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PONTIAC FEVER

AN EPIDEMIC OF UNKNOWN ETIOLOGY IN A HEALTH DEPARTMENT: I. CLINICAL AND EPIDEMIOLOGIC ASPECTS

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In July 1968, an explosive epidemic of acute febrile illness occurred at a county health department facility in Pontiac, Michigan. Illness characterized principally by fever, headache, myalgia, and malaise affected at least 144 persons, including 95 of 100 persons employed in the health department building. The mean incubation period was approximately 36 hours. Illness was self-limited, generally lasting from two to five days. Secondary cases did not occur in family contacts and second attacks did not consistently follow re-exposure in the building. A defective air-conditioning system was implicated as the source and mechanism of spread of the causative factor. However, extensive laboratory and environmental investigations failed to identify the etiologic agent. Since these investigations a bacterium similar to or identical with the agent responsible for Legionnaires' Disease has been isolated from guinea pigs exposed to the Pontiac health department building in 1968 as well as from guinea pigs exposed to water from the evaporative condenser. Paired sera from 32 cases of Pontiac Fever showed seroconversion or diagnostic rises in antibody titers to this bacterium.

air-conditioning; bacterial infections; disease outbreaks; environmental pollution; fever of unknown origin; Legionnaires' Disease; myalgia, epidemic

In July and early August 1968, an epidemic of acute febrile myalgia affecting at least 144 people occurred in a county health department building in Pontiac, Michigan. A relatively uniform, self-limiting illness of chills, fever, headache, and myalgia lasting two to five days affected 95 per cent of employees working in the county health department building. Only one person was hospitalized. Epidemiologic investigations incriminated a defective air-conditioning system as the proba-

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ble source and mode of spread of the causative agent. The remarkable features of this epidemic were an extraordinarily high attack rate, a relationship to one building, a common source, airborne spread, the lack of definite secondary cases among contacts, and the elusiveness of the agent despite intensive, prolonged environmental and laboratory investigation.

The clinical, epidemiologic, and laboratory investigations of this epidemic are detailed in this and another paper (1) to: 1) document this outbreak in the medical literature, 2) demonstrate the usefulness of epidemiologic and laboratory methods in identifying causative events, and 3) alert members of the health professions to the possibility of introductions in our environment of previously unknown or unrecognized agents.

Background

Oakland County, north of Detroit in southeast Michigan, is comprised of many residential suburbs, including Pontiac, an industrial city of approximately 84,000 persons (1965 Census). The Pontiac facility of the Oakland County Health Department is situated west of the center of Pontiac on a spacious "campus" of county service buildings. The health department building itself, a single structure built in 1956, has ground-level and basement floors. The main floor of the building is occupied by offices, an auditorium, a library, medical and dental clinic rooms, storage areas, and a small x-ray department. The laboratory, additional storage and utility rooms, and the equipment room which houses the air-conditioning machinery are located in the basement. The central air-conditioning system had been functional since the building opened.

The Pontiac facility serves as the administrative headquarters for the Oakland County Health Department, and, in addition, dental, chest x-ray, venereal disease, and immunization clinics operate there on a regular basis. Routine bacteriologic studies and serologic tests are performed in the basement laboratory. No virologic or fungal studies are conducted on the premises.

No major alterations had been made in the physical plant since its construction. During the first three weeks of June 1968, however, the ground adjacent to the building was regraded and paved, which raised clouds of dust that at times enveloped the building. Torrential rains occurred during the last week of June followed by a dramatic rise in temperature from a mean of 15.2 C on June 29 to 27.4 C on June 30.

Description of the epidemic

The epidemic of acute febrile illness at the Pontiac facility of the Oakland County Health Department began on July 1, 1968 (figure 1). Health department employees reporting to work on Monday morning, July 1, did not become ill during regular working hours; however, the first case occurred that evening. By the end of July 2, 67 cases had developed, and on Wednesday, July 3, an additional 22 employees and 15 visitors to the building had become ill. On July 4, the building was closed for the holiday and was reopened briefly the next morning. Meanwhile, a preliminary investigation was begun by personnel who were themselves ill.

On Saturday morning, July 6, operating components of the air-conditioning system were turned off for the weekend, while three newly-arrived medical investigators worked in the building. The building was reopened on Monday, July 8, with the air-conditioning system in operation. The three physicians who had remained well after exposure on the weekend, but who continued to work in the building on Monday, all became ill late Tuesday night. On Thursday, July 11, three additional investigators first worked within the building; approximately 36 hours thereafter, they, too, developed the syndrome. The health department building was completely closed to the public after Friday, July 12.

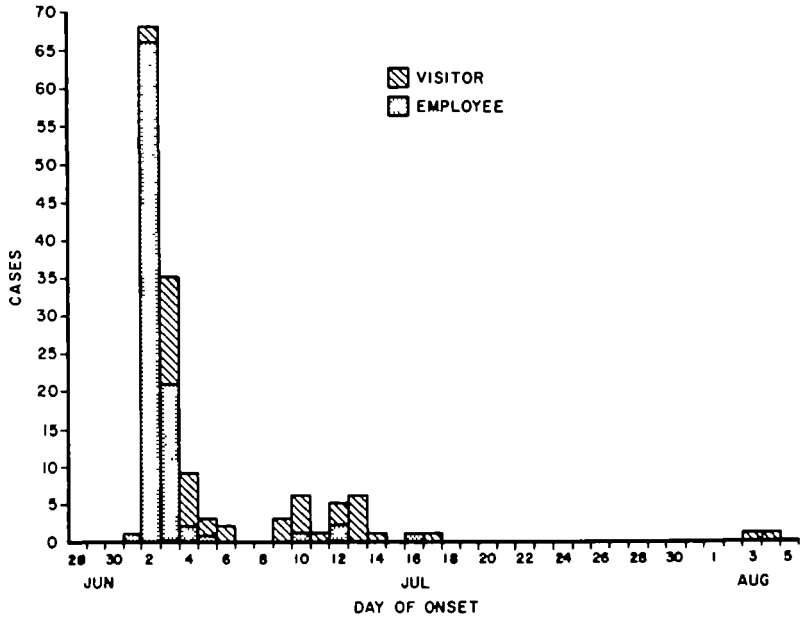

FIGURE 1. Cases of Pontiac Fever, by day of onset, Oakland County (Michigan) Health Department, June 28–August 5, 1968.

The only subsequent cases occurred in two additional investigators who worked in the building during the first week of August. A total of 144 cases occurred, 95 among 100 employees and 49 among 170 visitors to the building.

MATERIALS AND METHODS

One hundred employees of the health department, including public health and clinic nurses, sanitarians, administrative personnel, and several physicians and dentists were working at the Pontiac facility during the epidemic period. In addition, intermittent or transient visitors to the health department included maintenance men, consultants, and clinic patients; such persons, together with outside personnel involved in the investigation, have been collectively termed "visitors," a diverse group with respect to age and sex.

Every employee provided information on symptoms, time and activities in the health department building, and state of health of family members. Physical examination and clinical laboratory tests on 31 patients selected for acute or severe complaints were performed immediately after onset in some cases, and in most other instances within four days.

Visitors to the building from Friday, June 28, through Tuesday, July 2, were traced and information on visitors after July 2 was gathered insofar as time and available records permitted. While 170 visitors were recorded and have been included in the analysis, an undetermined number of additional persons, mostly clinic visitors, entered the building during the epidemic period, but were not traced. Since the quality of data on employees was superior to that on visitors, as a whole, a distinction between the two groups has been maintained throughout the analysis.

Additional case detection efforts included investigations of other institutions on the county campus, a control group of personnel of another Oakland County Health Department facility, analysis of emergency room visits and employee absenteeism at the two large general hospitals serving Pontiac, a survey of physicians in Pontiac, and a review of absentee

and sick-leave statistics of a large industrial corporation in Pontiac.

Preliminary observation of ill employees quickly revealed a notable uniformity of major symptoms. Illnesses were then graded by typicality of symptoms as follows: Grade I, which was considered as Pontiac Fever, included acute illness consisting of three or more of the following symptoms: 1) fever and/or chills, 2) generalized myalgia, 3) malaise, and 4) headache. Grade II included illness characterized by only one or two of the above symptoms, and was not considered as Pontiac Fever although a few may have been so. In addition, persons who suffered no acute symptoms three days following exposure were categorized as "well."

Specimens for culture and serologic testing were collected from approximately 280 persons, including employees, their family members, visitors, and employees from another office of the health department. Sera were tested against standard microbial antigens and against antigens prepared from pure cultures of certain agents cultured from exposed environmental materials or test animals. An extensive series of animal experiments and bacteriologic isolations and characterizations are described in another paper (1).

The initial team of two epidemiologists and a virologist were later joined by engineers specializing in air-conditioning and water systems, zoologists, veterinarians, industrial toxicologists, a mycologist, bacteriologists, and additional epidemiologists. Changes in the internal and external environment of the health department building were reviewed in detail including the study of the building's air and its circulation, and specifically: sources of possible aerosol production, such as dental drills; presence of contaminants, either microbiologic or chemical, as determined by testing of air samples; and patterns of air flow within the components of the air-conditioning system and in the rooms of the building. Examination of the air-conditioning system also included visualization of parts of the duct system and investigation of cross-contamination of air between separate components of the system. Other environmental studies included examination of the water and sewerage systems, and search for bird, rodent, or other infestations.

Clinical features

Fever and chills, myalgia, malaise, and headache were the most common symptoms elicited (table 1). The illness sometimes began quite abruptly, occasionally with shaking chills. More often, however, patients first noted progressive malaise, diffuse myalgia, or headache. Usually the complete syndrome appeared within six

Table 1

Symptoms in patients with "Pontiac Fever"

Symptom	Employee patients*		Visitor patients†	
	No.	%	No.	%
Malaise	93	98	47	96
Myalgia	90	95	47	96
Fever	86	91	38	78
Chills	86	91	34	69
Headache	86	91	41	84
Cough	54	57	12	24
Dizziness	51	54	23	47
Painful "stiff" neck	45	47	11	22
Nausea	44	46	17	35
Chest pain	43	45	12	24
Joint pain	41	43	19	39
Sore or dry throat	31	33	9	18
Sore eyes	30	32	13	27
Abdominal pain	26	27	8	16
Confusion	22	23	5	10
Coryza	20	21	5	10
Photophobia	18	19	4	8
Sensitive skin	15	16	8	16
Diarrhea	14	15	16	33
Poor coordination	13	14	4	8
Anorexia	12	13	5	10
Nose bleed	12	13	2	4
Vomiting	11	12	4	8
Insomnia	10	11	3	6
Bizarre dreams	8	8	2	4
Rash	7	7	2	4
Irritability	3	3	1	2

* Total number = 95.

† Total number = 49.

hours of the first symptom, and almost invariably within 12 hours.

Apart from these cardinal symptoms, localized muscle pains, dizziness, cough, and nausea were commonly mentioned. Among ill employees, diarrhea was reported in 15 per cent. Respiratory symptoms were not prominent in degree, but 57 per cent complained of a slight, usually dry cough. Sore or dry throat was present in 33 per cent of ill employees and midsternal chest pain or constrictive sensations were noted in 45 per cent. Pleuritic pain was rare.

A variety of neurologic symptoms was experienced by both ill employees and visitors, though reported less frequently by the latter. Fifty-four per cent of ill employees complained of dizziness and 19 per cent reported photophobia without neck stiffness or pain. Vague mental or other neurologic symptoms such as confusion, poor coordination, nightmares, insomnia, difficulty with memory or concentration, and general irritability were also reported.

As noted, fever and/or chills were recognized in over 90 per cent of ill employees epidemiologically related to exposure in the health department. Oral temperatures ranged up to 40.5 C but usually not above 39.4 C. In five of 49 cases where oral temperatures were well documented, values were above 40 C. Vital signs were not systematically observed in most patients in the acute state, but three physicians noted transient tachycardia and tachypnea early in their own illness. There were no other signs of upper or lower respiratory tract disease and no other significant physical findings.

In the acute stages of illness, white blood cell and differential counts were performed on seven acutely ill employees, revealing a polymorphonuclear leukocytosis ranging from 9400 to 17700 WBC/mm^3. Two weeks later, counts on 10 other patients after convalescence ranged from 5300 to 9077 cells per mm^3. A series of standard chemical determinations on sera of five patients who were still ill or in early convalescence revealed no consistent contributory findings. The battery of tests consisted of serum glutamic oxaloacetic transaminase, lactic dehydrogenase, alkaline phosphatase, bilirubin, albumin, globulin, cholesterol, total lipids, amylase, creatinine, blood urea nitrogen, uric acid, blood glucose, calcium, and phosphorus. Urinalysis on samples from three febrile patients revealed trace albumin in one, rare or occasional red blood cells in two, and occasional white blood cells in all three. A small number of throat and blood specimens were all negative on routine bacteriologic culture.

During the first week after onset, chest x-rays of 17 patients were negative for any acute process. Repeat examinations two weeks later were also negative, as were follow-up chest x-rays performed on most employees one to six months subsequently. Electrocardiograms in 13 persons without previous heart disease were normal.

Eleven patients received antimicrobial drugs, including penicillin, tetracycline, and sulfonamides, for treatment of the acute illness without noticeable effect. In addition, at the time of exposure two persons were receiving tetracycline for preexisting respiratory ailments; one of these individuals remained well. Only one patient was hospitalized, being admitted to a local hospital one week after onset. Physical examination and routine tests of this patient, including lumbar puncture, were negative and recovery was uncomplicated.

Acute illness tended to last two to five days. Specific physical sequelae were not apparent with several possible exceptions: one patient developed lymphangitis or thrombophlebitis in one leg; another experienced a brief episode of pleuritic chest pain with a transient friction rub approximately two weeks after the acute illness.

Many patients experienced lassitude in the aftermath of the acute illness. Other

frequent residual complaints, such as forgetfulness and poor concentration, persisted for as much as several months in a few patients. Prolonged convalescence was required in three patients with prior underlying illness. No significant chronic residua have been reported in these or other patients. There were no deaths.

Identification of source of causative agent

Early investigations. The probable relationship of illness to exposure in the health department building became apparent early in the epidemic. Initially, only employees who had been in the building on Monday, July 1, became ill. Exposure prior to Monday, July 1, did not produce illness, with the possible exception of one employee who was present in the building early June 29 as well as on July 1, and became ill during the evening of July 1. Many visitors and one employee who had not been in the building at all in the latter part of June, and some of them never before, developed illness after exposure on July 1.

There were no common exposures outside the building. A survey in adjacent buildings of the county service complex and in the community detected no unusual incidence of illness. There was no common exposure to foods in the employee group, nor had all affected persons used water from the building for drinking or washing. Moreover, numerous visitors became ill without prior consumption of any food or water from the building. In addition, illness in six investigators who had minimal community contact provided strong evidence for localization of exposure in the health department building. Thus, simply being in the health department building appeared to constitute exposure, since no specific activity appeared to entail exclusive or increased risk.

Particular areas in the building did not appear to be associated with higher risk, nor did any section of the building clearly confer protection. The explosive onset of the epidemic, as well as lack of evidence supporting other modes of exposure, suggested airborne spread of disease and drew attention to the air-conditioning system.

Certain days were associated with higher risk than others. The air-conditioning system was turned off on Saturday, July 6, and persons newly exposed that day did not become ill within the range of expected incubation periods, but did become ill approximately 40 hours following exposure to the building, after the system was restarted on Monday, July 8. Moreover, attack rates were higher in persons exposed during that morning than in those first exposed in the afternoon or evening, suggesting increased risk after restarting the air-conditioning system. Again, late Thursday morning, July 11, the entire air-conditioning system was turned off for approximately one-half hour and then restarted. Five persons present in both the morning and the afternoon became ill; two persons present only in the morning did not become ill, while five persons present only in the afternoon became ill.

Investigation of the air-conditioning system. By July 25, extensive laboratory and environmental investigation had not yet uncovered an etiologic agent. Since all epidemiologic evidence pointed to the air-conditioning system, a detailed examination of the structure and function of the system was undertaken.

The air-conditioning system consisted of two air circulation systems that were separate but had ducts next to each other (figure 2). The first system cooled refrigerant gas for the second system, which cooled air for the entire building. The first system circulated air from the basement through an evaporative condenser to the outside via a metal duct and discharge vent on the roof at a point less than 2 meters from the outside air intake of the second system. The air of the first system flowed through water sprayed within the evaporative condenser from a reservoir at

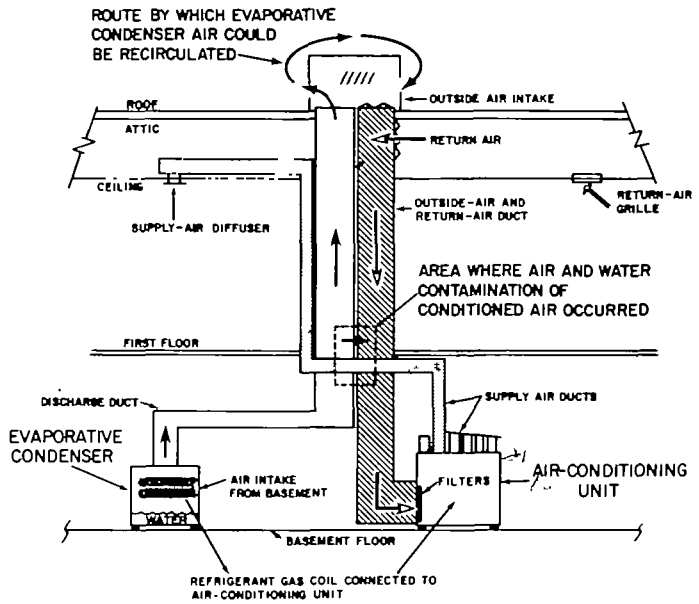

FIGURE 2. Schematic of air-conditioning system, Pontiac building, Oakland County (Michigan) Health Department, 1968.

the base of the unit to which algicide was periodically added. This air was supersaturated with water from the sprays as it moved up the metal duct.

The second air circulation system used fresh air from outside, as well as a percentage of recirculated air from the building, to cool the building. Outside air was passed through a low efficiency filter, cooled, and dehumidified in the air-conditioning unit proper, and distributed throughout the building by a system of supply-air ducts.

On July 29, several openings were made in one of the six main supply-air ducts of the air-conditioning system. Looking through these holes revealed that condensate from the water aerosol in the evaporative condenser discharge duct could, and in fact did, at times drain directly into an adjacent supply-air duct through cracks in both duct systems (figure 2). Furthermore, by means of smoke artificially generated and a non-toxic tracer gas dispersed in the discharge duct of the evaporative condenser, it was readily established that exhaust air from the evaporative condenser could contaminate the independent circulation of conditioned air in ducts supplying the building. This occurred both by simple leakage from duct to adjacent duct and by airflow between closely spaced exhaust and intake vents on the roof (figure 2).

LABORATORY AND ECOLOGIC FINDINGS

Throat swabs, stool, clotted blood, acute serum, and a variety of other specimens collected from a large number of typical, as well as especially severe, cases were cultured in Rhesus monkey kidney, baby hamster kidney, African green monkey kidney, HEp-2, WI-38, RO-1, human amnion cell systems, embryonated eggs, suckling mice, and numerous bacteriologic and fungal media. Aside from isolation of Herpes simplex virus from a throat swab in one case, there were no viral or rickettsial agents recovered. Species of *Mycoplasma* (*M. orale* type 1 and/or *M. salivarium*) were cultured from 15 throat swabs. Fungal and bacterial isolations from stool and throat swab specimens did not indicate a widespread, predominant, or unu-

sual agent. Thermophilic actinomycetes were specifically sought, but not found. Serologic screening tests were nondiagnostic (table 2). Toxicologic screening of urine samples did not reveal any abnormality.

Radial immunodiffusion studies were performed on 16 pairs of acute and convalescent sera from persons with characteristic Pontiac Fever (2). A 15 per cent or more rise in serum IgM globulins was revealed between acute and convalescent sera from 10 out of 16 patients. Four of the 16 showed a similar rise in serum IgA level and four showed a 15 per cent or more rise in IgG level.

Samples of air, drinking water, sewage, and soil, as well as swabs of many different surfaces including components of the air-conditioning system taken early in the second week of the epidemic did not uncover a significant or widespread pathogen or any predominant microorganism. Special attention was paid to microorganisms in the water used to fill the reservoir at the base of the evaporative condenser of the air-conditioning system. However, no organism isolated from this source (table 3) was serologically related to human illness.

Spectrographic analysis of air and drinking water samples obtained July 17, 30, and 31 detected no abnormal concentrations of trace metals or unusual chemicals. Spectrophotometric and chromatographic analysis of extracts from air-conditioning filters revealed no definite abnormalities. There was no evidence of leakage of dichlorodifluoromethane from the coils of the air-conditioning system.

Investigation for animal or arthropod habitation as well as a detailed search of the interior of the building for evidence of contamination by laboratory specimens or other foreign materials, was unrevealing.

Epidemiologic characteristics

Conditions of exposure and attack rates. Of the 100 employees at risk, 95 were classified as having had Pontiac Fever, for an attack rate of 95 per cent. Comprehensive medical and epidemiologic histories were elicited for the three unaffected

Table 2

Serologic tests performed on selected Pontiac sera upon which no diagnostic rise was demonstrated

Agent/antigen	Test	Agent/antigen	Test
Influenza – A/Japan/107/62	CF*	Murine reovirus 3	HI†
Influenza – A/Hong Kong/8/68	CF	Mouse adenovirus	CF
Influenza – B/Mass/366	CF	*Mycoplasma pneumoniae*	CF
Parainfluenza 1	CF	*Chlamydia psittaci*	CF
Parainfluenza 2	CF	Q fever	CF
Parainfluenza 3	CF	Rickettsialpox	CF
Parainfluenza 4a	CF	*H. capsulatum*	CF, Precipitins
ECHO 4	CF	*B. dermatitidis*	CF
ECHO 10	CF	Coccidiodin	CF
Lymphocytic choriomeningitis	CF	*C. neoformans*	Indirect fluorescent antibody
Vaccinia	HI		Latex agglutination
Adenovirus	CF	Salmonella	Agglutination
Murine Sendai	HI	Proteus	Agglutination
Pneumonitis virus of mice	HI	Brucella	Agglutination
Herpes simplex	CF	*Pseudomonas pseudomallei*	Agglutination
Venezuelan equine encephalomyelitis	HI	*F. tularensis*	Agglutination

* CF, complement fixation.

† HI, hemagglutination inhibition.

men (ages 28, 29 and 64) and two unaffected women (ages 28 and 47). They shared no common traits or unusual features to distinguish them, as a group, from the employees who became ill. In addition to these five exposed employees, four others remained well after initial exposure, only to contract the illness after later re-exposure. Of 170 persons analyzed in the visitor group, there were 49 cases for an attack rate of 29 per cent. There was no significant difference in incidence of illness on the basis of age or sex, in either the employee or visitor group.

Within the first two weeks, the attack rate was extraordinarily high in both employees and visitors exposed for more than brief periods. However, the risk of illness for equivalent duration of exposure generally diminished after the first two weeks of the epidemic. For example, in the nine visitors exposed for more than a six-hour period during the first two weeks of the epidemic, the attack rate was 89 per cent, but in the eight persons exposed for similar duration thereafter the attack rate was 25 per cent.

Virtually all employees were exposed for periods of at least two hours, and no significant variation of attack rate according to duration of exposure was noted among this group. The attack rate for visitors exposed for less than one hour was 9 per cent, as compared with 59 per cent in visitors exposed for more than six hours, and 98 per cent in employees exposed for more than six hours. However, some exposures lasting for less than one-half hour did produce characteristic illness.

Incubation period. The median incubation period, calculated from hour of first exposure in the building to approximate hour of first symptoms, fell in the 33–36-hour range for employee-patients and in the 37–40-hour range for visitor-patients (figure 3). The overall range was 5 to 66 hours, and with three exceptions all employee-patients developed illness between 21 and 56 hours after first exposure. Duration of exposure did not significantly affect the incubation period of cases. Most persons with atypical illness not believed to be Pontiac Fever had incubation periods at the extremes of, or outside the range for, illnesses classified as cases. The median duration of illness in all patients was three days. In 12 patients illness lasted for only one day, while in 17 it continued for six or more days. Duration of illness was increased only slightly in older patients and was not influenced consistently by duration of exposure.

TABLE 3

Predominant bacterial species isolated from water at base of evaporative condenser

Corynebacterium sp.	*Pseudomonas* – Group IA
Corynebacterium equi	*Pseudomonas stutzeri*
Bacillus sp. – similar to *B. cereus* (salicin neg.)	*Pseudomonas maltophila*
Pseudomonas sp.	*Pseudomonas alcaligenes* or *pseudoalcaligenes*
Flavobacterium sp.	

Secondary attack rate. In 231 contacts of 95 ill employees there were five cases consistent with Grade I illness. All were adults, and none was exposed to the building. Onset occurred from one to eight days after onset of illness in the index patient. Two persons with symptoms consistent with Grade I illness were reported in 95 contacts of visitor patients.

Re-exposure and recurrent symptoms. Forty-three of 91 ill employees who had comparable re-exposure during the second week of July claimed recurrent symptoms; however, the majority of recurrent syndromes were dissimilar to the prototype illness. Only 13 re-exposed employees claimed recurrent symptoms which would be classified as Grade I illness. Of four employees who had been ill and were not re-exposed, one subsequently experienced symptoms atypical of Pontiac Fever. Two employees claimed multiple recurrences.

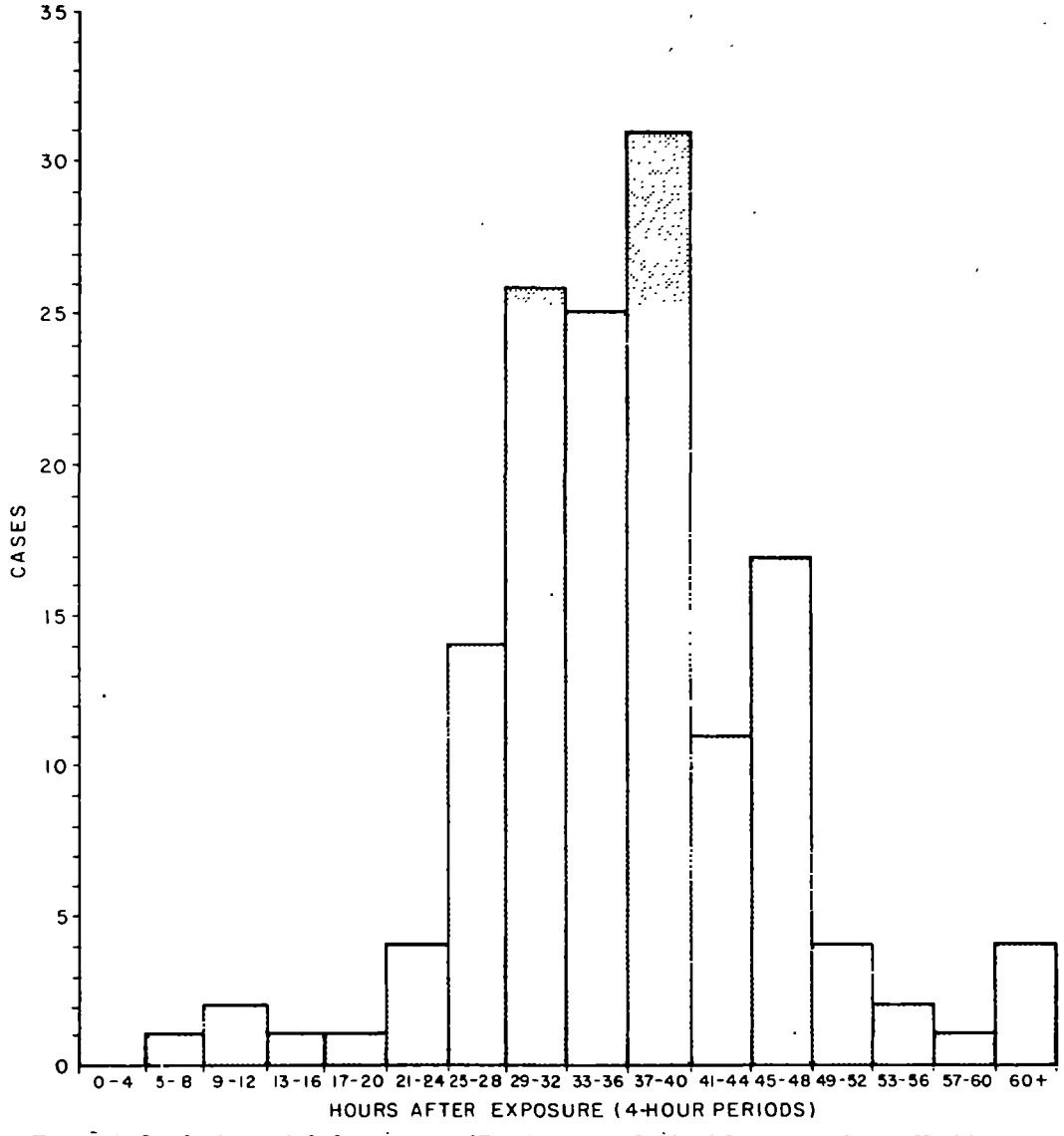

FIGURE 3. Incubation periods for 144 cases of Pontiac Fever, Oakland County (Michigan) Health Department, July–August 1968.

Two of the 26 visitors who were re-exposed suffered recurrent symptoms which were not, however, classified as Grade I illness. In a control group of 25 non-exposed employees none developed illness during the first week of July that could be classified as Pontiac Fever.

DISCUSSION

Although Pontiac Fever was a self-limited, relatively benign febrile disease, the involvement of a public health facility, an extremely high attack rate, and the enigma of its etiology generated an extraordinary amount of epidemiologic and laboratory investigation. The occurrence of this epidemic in a health department appeared fortuitous since no operations peculiar to this building as a health department could be etiologically implicated. The preceding events of earth turning, heavy rains, and high temperatures sug-

gested a critical interplay of environmental factors; however, none of these factors could be directly implicated. On the other hand, the explosive nature of the epidemic involving only those entering the building plus the identification of an air-conditioning system, defective in design and operation, strongly suggested that this was the mode of spread, as in other reports (3, 4).

The clinical characteristics of Pontiac Fever did not elucidate the pathogenesis of the illness nor the nature of the responsible agent. While the cardinal symptoms appeared consistently in the affected population, they were non-specific and did not suggest a unique syndrome. They resembled quite closely the characteristic symptoms of a systemic viral infection such as influenza or Venezuelan equine encephalitis, of metal-fume fever (5), polymer-fume fever (6, 7), acute airborne histoplasmosis (8, 9), and bore some resemblance to syndromes arising from inhalation of organic dusts such as Farmer's lung (7, 10). Physical examination and routine clinical laboratory tests added no positive information. Particularly significant negative findings were the lack of pulmonary involvement as seen by serial x-ray examinations.

Epidemiologic analysis revealed an epidemic of explosive nature with an extraordinarily high attack rate indicating a common source without evidence of any common exposure outside the building. The agent appeared clearly to be spread by the airborne route. The rapid onset was attributable to the simultaneous exposure on a Monday morning of a large group of susceptible persons. The syndrome followed exposure in the health department building by an incubation period averaging approximately 36 hours, an interval greater than that expected for acute intoxication by known metal or polymer fumes, but less than that expected for pulmonary histoplasmosis or bacterial and rickettsial diseases commonly spread by the airborne route. While risk of contracting illness was not entirely directly proportional to duration of exposure, the attack rate was lower in the group of persons only briefly exposed. Neither severity nor duration of illness could be definitely related to duration of exposure. Presence or absence of pre-exposure to the building was not a factor. Person-to-person spread could not clearly be established, and it seems likely that the similar, though non-specific symptoms that occurred rarely in contacts, were etiologically unrelated. The problem of recurrence of symptoms after re-exposure was more perplexing. If exposure to a toxic compound were involved, consistent recurrence of symptoms upon re-exposure might have been expected. However, illness apparently did confer resistance to subsequent attacks in all but a troubling minority of cases.

The etiologic agent persisted in the building for a minimum of two weeks and presumably existed in parts of the air-conditioning ducts or in the machinery room at least five weeks after first appearance. This suggested intermittent if not continuous production of the offending agent, or survival of such an agent over this prolonged time period. While viral or rickettsial agents could not be positively excluded, it seems more likely that a bacterial or fungal agent was introduced into and replicated in an organic medium in some part of the building. The only likely source of seeding of microbiologic particles, the open reservoir of the evaporative condenser of the air-conditioning system, was a menstruum which was suitable for the growth and propagation of bacteria or fungi. As previously noted, aerosolization of this tank water occurred, and air so contaminated was distributed throughout the building. Similarly, it seems likely that microbiologic particles were widely spread, probably in intermittent fashion, depending on the operating status of the air-conditioning system. Distribution to the building appeared relatively uniform, since there was no localization of cases

within the building nor sanctuary.

Following extensive cleaning of the air-conditioning system and duct work, the building was reopened to the public on September 15, 1968. However, the air conditioning system was not turned back on. Furthermore, during the next year the air-conditioning system was rebuilt including relocation of the evaporative condenser system to the roof. No recurrence of symptoms similar to Pontiac Fever was noted thereafter.

In sum, it seems possible that a microbiologic particle was introduced into the air-conditioning system some time prior to the epidemic; such an organism could have proliferated in the tank of the evaporative condenser and/or duct system, a process perhaps facilitated by the preceding days of high temperature and humidity. The pathogenesis of symptoms may have involved the release, either prior to airborne spread or after entry through the respiratory portal, of toxic, pyrogenic products or components (10, 11). In any event, this episode stands, at least for the present, as an example of the hazards that may in obscure ways be associated with man's manipulation of his environment.

Addendum

Since the completion of the above manuscript in November 1976, 37 paired sera from persons classified as Grade 1 Pontiac Fever as well as 10 pairs of control patients' sera were tested by the indirect fluorescent antibody technique against the bacterium that caused the Legionnaires' Disease (12, 13). Thirty-two sera from patients showed diagnostic rises or seroconversion to the Legionnaires' agent and all control sera were negative, indicating that the agent that caused Pontiac Fever is similar if not identical to the bacterium that caused Legionnaires' Disease. Furthermore, lung tissue from guinea pigs exposed to the Pontiac facility in 1968 as well as exposed to aerosols of water from the evaporative condenser have revealed bacteria similar or identical to the Legionnaires' agent, adding further evidence that this bacterium was the etiologic agent responsible for Pontiac Fever. When appropriate serologic studies with the Pontiac strain of the bacterium can be completed, a further analysis will be published in the *American Journal of Epidemiology*.

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