Nonpneumonic, Short-Incubation-Period Legionellosis (Pontiac Fever) in Men Who Cleaned a Steam Turbine Condenser

Abstract. *Pontiac fever affected ten men who had cleaned a steam turbine condenser with compressed air. Previous epidemics of Pontiac fever and Legionnaires' disease—both caused by* Legionella pneumophila *(proposed sp. nov.)—involved "airborne spread" from air-conditioning cooling towers or evaporative condensers. Aerosols of contaminated water in heat-rejection systems appear to be important sources of epidemic legionellosis.*

Two similar outbreaks of acute febrile myalgia occurred in 1973 in workers after they had cleaned steam turbine condensers (*1*). At the time, the cause of neither outbreak was determined. We have recently found that one of these outbreaks was caused by infection with *Legionella pneumophila* (genus novum, species nova) (*2*), the bacterial agent of Legionnaires' disease.

On 30 July 1973, ten previously healthy 18- to 39-year-old men spent 9 hours cleaning a steam turbine condenser located on the James River in Virginia. All subsequently became ill with a syndrome of fever with shaking chills (10/10), headache (9/10), severe generalized myalgia (9/10), sore throat (7/10), nausea or vomiting (6/10), and occasional dry cough (6/10). The mean incubation time, calculated from the beginning of the work shift, was 37 hours with a range of 17 to 43 hours. Nine were hospitalized; temperatures on admission were 37.9° to 40.2°C (mean, 39.1°C) and at maximum 39.1° to 40.6°C (mean, 39.7°C), and leukocyte counts on admission were 12,700 to 27,400 (mean, 16,100) per cubic millimeter. No patient had pneumonia or objective evidence of other organ system involvement. All defervesced within 2 days.

The condenser was a cast-iron cylinder approximately 4 m in diameter and 7 m long. Chambers on each end were connected by two sets of copper alloy tubes (diameter, 1.9 cm), which were surrounded by steam from the turbine during operation. Water from the James River was pumped into the chamber at one end and through one set of tubes in which the water absorbed heat from the turbine steam. The water then passed to the second chamber and back through the second set of tubes, where more heat was absorbed, before it was discarded back into the river; in the summer the temperature of the discharged water was approximately 36°C. Before being cleaned, the turbine was allowed to cool for 2 days, but there was no chemical pretreatment of the condenser. During the cleaning operation, the men entered the end chambers, forced slime and silt from the tubes with blasts of compressed air, washed the chamber walls, and removed the debris. The men worked in rotations of 7 to 10 minutes in the chambers and 15 to 30 minutes outside.

Serum obtained on 1 August and 21 August 1973 was tested in 1979 by indirect immunofluorescence according to the method of McDade *et al.* (*3*), using as antigens agar-grown *Legionella* of four serogroups diluted in 0.5 percent yolk sac: strain Philadelphia 1 (serogroup 1), strain Togus 1 (serogroup 2), strain Bloomington 2 (serogroup 3), and strain Los Angeles 1 (serogroup 4) (*4*). Titers were expressed as the reciprocal of the greatest dilution with distinct fluorescence.

Serum from the acute and convalescent phases was available from nine patients and from the convalescent phase only from the tenth. Five showed fourfold or greater rises in titer to serogroup 1 antigen: from <32 to 256, <32 to 128, <32 to 128, 32 to 128, and <32 to 64; one of the five also showed a fourfold or greater rise to serogroup 4 antigen but none had rises in titer to antigens of serogroups 2 or 3. Four patients showed insignificant rises in titer to all four antigens; titers to serogroup 1 antigens were from 64 to 128, 64 to 64, and <32 to 32. The last patient had a single convalescent-phase titer of <32 to serogroup 1 antigen. Workers with or without demonstrated seroconversion were similar in age, length of employment, frequency of symptoms, admission and maximal temperatures, leukocyte count, and antibody titer during the acute phase.

Two distinct patterns of epidemic illness caused by *L. pneumophila* have been observed. Legionnaires' disease, as it occurred in Philadelphia in 1976 (*5*) and elsewhere (*6*), is a multisystem illness involving gastrointestinal tract, kidney, and central nervous system, but pneumonia is the most prominent feature in most cases. From 1 to 5 percent of persons exposed developed illness, with an incubation period that averages 5 to 6 days and ranges from 2 to 10 days. The case-fatality ratio has averaged 15 percent. In sharp contrast is Pontiac fever, which has been reported in a single outbreak that affected people who entered one building of the Oakland County Health Department in Pontiac, Michigan (*7*). In that outbreak, Pontiac fever was characterized by fever, headache, and myalgia. Cough, diarrhea, vomiting, chest pain, and sore throat were observed but were not prominent. No pneumonia was seen, although one patient had a pleural friction rub. The attack rate was 95 percent for exposed people. The incubation period averaged 36 hours and ranged from 24 to 48 hours, and none of 144 cases was fatal. In this report, the term legionellosis is used to describe any infection by *L. pneumophila*, but the terms Legionnaires' disease and Pontiac fever refer to the respective clinical and epidemiologic syndromes.

The James River outbreak reported here appears clinically and epidemiologically to resemble the Pontiac fever syndrome of legionellosis. The high attack rate, short incubation period, and absence of pneumonia are typical. The demonstration that five of the ten patients showed seroconversion and that three others had convalescent-phase titers of ≥64 confirms the association with *L. pneumophila*. Experience from other outbreaks indicates that seroconversion may be delayed as much as 6 weeks after onset of symptoms (*3*, *8*)—a possible explanation for the failure to demonstrate antibody titer rises for all ill workers, since serum specimens were not obtained after the 21st day of illness.

Evidence is accumulating that aerosolization of contaminated water may be a prime method for epidemic spread of *L. pneumophila* and that the organism may be particularly well adapted to warm water. On three occasions (including the previous episode of Pontiac fever), common-source outbreaks of legionellosis have occurred in such a pattern as to suggest that they were caused by "airborne spread" of droplet nuclei of aerosols generated by air-conditioning cooling towers (*9*) or evaporative condensers (*7*, *10*) documented to be contaminated with the organism. The temperature of water in cooling towers and evaporative condensers is usually 33° to 37°C, which corresponds to the observation that on agar *L. pneumophila* grows well at 37°C, but poorly or not at all at 25°, 30°, and 42°C. The organism also has been isolated repeatedly from water and riparian soil from a thermally polluted river (*11*) and can survive in water for more than a year (*12*). During the cleaning of the steam turbine condenser, all ten workers were exposed to water and debris, previously warmed to 36°C in the exchange of heat from the turbine, that

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was aerosolized in the pneumatic cleaning process. In this outbreak, however, the relative importance of direct contact or aerosolization in spread cannot be determined.

The earliest outbreak of legionellosis documented so far appeared to result from airborne spread from sites of excavation of soil (*13*), and sporadic cases of legionellosis have been associated with excavation and construction (*14*). It may be that *L. pneumophila* is basically a soil organism, the ecologic niche and epidemic potential of which are expanded by the increasing use of water in various heat-rejection systems.

What determines whether *L. pneumophila* will cause Legionnaires' disease or Pontiac fever is obscure. It is unlikely that dose of organism alone suffices to explain the difference, since one would expect the disease with the larger dose to have both the shorter incubation period and the more severe course. Perhaps Pontiac fever results from a large dose of nontoxigenic organisms, but no differences of obvious importance—including presence of toxins—have been found in laboratory testing of strains of *L. pneumophila* that caused Legionnaires' disease or Pontiac fever. Eickhoff has suggested that Pontiac fever results from exposure to a large number of dead *L. pneumophila* organisms (*6*). Although an attractive hypothesis, it does not explain the success in recovering live *L. pneumophila* from the lungs of guinea pigs that developed pneumonia following exposure in the building where the Pontiac fever epidemic occurred (*3*).

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Cycloheximide-Dependent Reversion of Human Cells Transformed by MSV and Chemical Carcinogen

Abstract. *The protein synthesis inhibitor cycloheximide, at a concentration of 0.08 microgram per milliliter, induced flat morphology within 24 to 48 hours and low saturation density in human osteosarcoma cells transformed by Kirsten murine sarcoma virus (Ki-MSV) or* N-*methyl*-N′-*nitro*-N-*nitrosoguanidine. Removal of the protein synthesis inhibitor caused both transformed cells to revert to the transformed phenotype. The demonstration of cell-surface antigens, cross-reacted with antiserums induced by extracts of both types of transformed human cells, was dependent on the presence or absence of cycloheximide in the culture medium. The results show that protein synthesis is required to maintain the transformed state in virally or chemically transformed human cells.*

Flat morphology and low saturation density of cells studied in vitro are often regarded as markers of normal behavior. Cells transformed by oncogenic DNA and RNA viruses or by chemical carcinogens can revert to variant forms in which their morphology and function resemble those of normal cells (*1*-*5*). In attempts to understand the basis for contact inhibition of mitosis, a number of agents, including inhibitors of protease and hyaluronidase enzymes, have been used to induce flat morphology in cultured transformed cells (*6*, *7*). However the mechanism of reversion is not known. Recently, Krzyzek *et al.* (*8*) observed that revertant subclones of cells infected with Rous sarcoma virus (RSV) contain as much sarcoma-specific RNA as the transformed cells from which they were derived. This suggests that reversion might be caused by a posttranscriptional restriction of the expression of the viral transforming gene or genes. Addition of protein synthesis inhibitors to rat kidney cells transformed by a temperature-sensitive mutant of RSV at a permissive temperature caused the cells to revert temporarily to normal phenotype (*9*). This finding implies that protein synthesis, presumably of an unstable product of the transforming gene of the temperature-sensitive virus, is required to maintain the transformed state in these infected cells at the permissive temperature. Recently a transformation-specific antigen from cells transformed by avian sarcoma virus has been identified (*10*).

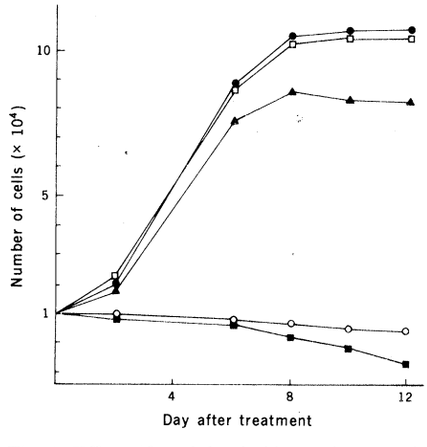

Fig. 1. Effect of cycloheximide on the growth of human osteosarcoma TE-85, clone F-5, cells (●) grown in EMEM plus 10 percent FBS medium without cycloheximide or in the medium containing cycloheximide at (□) 0.08 μg/ml, (▲) 0.1 μg/ml, (○) 1.0 μg/ml, or (■) 10 μg/ml.

In view of these results, we reasoned that inhibition of protein synthesis might affect the rate of growth and morphology of human cells transformed by oncogenic viruses. Further, chemically transformed human cells could also revert to an untransformed state by restricting the expression of the transforming gene or genes. In this report we present evidence that morphologic reversion and selective inhibition of growth can be observed in

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