

AN OUTBREAK OF PRIMARY PNEUMONIC TULAREMIA
ON MARTHA'S VINEYARD

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ABSTRACT

Background In the summer of 2000, an outbreak of primary pneumonic tularemia occurred on Martha's Vineyard, Massachusetts. The only previously reported outbreak of pneumonic tularemia in the United States also occurred on the island in 1978.

Methods We conducted a case-control study of adults with pneumonic tularemia and investigated the environment to identify risk factors for primary pneumonic tularemia. Patients with confirmed cases were residents of or visitors to Martha's Vineyard who had symptoms suggestive of primary pneumonic tularemia, were ill between May 15 and October 31, 2000, and had a positive laboratory test for tularemia. Controls were adults who had spent at least 15 days on Martha's Vineyard between May 15 and September 28, 2000.

Results We identified 15 patients with tularemia; 11 of these cases were primary pneumonic tularemia. *Francisella tularensis* type A was isolated from blood and lung tissue of the one man who died. Patients were more likely than controls to have used a lawn mower or brush cutter in the two weeks before the illness (odds ratio, 9.2; 95 percent confidence interval, 1.6 to 68.0) and during the summer (odds ratio, undefined; 95 percent confidence interval, 1.8 to ∞). Lawn mowing and brush cutting remained significant risk factors after adjustment for other potentially confounding variables. Only one patient reported being exposed to a rabbit while cutting brush. Of 40 trapped animals, 1 striped skunk and 1 Norway rat were seropositive for antibodies against *F. tularensis*.

Conclusions Study of this outbreak of primary pneumonic tularemia implicates lawn mowing and brush cutting as risk factors for this infection. (N Engl J Med 2001;345:1601-6.)

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TULAREMIA is a bacterial zoonosis caused by the small, gram-negative coccobacillus *Francisella tularensis*. The organism may be found in contaminated water or soil, infected ticks, wild and domestic animals, and decaying animal carcasses. Mammals can acquire the infection through arthropod bites, direct contact with infected tissues, inhalation, or ingestion; person-to-person transmission has not been documented.

After an incubation period of 3 to 5 days (range,

1 to 21), infection with *F. tularensis* can result in various clinical presentations, depending on the route of inoculation, the dose of the inoculum, and the virulence of the organism. Primary pneumonic tularemia results from the inhalation of *F. tularensis*; although uncommon, it is the most severe clinical form of tularemia, with a mortality rate as high as 60 percent in the absence of treatment.¹ The more virulent type A *F. tularensis* can be differentiated from the milder type B on the basis of biochemical reactions, virulence, and epidemiologic features.¹⁻⁴ Infection with type B rarely results in death, as evidenced by the mild clinical illness of patients who have pneumonic tularemia in Europe, where only type B causes disease in humans.⁵

Each year 100 to 200 cases of tularemia are reported in the United States. The disease occurs throughout the United States, but Arkansas, Missouri, and Oklahoma generally account for over half the cases.⁶ Cottontail rabbits from Arkansas and Missouri were introduced to Cape Cod and Martha's Vineyard, an island off the coast of Massachusetts, by game clubs in the late 1930s, and the first locally acquired cases of tularemia were reported shortly thereafter.^{7,8} Since 1975, Massachusetts has reported as many as seven cases of tularemia annually, with two or fewer cases reported on Martha's Vineyard except in 1978 and 2000. In 1978, the only previously reported cluster of primary pneumonic tularemia in the United States occurred on Martha's Vineyard, with seven cases among the residents of a single cottage. A definitive source was never identified; however, the investigators speculated that the inhabitants became infected after a wet dog aerosolized *F. tularensis* by shaking itself inside the cottage.⁹

In July 2000, five cases of primary pneumonic tularemia were reported on Martha's Vineyard, with dates of onset from May 30 to June 22. We began active surveillance for tularemia on Martha's Vineyard, and by late August, six additional cases were identified, including four cases of primary pneumonic tularemia. One patient cut brush over a rabbit, and six other pa-

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tients mowed lawns or cut brush within one week before becoming ill. Therefore, we conducted case-control and environmental studies to test the hypothesis that mowing lawns and cutting brush were risk factors for primary pneumonic tularemia.

METHODS

We identified cases of tularemia through active surveillance of health care providers on Martha's Vineyard. We also reviewed medical records with a discharge diagnosis of unspecified pneumonia (*International Classification of Diseases, 9th Revision, Clinical Modification*, code 486) from the Martha's Vineyard, Falmouth, Cape Cod, and Nantucket Cottage hospitals. The Massachusetts Department of Public Health enhanced its passive surveillance for tularemia statewide.

Epidemiologic Investigation

For surveillance purposes, a patient was defined as any resident of or visitor to Martha's Vineyard between May 15 and October 31, 2000, who had symptoms suggestive of tularemia (e.g., acute onset of fever with lymphadenopathy, malaise, skin ulcer, or cough) and a serum titer of anti-*F. tularensis* antibody of at least 1:128 on an agglutination assay,¹⁰ a positive result for *F. tularensis* antigen on direct fluorescence antibody testing, or a positive culture for *F. tularensis*.¹¹ For the case-control study, a patient was defined as any person 18 years of age or older who met the case definition and who had clinical features of primary pneumonia at presentation. Through random-digit telephone dialing to Martha's Vineyard residents, we enrolled 100 control subjects who were at least 18 years old and who had spent at least 15 days on Martha's Vineyard between May 15 and the time they were interviewed in September 2000.

We conducted interviews from September 5 to 28, 2000, using a questionnaire to obtain the following information for each subject: occupation, landscaping activities and exposure to landscaping products, exposure to animals and arthropods, recreational activities, average amount of time spent outdoors each day, and history of tularemia, smoking, asthma, and pneumonia. We obtained information about exposure to possible risk factors between May 15 and the time of the interview, and during the two weeks before illness in the case of the patients and the two weeks before the interview in the case of the controls. One patient became ill in October and was interviewed shortly thereafter.

A human-subjects coordinator for the Centers for Disease Control and Prevention reviewed the study plan and determined that the study represented a public health response that did not require additional ethics review. The study plan received expedited approval from the Massachusetts Department of Public Health Human Subjects Committee.

Environmental Investigation

We visited the suspected site of exposure of each patient and the 1978 outbreak site. At three sites we recreated possible activities that led to exposure, such as mowing the lawn and cutting weeds ("weed whacking"), and collected air samples using personal air samplers attached to the lawn mower and to the person who used the mowing equipment. Investigators wore protective gear while performing these activities. Samples of grass clippings, water, and soil were also collected. Small mammals were trapped at five properties, and we obtained serum samples from all dogs that lived at suspected sites of exposure. Samples of mammal tissue were examined by direct-fluorescence antibody staining, and mammal serum was tested for antibodies with use of an agglutination assay. Samples of air, grass, water, soil, and animal tissue were cultured for *F. tularensis*.

Statistical Analysis

We used Epi Info version 6¹² to calculate crude odds ratios and Cornfield's 95 percent confidence intervals for categorical variables.

When the odds ratio was undefined, the lower confidence limit was calculated with the use of StatXact software.¹³ Continuous variables were tested with use of the Mann-Whitney U test. Using SAS software,¹⁴ we constructed a multivariate model with variables referring to the two weeks before illness or interview that were significantly associated with illness or that approached statistical significance on univariate analysis and were biologically plausible risk factors.

RESULTS

Characteristics of the Patients

We identified 15 patients with confirmed cases of tularemia: 11 patients had primary pneumonic tularemia, 2 had ulceroglandular disease (fever with skin ulcers and lymphadenopathy), and 2 had fever and malaise but no localizing signs (Fig. 1). All but one of the patients were male; the median age was 43 years (range, 13 to 59). Examination of paired serum samples in eight patients showed that the serum titer increased by a factor of four, with at least one measurement of at least 1:128. Analysis of single serum samples in six patients showed a titer of at least 1:128. In addition, *F. tularensis* was cultured from blood and lung tissue of a 43-year-old man who died of primary pneumonic tularemia. He delayed seeking medical care for his illness, which began within one week after he mowed a lawn. The culture isolates were identified as type A *F. tularensis* biovar tularensis and had growth, biochemical, and antigenic profiles typical of those of other naturally occurring isolates of *F. tularensis*.

The residences of the patients were located throughout Martha's Vineyard; however, all but one of the properties where patients had mowed the lawn or cut brush before becoming ill were along the southern coast of the island, as was the site of the 1978 outbreak. The patient who mowed the lawn at the property that was not on the southern coast had also mowed lawns at two properties along the southern coast. No patients were identified from Cape Cod or Nantucket.

Case-Control Study

Ten patients met the case definition for the case-control study (1 of the 11 patients with primary pneumonic tularemia was 13 years old and was excluded because controls had to be 18 years old or older). Of 100 controls, 1 reported having had tularemia in the past and was excluded from the analysis. Table 1 shows the frequency of selected possible risk factors for primary pneumonic tularemia among the patients and controls. In contrast to the control subjects, all patients were male and half were professional landscapers (odds ratio, 32.0; 95 percent confidence interval, 4.6 to 257). In the two weeks before becoming ill (or being interviewed, in the case of controls), 80 percent of patients (8 of 10) had used a lawn mower or brush cutter, as compared with 30 percent of controls (odds ratio, 9.2; 95 percent confidence interval, 1.6 to 68.0). Of these eight, four patients mowed four or five days before they became ill, two were professional landscap-

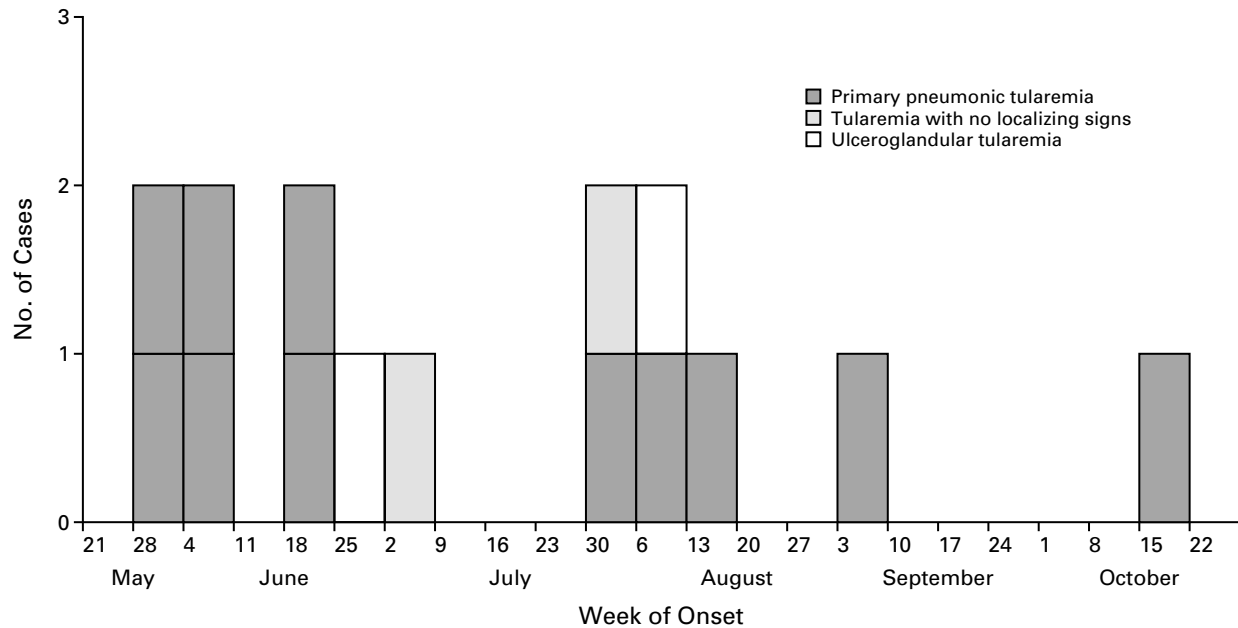


Figure 1. Cases of Primary Pneumonic Tularemia, Tularemia with No Localizing Signs, and Ulceroglandular Tularemia on Martha's Vineyard, May 21 through October 28, 2000, According to the Week of Onset of Illness.

TABLE 1. FREQUENCY OF SELECTED RISK FACTORS FOR PRIMARY PNEUMONIC TULAREMIA.

RISK FACTOR*	PERIOD ANALYZED†	PATIENTS (N=10)	CONTROLS (N=99)	ODDS RATIO (95% CI)‡
		no. (%)		
Male sex		10 (100)	41 (41)	— (2.9 to ∞)
Worked as landscaper		5 (50)	3 (3)	32.0 (4.6 to 257)
Used lawn mower or brush cutter	2 Wk before illness or control period	8 (80)	30 (30)	9.2 (1.6 to 68.0)
Used lawn mower or brush cutter	Summer	10 (100)	48 (48)	— (1.8 to ∞)
Cut brush or mowed over rabbit	2 Wk before illness or control period	1 (10)	0	— (0.3 to ∞)
Worked with bark chips	2 Wk before illness or control period	3 (30)	5 (5)	8.1 (1.2 to 53.7)
Worked with weed whacker	Summer	7 (70)	27 (27)	6.2 (1.3 to 33.6)
Worked with lumber	Summer	7 (70)	29 (29)	5.6 (1.2 to 30.3)
Owned a dog on Martha's Vineyard		8 (80)	44 (44)	5.0 (0.9 to 36.6)
Smoked	2 Wk before illness or control period	5 (50)	18 (18)	4.5 (1.0 to 20.9)
Saw dead rabbit on property	2 Wk before illness or control period	2 (20)	11 (11)	2.3 (0.3 to 14.9)
Found ticks crawling on person	Summer	8 (80)	55 (56)	3.2 (0.6 to 23.4)

*All other risk factors (not shown) were not significantly associated with primary pneumonic tularemia.

†Summer was defined as the period from May 15 to the time of interview. The control period refers to the two weeks before controls were interviewed.

‡The dashes indicate that the odds ratio was undefined. CI denotes confidence interval.

ers who mowed daily, and two had mowed sometime within the week before their illness. All patients had used a lawn mower or brush cutter at some time during the summer, as compared with 48 percent of the controls (odds ratio, undefined; 95 percent confidence interval, 1.8 to ∞).

Only one patient remembered being exposed to a dead rabbit, and the exposure occurred while he was cutting brush. Patients were more likely than controls to have worked with bark chips in the two weeks preceding illness (odds ratio, 8.1; 95 percent confidence interval, 1.2 to 53.7), although only three patients had worked with bark chips. Patients were significantly more likely than controls to have worked with a weed whacker (odds ratio, 6.2; 95 percent confidence interval, 1.3 to 33.6) or with lumber (odds ratio, 5.6; 95 percent confidence interval, 1.2 to 30.3) during the summer, but neither of these activities performed within the two weeks before illness was a significant risk factor for primary pneumonic tularemia. Both dog ownership (odds ratio, 5.0; 95 percent confidence interval, 0.9 to 36.6) and smoking (odds ratio, 4.5; 95 percent confidence interval, 1.0 to 20.9) were more frequently reported by patients than controls. There was no significant difference in the proportions of patients and controls who were exposed to rabbits or ticks. Patients spent significantly more time outdoors than did controls (mean, 8.4 vs. 5.2 hours per day; $P=0.01$).

As Table 2 shows, after adjustment for the presence or absence of a recent history of working with bark chips, average time spent outdoors, smoking status, and dog-ownership status, patients with primary pneumonic tularemia were more likely than controls to have used a lawn mower or brush cutter in the two weeks before illness (odds ratio, 6.7; 95 percent confidence interval, 1.1 to 39.9). We also used backward, forward,

and stepwise selection procedures to obtain a parsimonious model that considered the effects of all variables. This parsimonious model retained only two variables: lawn mowing (odds ratio, 9.1; 95 percent confidence interval, 1.7 to 47.6) and working with bark chips (odds ratio, 7.8; 95 percent confidence interval, 1.3 to 48.2).

Environmental Investigation

Cultures of three lawn-mower filters, 15 samples of cut grass, 11 air samples, 3 samples of raw water, and 9 samples of soil and mulch were all negative for *F. tularensis*.

We set traps for a total of 442 trap-nights, with a success rate of 9.3 percent. Of 40 animals trapped, 2 were seropositive for antibodies against *F. tularensis*: a striped skunk (*Mephitis mephitis*) that was trapped where the patient who died had mowed before becoming ill and a Norway rat (*Rattus norvegicus*) that was trapped where another patient had mowed. Other species trapped were a house mouse (*Mus musculus*), white-footed mice (*Peromyscus leucopus*), an eastern cottontail rabbit (*Sylvilagus floridanus*), and meadow voles (*Microtus pennsylvanicus*). Direct fluorescence antibody tests and cultures of mammal tissues were negative. All five dogs that were tested were seronegative. Of seven animals trapped at the site of the 1978 outbreak, none were seropositive.

DISCUSSION

In this outbreak of primary pneumonic tularemia, lawn mowing and brush cutting were risk factors. Clinicians should be aware that primary pneumonic tularemia can occur after activities that aerosolize the organism from the environment. This is particularly important, since these are such common outdoor activities; 30 percent of the control subjects in the study reported mowing or cutting brush in the two weeks before being interviewed, and 48 percent reported engaging in these activities at some time during the summer.

Primary pneumonic tularemia has been reported in persons who disturbed the carcasses of infected rabbits,^{15,16} in European farmers who worked with contaminated hay,⁵ in two boys who mowed over a rabbit,¹⁷ and in a man who used a brush cutter to clear a lot where many rabbits lived.¹⁸ Lawn mowing has been epidemiologically implicated in an outbreak of psittacosis, in which patients were no more likely than controls to keep, handle, or feed birds but were more likely to have mowed lawns.¹⁹ The authors hypothesized that lawn mowing aerosolized *Chlamydia psittaci* shed by sick birds. Rodents can excrete viable *F. tularensis* in both urine and feces,^{20,21} and we propose that on Martha's Vineyard, *F. tularensis* was shed in animal excreta, persisted in the environment, and infected people after being mechanically aerosolized and inhaled. Although one patient did cut brush over a

TABLE 2. LOGISTIC-REGRESSION MODEL OF RISK FACTORS FOR PRIMARY PNEUMONIC TULAREMIA.

POTENTIAL RISK FACTOR	ADJUSTED ODDS RATIO (95% CI)*	P VALUE
Used lawn mower or brush cutter	6.7 (1.1–39.9)	0.04
Worked with bark chips	5.1 (0.7–39.8)	0.12
Average no. of hours spent outside per day	1.1 (0.8–1.4)†	0.59
Smoked	3.0 (0.6–14.7)	0.18
Owned a dog on Martha's Vineyard	2.4 (0.4–14.4)	0.33

*The model included variables that were significantly associated with illness or approached significance on univariate analysis and were biologically plausible risk factors. Every variable in the odds ratio was adjusted for the other listed variables. All variables refer to the two weeks before illness or interview. CI denotes confidence interval.

†The odds ratio is for each additional hour spent outside.

rabbit, this outbreak indicates that people can acquire primary pneumonic tularemia from mowing in the absence of any obvious exposure to infected animal tissue.

Exposure to cigarette smoke increases the risk and severity of a variety of pulmonary infections.²² In our study, smoking was associated with a risk of illness on univariate analysis; however, this finding was not statistically significant after adjustment for other variables. This finding may have been due to the low statistical power of our analysis, related to the small number of patients. Similarly, although dog ownership was reported by 80 percent of patients, dog ownership was not significantly associated with illness after adjustment for other variables.

Although *F. tularensis* does not form spores, it can survive in water, soil, and decaying animal carcasses.⁶ The organism persists in water and mud for as long as 14 weeks,²¹ in straw for 6 months,³ and in oats for 4 months.²³ We were unsuccessful in culturing *F. tularensis* from environmental samples, but the optimal methods of collecting and isolating the organism from grass and air have not been determined. In addition, we may have collected samples under environmental conditions that differed from those existing when the patients were exposed. We did identify a seropositive skunk and a seropositive rat on properties where patients had mowed the lawn before becoming ill. Natural infection with *F. tularensis* has been reported in skunks and rats,^{24,25} but whether either of these species contributes to the maintenance and transmission of *F. tularensis* on Martha's Vineyard could not be determined. *Dermacentor variabilis*, the American dog tick, is a recognized reservoir and vector of tularemia,¹¹ is present throughout Martha's Vineyard, and feeds on small mammals.²⁶ The contribution of ticks to environmental contamination with *F. tularensis* is unclear.

The probable exposure sites of patients in this outbreak and in the 1978 outbreak were concentrated along the island's southern coast. Such variables as proximity to brackish ponds and the level of wind, humidity, and precipitation arising from the sea might influence the presence and persistence of *F. tularensis* in the environment.

One possible means of preventing primary pneumonic tularemia would be to minimize exposure to aerosolized bacteria during landscaping activities by surveying the area for carcasses or excreta before mowing. The use of protective skirting and collection bags on lawn mowers might help reduce the operators' exposure to aerosols. Little is known about the degree of protection against aerosolized *F. tularensis* afforded by respirators. Respirators certified by the National Institute for Occupational Safety and Health that have a rating of 95 remove 95 percent of particulate matter with a diameter of 0.3 μm from the air. *F. tularensis* measures 0.2 μm by 0.2 to 0.7 μm ,⁶ but it might be aerosolized in larger water droplets or on particles of

grass or soil. Suggestions for respiratory protection could be extrapolated from recommendations for other infectious agents including *Mycobacterium tuberculosis*,²⁷ Sin Nombre virus,²⁸ and *Histoplasma capsulatum*.²⁹

There are several possible limitations to our study. Patients and controls may have had difficulty recalling exposures that occurred one to three months before the interview. We tried to reduce recall bias by comparing exposures that had occurred in the two weeks before the interview in the case of controls with exposures that had occurred in the two weeks before the onset of illness in the case of patients. Using a lawn mower or brush cutter was the only type of exposure significantly associated with illness both in the two-week period and at any time during the summer. Controls were not tested serologically, and some may have had an inapparent infection. However, this factor would result in nondifferential misclassification and would bias our results toward the null.

People who mow lawns or cut brush in areas where tularemia is endemic may be at increased risk for primary pneumonic tularemia. Health care providers should consider the possibility of tularemia in patients in whom fever or pneumonia develops after such activities in areas where the disease is endemic.

We are indebted to the residents and the medical community of Martha's Vineyard for their cooperation; to Dr. Alfred DeMaria, Jr., Susan Soliva, Tracy LaPorte, and the many interviewers from the Massachusetts Department of Public Health for their contributions; to Dr. May Chu, Leon Carter, Brook Yockey, Todd Deppe, Dr. Brad Biggerstaff, Dr. Richard Meyer, and William Morrill from the Centers for Disease Control and Prevention for their assistance in this investigation; to Dr. Chris Andry, Dr. Ola El-Zammar, Don Schwartz, and Dr. Dan Shapiro for obtaining and forwarding tissue samples from the Boston Medical Center; and to the staff of the Connecticut, New Jersey, and New Hampshire Departments of Public Health.

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