.

Carter et al [6] compared the toxicity of the pyrolysis products of PTFE with those of a polymer of vinylidene fluoride with hexafluoropropylene (VF2-HFP), of a polymer of vinylidene fluoride with hexafluoropropene and unspecified additives (VF2-HFP-A), and of a terpolymer of vinylidene fluoride with both hexafluoropropylene and tetrafluoroethylene (VF2-HFP-TFE). The three polymers containing vinylidene fluoride were pyrolyzed at 550 and 800 C, whereas PTFE was pyrolyzed at 625 and 800 C. Rats were exposed in the static mode after the chamber had been charged with the desired concentration of pyrolysis products. Of the three polymers containing vinylidene fluoride, the copolymer with hexafluoropropylene was the least toxic at both pyrolysis temperatures. All three polymers containing vinylidene fluoride and

pyrolyzed at either 550 or 800 C were less toxic than PTFE pyrolyzed at either 625 or 800 C. The pyrolysis products of all four polymers heated to 800 C were more toxic than those of the corresponding polymers heated to 550 or 625 C. Toxicity was not strictly related to the concentrations of either carbon monoxide, carbon dioxide, or fluoride in the pyrolysis products. The toxicities of the pyrolysis products from the four polymers heated at 800 C were much more alike than those from the same four polymers heated at 550 or 625 C. Deaths resulted from congestion and acute edema of the lungs. Animals that did not die within 48 hours after the exposures resolved the edema within 8 days.

Scheel et al [69] determined the LC50 for a 2-hour exposure of male rats to the decomposition products of a copolymer of ethylene and chlorotrifluoroethylene (E-CTFE) heated at 550 C in air as the decomposition products from 7.5 g of polymer/cu m. This corresponded to a concentration of hydrogen fluoride in the exposure chamber of 42.5 ppm (about 34.8 mg/cu m). Hydrogen fluoride was the only pyrolysis product whose concentration in the exposure chamber seemed to be related to mortality in the exposed rats. The principal effects of the exposure on rats were irritation of the respiratory tract, pulmonary edema, hemorrhage in the lungs, congestion of the liver, vacuolation of hepatocytes, tubular necrosis in the kidneys, and proteinaceous material in the renal tubules.

Ehrsam [70] has shown that the pyrolysis products of PTFE are more toxic to birds than to mice or guinea pigs. Similarly, Griffith et al [71] has reported that Japanese quail and parakeets were killed by effluvia from a frying pan coated with PTFE and heated to 330 C and 280 C, respectively, whereas rats appeared not to be harmed until the pan was heated to 450 C.

Some investigators [72,73] have reported that subcutaneous implantation of PTFE into rats resulted in the formation of fibrosarcomas. However, Bryson and Bischoff [74] were unable to duplicate these results.

Correlation of Exposure and Effects

The most frequently reported effect of workplace exposure to the pyrolysis products of PTFE is an influenza-like syndrome designated polymer fume fever [10,34,37,39-41]. No effects of workplace exposure to the pyrolysis products of other fluorocarbon polymers were found in the literature. The major signs and symptoms associated with polymer fume fever are chest discomfort [10,23,34,36-41], fever [10,23,36,39, 40], leukocytosis [10,36], headache [23,34,36,37,40,41], chills [10,23,34,36-38,40,41], achy feeling [10,23,34,36,38], and weakness [10,23,36]. Complete recovery usually occurred within 12-48 hours after the exposure ended [10,23,34]. Other effects reported in humans exposed to the pyrolysis products of PTFE were nausea [40], malaise [10,36], congested throat and pharynx [37], basal rales of the lungs [39,40], pulmonary edema [39,40], hyperpnea [10,40], and increased pulse rate [40].

Damage to the respiratory tract, occasionally severe enough to result in pulmonary edema, was found in humans exposed to the pyrolysis products of PTFE [10,34,39,40] and in animals exposed to the pyrolysis products of PTFE [7,55], PCTFE [14], VF2-HFP [6,23], VF2-HFP-TFE [6,23], and E-CTFE [69]. Effects such as leukocytosis and elevated temperature were difficult to produce in animals [49,57,65].

Polymer fume fever has resulted when there was an insufficient amount of ventilation in molding operations [10,47] and when PTFE processing

temperatures were not controlled because of malfunctioning thermostats [10]. Polymer fume fever has also resulted from the smoking of PTFE-contaminated tobacco [22,23,34]. As little as 0.3 mg of a TFE fluorocarbon telomer added to the cigarettes of volunteers produced polymer fume fever [23].

Polakoff et al [46] reported that concentrations of undecomposed PTFE dust ranged from 0 to 5.5 mg/cu m in a PTFE-fabricating plant, but these concentrations were not associated with any harmful effects. No other epidemiologic studies on PTFE dust or other fluorocarbon polymers were found in the literature.

Sherwood [47] detected as much as 3.5 mg/cu m of fluoride (expressed as PTFE) in a PTFE sintering and machining workshop. After installation of a local exhaust ventilation system, fluoride levels were reduced to 10% of the previous levels. Sherwood's findings are difficult to interpret because of the lack of experimental details. Adams [22] found 6 ppm of hydrogen fluoride on some occasions near ovens that heated PTFE to temperatures above 300 C. He also reported finding 35 ppm of hydrogen chloride but offered no explanation for its presence.

Waritz and Kwon [7] found that the particulate fraction was the most toxic component of the pyrolysis products of PTFE heated at 450 C. All rats survived a 4-hour exposure to the pyrolysis products of PTFE heated at 400 C. When PTFE was pyrolyzed at 450 C, all rats survived a 4-hour exposure if the pyrolysis products were filtered (0.20-0.25 μm pore size), but all rats were killed when exposed to unfiltered pyrolysis products at lower concentrations. The amount of particulate collected on the filters indicated that there was 1.4 mg/cu m of particulate in the exposure chamber

in the unfiltered experiments. In both experiments, octafluorocyclobutane, tetrafluoroethylene, hexafluoropropylene, perfluoroisobutylene, and hydrolyzable fluoride were present at nonlethal concentrations.

The total amount of hydrolyzable fluoride produced when PTFE was pyrolyzed at 450 C was greater than that produced when PTFE was pyrolyzed at 400 C [7]. The concentrations of hydrolyzable fluoride in the exposure chamber, however, were approximately equal because different dilutions were used. Because all rats survived exposure to the filtered pyrolysis products of PTFE heated at 450 C, it is not possible to correlate lethality with the concentration of hydrolyzable fluoride.

Scheel et al [55] found that the principal toxic component in the pyrolysis products of PTFE heated at 550 C was carbonyl fluoride. Coleman et al [8] have shown that approximately 60% of PTFE was converted to carbonyl fluoride at a pyrolysis temperature of 550 C. For a 1-hour exposure, the 24-hour LC50 for carbonyl fluoride was 360 ppm, and the 24-hour LC50 for the pyrolysis products of PTFE heated at 550 C was 370 ppm of hydrolyzable fluoride, expressed as carbonyl fluoride [55]. For a 1-hour exposure, the 14-day LC50 for carbonyl fluoride was 350 ppm, and the 14-day LC50 for the pyrolysis products of PTFE heated at 550 C was 290 ppm, expressed as carbonyl fluoride. From these data, the authors [55] concluded that PTFE pyrolysis products caused delayed deaths, which they attributed to a particulate. They also concluded that the mortality produced by PTFE pyrolysis products during the first 24 hours postexposure was caused by carbonyl fluoride. The authors [55] did not report either the confidence limits for LC50 values or slopes of the dose-response curve. Without these data, it is difficult to determine whether the authors'

conclusions were justified.

Clayton et al [64] also concluded that the toxicity of the pyrolysis products of PTFE heated at 350 C was caused by a particulate. Seven of 36 (19.4%) rats were killed when the pyrolysis products of PTFE heated at 350 C were filtered (Millipore filter, 0.45 μm pore size). The expected mortality was 100%. When PTFE was pyrolyzed at 325 C, the unfiltered fume killed 6/16 rats (37.5%). The same pyrolysis products after filtration through a filter of 0.45 μm pore size killed 0/8 rats. These results are in agreement with the findings of Waritz and Kwon [7], since filtration of the pyrolysis products reduced mortality. However, Waritz and Kwon [7] reported that the unfiltered pyrolysis products of PTFE heated at 400 C were not lethal to rats. This discrepancy may be related to the finding of Clayton et al [64] that low-molecular-weight PTFE yielded pyrolysis products more toxic than those from high-molecular-weight PTFE; Clayton et al and Waritz and Kwon perhaps used samples of PTFE of different molecular weights.

In animal studies, Scheel [69] found a correlation of lethality with the amount of hydrolyzable fluoride produced when E-CTFE was pyrolyzed at 550 C, but the amount of hydrolyzable fluoride produced was not correlated with the amount of E-CTFE pyrolyzed. Other investigators found no correlation of lethality with the amount of hydrolyzable fluoride produced by pyrolysis of PCTFE [14], VF2-HFP [6], or VF2-HFP-TFE [6].

Waritz and Kwon [7] reported that traces of perfluoroisobutylene (PFIB) were produced when PTFE was pyrolyzed at 475 C and that pyrolysis at 480 C produced 5 ppm of PFIB. Clayton [57] has reported that the LC50 for PFIB in rats after a 6-hour exposure was 0.5 ppm. Although PFIB appears to

be the most toxic gas produced by the pyrolysis of PTFE, no studies correlating the concentration of PFIB with the toxicity of the pyrolysis products of PTFE were found in the literature.

In the absence of pertinent data, no useful correlation can be made between the type and extent of exposure and the degree of human intoxication produced by the decomposition products of fluorocarbon polymers. However, compiling and summarizing the signs and symptoms reported in humans is a useful first step in the attempt to understand the adverse effects of these substances.

Carcinogenicity, Mutagenicity, Teratogenicity, and Effects on Reproduction

No reports of reproductive impairment, mutagenicity, or teratogenicity resulting from exposure to fluorocarbon polymer decomposition products were found in the literature. Fibrosarcomas developed adjacent to PTFE implantations in rats [72,73], but implantation studies have little relationship to occupational exposure to the decomposition products of fluorocarbon polymers. A fibrosarcoma developed in a man who had received a PTFE-Dacron vascular graft [43], but the author was not able to justify a conclusion that the tumor arose because of the presence of PTFE. No report of an excess incidence of malignant tumors in humans exposed in the workplace to fluorocarbon polymers or their decomposition products was found in the literature.

TABLE III-2

EFFECTS FROM INHALATION OF FILTERED AND UNFILTERED PTFE PYROLYSIS PRODUCTS ON ANIMALS

Species	Pyrolysis Temperature (C)	Exposure Duration	Hydrolyzable Fluoride (mg/cu m)	Effects	Reference
Rats	550	1 hr	576.2	LC50 (24 hr)	55
"	550	"	452	LC50 (14 d)	55
"	550	1 hr/d X 5 d	288.1	Pulmonary edema; recovery in 7-10 d	55
"	450	4 hr	257.0*	No mortality or pulmonary hemorrhage	7
"	450	"	255.0*	"	7
"	450	"	231.0*	"	7
"	800	5 min	201.0	LD50 (expressed as 0.38 g PTFE); pulmonary edema	6
"	400	4 hr	24.3	No mortality or pulmonary hemorrhage	7
"	450	"	21.6	Mortality 100%; pulmonary hemorrhage	7
"	450	"	19.8	"	7
"	625	30 min	18.7	Mortality 100% (0.5 g PTFE); pulmonary edema	6
"	450	4 hr	17.6	Mortality 66%; pulmonary hemorrhage	7
"	625	30 min	16.8	Mortality 0 (0.45 g PTFE)	6
"	450	4 hr	15.8	Mortality 0; pulmonary hemorrhage	7

TABLE III-2 (CONTINUED)

EFFECTS FROM INHALATION OF FILTERED AND UNFILTERED PTFE PYROLYSIS PRODUCTS ON ANIMALS

Species	Pyrolysis Temperature (C)	Exposure Duration	Hydrolyzable Fluoride (mg/cu m)	Effects	Reference
Rabbits	550	1 hr	20	Death within 4-5 hr; pulmonary edema, congestion in all organs	49
"	550	30 min	20	Serious dyspnea, bradypnea, cough, hypothermia, recovery in 2-3 d	49
"	450	1 hr	11.4	Moderate dyspnea, bradypnea, cough, hypothermia, bronchitis	49
"	400	30 min	7.6	Moderate respiratory tract irritation, hypothermia	49
"	350	"	0.95	Slight respiratory tract irritation, moderate hypothermia	49

*Airstream filtered to remove particles

TABLE III-3

EFFECTS FROM INHALATION
OF INDIVIDUAL PYROLYSIS PRODUCTS
OF FLUOROCARBON POLYMERS ON ANIMALS

Compound	Species	Concentration	Exposure Duration	Lethality and Other Effects	Reference
TFE	Rats	40,000 ppm	4 hr	LC50; lung irritation	57
"	"	25,000 ppm	2 hr	Lowest LC; brain congestion, lung changes, dystrophic kidney changes	56
"	Rabbits	40,000 ppm	"	Lowest LC; brain congestion, pulmonary hemorrhage, and dystrophic kidney changes	56
HFP	"	4,000 ppm	"	LC50	60
"	"	3,000 ppm	4 hr	LC50; lung irritation	57
"	"	1,200 ppm	2 hr	LC50	60
"	"	735 ppm	6 hr	LC50; tubular nephritis	19
PFIB	Rats	0.5 ppm	"	Pulmonary edema	54
OFCB	"	800,000 ppm in O2	4 hr	No effects	57
"	Rats, Rabbits, Mice, Dogs	100,000 ppm	6 hr/d 90 d	"	54
COF2	Rats	350 ppm	1 hr	LC50 (14 d); lung edema	55
"	"	90 ppm	4 hr	"	55

TABLE III-3 (CONTINUED)

EFFECTS FROM INHALATION
OF INDIVIDUAL PYROLYSIS PRODUCTS
OF FLUOROCARBON POLYMERS ON ANIMALS

Compound	Species	Concentration	Exposure Duration	Lethality and Other Effects	Reference
SiF4	Rats	1,860 ppm	1 hr	LC50 (24 hr); lung irritation and edema	55
"	"	922 ppm	"	LC50 (14 d); lung edema	55
CTFE	"	5,040 ppm	2 hr	LC50; congestion of internal organs	58
"	"	1,000 ppm	4 hr	LC50; lung irritation and edema, tubular necrosis of kidneys	59
"	Rabbits	5,040 ppm	2 hr	LC50; kidney necrosis, brain changes	58
VF	Rats	800,000 ppm	0.5 hr	Loss of postural and righting reflex	62
"	Mice	690,000 ppm	4 hr	LC50; congestion of lungs and liver	62
VF2	Rats	800,000 ppm	19 hr	Slight intoxication	62
CF4	-	200,000 ppm	2 hr	No effects	23