

Cases of Cat-Associated Human Plague in the Western US, 1977–1998

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Exposure to cats infected with *Yersinia pestis* is a recently recognized risk for human plague in the US. Twenty-three cases of cat-associated human plague (5 of which were fatal) occurred in 8 western states from 1977 through 1998, which represent 7.7% of the total 297 cases reported in that period. Bites, scratches, or other contact with infectious materials while handling infected cats resulted in 17 cases of bubonic plague, 1 case of primary septicemic plague, and 5 cases of primary pneumonic plague. The 5 fatal cases were associated with misdiagnosis or delays in seeking treatment, which resulted in overwhelming infection and various manifestations of the systemic inflammatory response syndrome. Unlike infections acquired by flea bites, the occurrence of cat-associated human plague did not increase significantly during summer months. Plague epizootics in rodents also were observed less frequently at exposure sites for cases of cat-associated human plague than at exposure sites for other cases. The risk of cat-associated human plague is likely to increase as residential development continues in areas where plague foci exist in the western US. Enhanced awareness is needed for prompt diagnosis and treatment.

Plague is a bacterial zoonosis caused by infection with *Yersinia pestis*, a gram-negative coccobacillus. Active foci exist in wild rodent and flea populations in many regions of the world, including the western US (where the disease probably was first introduced in 1899–1900 by rat- and flea-infested ships) [1–3]. To date, surveillance programs have identified evidence of *Y. pestis* infection in mammal or flea samples collected from 17 western states (K.L.G., Plague Section, Centers for Disease Control and Prevention [CDC], unpublished data). A total of 297 human cases of plague were identified in 13 of these states from 1977 through 1998.

Most cases of human plague in the US result from bites by infectious fleas, but nearly 20% of all cases with identified modes of transmission are acquired through contact with *Y. pestis*-infected mammals, including domestic cats (*Felis catus*) [4–8]. The first well-documented case of cat-associated human plague in the US occurred in 1977 in Arizona [7]. Since then, 22 further cases have been identified (total of 23 cases in the 22-year period from 1977 through 1998), which suggests that exposure to infected cats is a significant plague risk in the US. Cases of cat-associated human plague are noteworthy because

they have a broad range of clinical presentations (including primary pneumonic plague) and unusual circumstances of exposure. Further, cases appear to be largely restricted to the US or have yet to be recognized routinely in other countries. Thornton et al. [9] reported a single case from South Africa, and Simpson [10] reported another likely case from that country. Mall and O'Leary [11] also presented anecdotal evidence of cat-associated human plague in Argentina and Brazil.

The purposes of this article are to review the epidemiological, ecological, and clinical aspects of the 23 cases of cat-associated human plague identified to date in the US, to provide detailed discussions of 4 recently identified cases of cat-associated human plague, and to discuss the risks cats may pose to their owners, veterinary staff, and other persons. Although a small number of cases of cat-associated human plague have been reported by other researchers, this article is the first comprehensive review of this topic [7, 12–16]. The review is intended to increase recognition and understanding of the problem and thereby reduce further preventable morbidity and deaths.

Methods

Under the provisions of the International Health Regulations for quarantinable diseases (plague, yellow fever, and cholera), all cases of plague must be investigated and reported to the World Health Organization [8]. Case investigations in the US involve the cooperative efforts of the CDC and state and local public health agencies. Records of these investigations are maintained in the Plague Section at the CDC. Our study included all cases of cat-associated human plague in the CDC records that met the following

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Table 1. Summary of data on cases of cat-associated human plague in the US, 1977–1998.

Case	State, county	Date of onset	Age (y), sex, ethnicity of patient	Outcome	Clinical presentation	Type of exposure
1	AZ, Coconino	6/13/77	23, F, W	Recovered	Bubonic (cervical)	Face-to-face contact
2	NM, Cibola	9/6/77	6, M, W	Recovered	Bubonic (axillary) ^a	Bite or scratch
3	NV, Douglas	12/25/78	77, F, W	Died	Septicemic	Cared for sick cat
4	CA, El Dorado	10/2/80	47, F, W	Died	Pneumonic	Inhalation
5	CO, Jefferson	4/15/81	49, M, W	Recovered	Bubonic (axillary)	Bite (veterinarian)
6	WY, Laramie	6/22/82	22, F, W	Recovered	Pneumonic	Inhalation (veterinary technician)
7	OR, Jefferson	8/15/82	10, F, NA	Recovered	Bubonic (axillary)	Scratched by cat that presumably had <i>Yersinia pestis</i> on its claws [8]
8	NM, McKinley	10/2/83	14, M, H	Recovered	Bubonic (axillary)	Handled sick cat
9	NM, McKinley	3/26/84	11, M, NA	Recovered	Bubonic (axillary)	Cared for sick cat
10	CA, Los Angeles	3/30/84	35, M, W	Recovered	Bubonic (axillary)	Cared for sick cat
11	CA, Kern	5/3/84	24, M, W	Died	Bubonic (axillary)	Buried dead cat that had been sick
12	NM, Rio Arriba	3/28/87	27, M, W	Recovered	Bubonic (axillary)	Bite
13	AZ, Apache	11/16/87	9, M, NA	Recovered	Bubonic (axillary)	Handled and slept with sick cat
14	CO, Montrose	10/19/91	41, F, W	Recovered	Bubonic (axillary)	Cared for sick cat (veterinary technician)
15	NM, San Miguel	7/13/92	28, M, H	Recovered	Bubonic (axillary)	Bite
16	CO, Chaffee	8/23/92	31, M, W	Died	Pneumonic	Inhalation; face-to-face contact while retrieving sick cat from under house
17	NM, Sandoval	3/13/93	44, M, W	Recovered	Bubonic (axillary and epitrochlear)	Scratch
18	CO, Boulder	5/19/93	31, F, W	Recovered	Pneumonic	Inhalation (veterinarian)
19	UT, Box Elder	7/6/94	15, F, W	Recovered	Pneumonic	Inhalation; face-to-face contact
20	CO, Delta	8/17/96	16, F, W	Died	Bubonic (axillary)	Cared for sick cat with submandibular abscess
21	CA, Modoc	8/7/97	58, M, W	Recovered	Bubonic (axillary)	Scratch (veterinarian)
22	NM, Santa Fe	5/19/98	45, F, W	Recovered	Bubonic (axillary)	Bite (veterinarian)
23	CO, Archuleta	6/10/98	39, F, W	Recovered	Bubonic (axillary)	Cared for sick cat

NOTE. W, white; H, Hispanic; NA, Native American.

^a Bilateral axillary lymphadenopathy.

2 criteria: development of clinical plague within 10 days after a cat considered to be infected with *Y. pestis* was handled (22 cases) or after a scratch by a cat believed to have had viable *Y. pestis* on its claws (case 7) and epidemiological evidence suggesting that other exposures were unlikely [12].

All case records were reviewed to identify dates of onset of illness, the patient's age, sex, ethnicity, the primary clinical presentation, secondary complications and other clinical manifestations, the outcome of the illness (recovered or fatal), the likely mode of transmission, and information on exposure sites for patients and the cats they had handled. Additional data were gathered from reports of on-site environmental investigations, including whether plague epizootics (outbreaks in susceptible species of rodents) had occurred at the exposure sites. Plague epizootics were considered to have occurred when *Y. pestis* infection was identified in typical epizootic hosts (ground squirrels, prairie dogs, chipmunks, or wood rats) or their fleas or when observers noted inactive burrows or nests of these animals [1]. Certain information for 7 of the 23 cases has been published previously in isolated case reports or has been discussed briefly by other investigators [7, 12–16]. We include here selected data from the CDC records on these 7 cases for the sake of completeness and to present information absent from the published reports.

Results

Evidence for Y. pestis in cats associated with cases of human plague. Twenty-two of the 23 cats associated with the human cases of plague described in this review were considered to have

had plague: *Y. pestis* was isolated from 5 cats (human cases 1, 2, 3, 4, and 19); 5 culture-negative cats were strongly seropositive by passive hemagglutination assays (titers to the F1 surface antigen of *Y. pestis* ≥ 1024 ; 4 cats were positive for *Y. pestis* by fluorescent antibody assays that used a rabbit polyclonal antibody that was specific for F1 antigen and conjugated to fluorescein isothiocyanate; and 8 cats had disappeared or had been killed before the arrival of investigators (human cases 9, 10, 11, 13, 14, 15, 16, and 21). Each of the 8 missing animals, however, had exhibited signs and symptoms of illness strongly suggestive of plague. The remaining cat (human case 7) did not exhibit evidence of *Y. pestis* infection but was thought to have had *Y. pestis* on its claws as a result of fighting with a cat that had a *Y. pestis*-positive cervical abscess [12].

Case Summaries

The 23 cat-associated cases of human plague identified in the US are summarized in table 1. These cases occurred in 8 western states, including New Mexico (7 cases), Colorado (6), California (4), Arizona (2), Nevada (1), Oregon (1), Utah (1), and Wyoming (1). Illness onset was in every month except January and February; there was no clear increase in incidence during the summer months of June, July, and August. The median age of the patients was 28 years (range, 6–77 years) (table 1). Eighteen patients were white, 3 were Native American, and 2 were Hispanic; 12 (52.2%) of the 23 were male. Seventeen patients

(73.9%) presented with manifestations of bubonic plague; 16 of these patients had axillary buboes, and 1 had a cervical bubo. Only 1 patient (4.3%) presented with primary septicemic plague. Five patients (21.7%) developed primary pneumonic plague, apparently as a result of inhaling infectious materials from cats with pneumonic plague or oral lesions (table 1). Of the 18 patients presenting with bubonic or septicemic plague, 8 had incurred antecedent scratches or bites, including 1 patient (case 7) who was scratched near her left nipple by a cat while intervening in a fight between this animal and another cat that had a *Y. pestis*-infected abscess on its neck (table 1) [12]. The remaining 10 patients who developed either septicemic plague (1 case) or bubonic plague (9 cases) had potential exposures while examining or caring for ill cats, sleeping with an ill cat, or burying a dead cat (table 1).

We compared the 23 patients with cat-associated human plague with the remaining 274 patients whose cases occurred during the same period (1977–1998) with respect to the following data: the patients' sex and ethnicity and the state of exposure, initial clinical presentation, outcome (fatal or recovered), bubo location (if present), and likely route of exposure (inhalation, direct contact, or not determined). Probable modes of transmission were determined for 228 of the 274 cases without known infective cat exposures. Only 2 of these 228 patients were thought to have acquired plague through inhalation of infectious materials (unknown sources for these 2 cases), compared with 5 of the 23 patients with cat-associated cases ($P < .0001$; Fisher's exact test). As expected, the proportion of patients who developed primary pneumonic plague also was higher among patients with cat-associated cases than among other patients (5 of 23 vs. 2 of 274, respectively; $P < .0001$; 2-tailed Fisher's exact test). Axillary buboes were observed much more frequently in cat-associated cases of bubonic plague (16 of 17 cases) than in other cases (76 of 210 cases with identified bubo locations; $P < .0001$; χ^2 test). None of the cat-associated cases included femoral or inguinal buboes, which occurred in most patients (52.9%) who acquired plague from other sources. Significant differences could not be demonstrated between cat-associated cases and other cases with respect to the relative proportion of cases of bubonic plague and septicemic plague, gender, ethnicity, state of exposure, and outcomes ($P > .05$; χ^2 or Fisher's exact tests, as appropriate). Incubation periods for cat-associated cases were similar in range (2–10 days) to those that have been reported for plague cases in general [17], but these cases could not be compared directly with most cases in our files because of the difficulties in determining precise exposure times for cases associated with flea bites or the lack of sufficiently detailed information in the case files.

Ecological Investigations

The methods used in ecological investigations and the intensity of sampling at sites where cats were believed to have ac-

quired infection varied between cases. However, in all but 2 cases (14 and 18), blood samples for serology were obtained from pet dogs or cats, rodents, rabbits, or wild carnivores, and attempts were made to collect fleas from trapped rodents or rabbits and from rodent burrows or nests. At 6 sites, *Y. pestis* infection was identified in various highly susceptible epizootic rodent hosts (or their fleas), including ground squirrels, prairie dogs, chipmunks, or wood rats (cases 4, 7, 8, 10, 16, and 18). Inactive rodent burrows suggestive of epizootics were noted at another 5 sites (cases 6, 9, 11, 14, and 20). On the basis of these observations, plague epizootics were thought to have occurred at only 11 (47.8%) of the 23 sites where cats became infected with *Y. pestis* before passing their infections on to humans. By comparison, similar evidence of epizootic activity was observed at 188 (68.6%) of the 274 exposure sites for human cases that were not associated with cats but had occurred during the same period (1977–1998; $P = .0417$; χ^2 test). *Y. pestis* infection also was identified at 2 sites in native mice (*Peromyscus* species), which often are considered to be partially resistant to plague (enzootic or maintenance hosts), and in a *Peromyscus*-infesting flea (*Aetheca wagneri*) at another site [1]. In addition to infected rodents, seropositive samples were obtained at 7 sites from dogs and at 2 sites from coyotes.

Description of Selected Cases

Because there is not space here to describe each of the 23 cases of cat-associated human plague in detail, we have selected 4 recent cases as instructive examples. Three of these patients presented with bubonic plague (cases 17, 21, and 23), and 1 presented with primary pneumonic plague (case 18).

Case 17: bubonic plague with axillary lymphadenopathy. This case occurred in a patient whose cat was treated by a veterinarian for an ulcerative oral lesion. Plague was not suspected, and the cat was treated with an oral tetracycline formulation. On the following day, the patient, who had undergone splenectomy, was scratched on the left arm while attempting to medicate the cat. Three days later, he had fatigue, prostration, diffuse myalgia, low-grade fever, nausea, and an episode of vomiting. The patient initially attributed these symptoms to chemotherapy (vinblastine sulfate and daily doses of prednisone) for idiopathic thrombocytopenic purpura. He also developed redness, induration, and sensitivity to touch in his upper left arm.

Two days after the onset of illness, he presented to an emergency department with fever, an enlarged left axillary lymph node (1 cm in diameter), and swelling of the distal epitrochlear node. Laboratory tests indicated an elevated leukocyte count (18,300/mm³) with a high proportion of immature neutrophils (27% band forms). The initial diagnosis was cellulitis with lymphangitis caused by a cat scratch and a possible relapse of idiopathic thrombocytopenic purpura. He was hospitalized and treated with ceftriaxone, an increased dosage of prednisone,

and a second dose of vinblastine sulfate. Four days after the onset of illness, his temperature had returned to normal, and cellulitis with lymphangitis had begun to resolve. On the following day, culture of blood obtained at admission yielded *Y. pestis*. Because ceftriaxone and other β -lactam antibiotics are not considered effective against *Y. pestis* in vivo, the patient's treatment was changed to intravenous gentamicin and oral doxycycline. He was released from the hospital after 6 days and recovered without complications.

The patient's mobile home was situated among other widely spaced (100–300 m) homesites in a semiarid grassland habitat containing scattered juniper trees, cholla, and 4-winged salt-bush. His homesite had numerous piles of lumber, scrap metal, and other potential rodent harborage, as did other nearby residences. None of the live rodents captured at the site was seropositive, and fleas infesting these animals were negative for *Y. pestis* by mouse inoculation assay. *Y. pestis* was, however, identified in 2 white-throated wood rat carcasses collected within 100 m of the patient's home. A flea (*Orchopeas sexdentatus*) recovered from 1 of these carcasses was positive for *Y. pestis* by mouse inoculation assay. Investigators also recovered 3 species of fleas from a wood rat nest located <10 m from the patient's home. A pool of 1 of these fleas (*Megarathroglossus divisus*) was found to be infected with *Y. pestis* by mouse inoculation assay. These findings indicated that an epizootic had occurred among the local wood rats, and it is likely that the cat became infected through contact with these animals. Abandoned rock squirrel burrows (20–25 burrows) were noted in an arroyo located about 100 m from the patient's house, which suggests that these animals also were affected by the epizootic.

Case 21: bubonic plague with axillary lymphadenopathy. This case occurred in a veterinarian who visited a ranch where he was scratched while examining a moribund cat that had a submandibular abscess, rectal temperature of 35.0°C, and dehydration. Two days later, the veterinarian developed fever (temperature, 40.0°C) and a swollen and tender left axillary lymph node (5 cm in diameter). Upon consulting a physician, he was noted to have hypotension (blood pressure, 80/40 mm Hg; pulse rate, 48) and leukocytosis (leukocyte count, 31,000/mm³); he was hospitalized and treated with intravenous ceftriaxone. Tetracycline therapy was begun 2 days after admission and continued after his discharge on the same day. Although this patient recovered completely, he was dissatisfied with the unspecified diagnosis and consulted a second physician who obtained a serum sample about 3 weeks after the onset of illness. The sample was forwarded to the California Department of Health Service's Microbial Diseases Laboratory (Berkeley) and the CDC, where it was reported to be positive for *Y. pestis* at a titer of 256 in passive hemagglutination assays. Six weeks later, the patient's titer had increased 4-fold to 1024, which confirmed that his illness was plague [18].

Several weeks later, investigators visited the site where the cat had lived but found no evidence of epizootic activity. Res-

idents did indicate, however, that another cat from this site had become ill and died with symptoms resembling those displayed by the cat that scratched the patient. The carcasses of both cats had been disposed of many weeks earlier and were unavailable for analysis.

Case 23: bubonic plague with axillary lymphadenopathy. This case occurred in a patient who probably became infected while cleaning a draining abscess on the head of her cat. The cat, which had been ill for many days, was taken to a veterinary clinic where it died. The veterinarian considered plague as a possible diagnosis but decided against it because the abscess was located on the top of the cat's head rather than in the submandibular lymph nodes, which is more typical for cats infected with *Y. pestis*. Two days after last contact with the cat, the patient developed aching and throbbing in the left arm. Over the next 3 days, her symptoms increased, and she had increasingly severe left axillary pain, fever (temperature as high as 40.0°C), chills, and myalgia. On day 4 after the onset of illness, she presented to an emergency department complaining of severe left axillary, chest, and back pain, an enlarged left axillary lymph node (2 cm in diameter), fever, chills, diffuse myalgias, and persistent nausea and vomiting without diarrhea. Her temperature was 38.2°C, and her chest radiogram was clear. Blood was collected for culture, and seropurulent fluid, which contained some WBCs but no obvious microorganisms, was aspirated from the left axillary region. Her WBC count was 8930/mm³ with a left shift. The patient mentioned the veterinarian's concern that her cat's illness might have been plague, and she was treated with ampicillin and gentamicin, along with supportive therapy.

On day 6 after the onset of illness, the patient was transferred to a larger health care facility with a suspected diagnosis of *Staphylococcus*-related cellulitis and necrotizing fasciitis; treatment with gentamicin was discontinued, and streptomycin and tobramycin therapy was initiated. Culture of blood obtained on day 4 after the onset of illness subsequently yielded a gram-negative rod that was confirmed to be *Y. pestis*. The patient was discharged after 3 days and recovered completely.

She lived in a mobile home park in a semirural area. Her cat reportedly hunted small rodents and was allowed to roam freely in a rocky canyon and other nearby natural areas. An ecological investigation did not identify signs of epizootic plague activity. Although numerous pet cats roamed the area, only the patient's cat was reported to have been ill. Tissue samples obtained from the exhumed carcass of this animal were positive for *Y. pestis* by fluorescent antibody assay.

Case 18: primary pneumonic plague. This case occurred in a veterinarian who examined a severely ill cat that had a small lesion on its lower lip and was febrile and dehydrated. Plague was not considered as a possible diagnosis for the animal, which died several hours after the examination. Four days later, the veterinarian developed fever, myalgia, and malaise. On the following day, her condition worsened, and she sought emergency

Table 2. Summary of data on fatal cases of cat-associated human plague.

Case	Clinical presentation	Initial diagnosis (place and time of diagnosis)	Method of diagnosis of <i>Yersinia pestis</i> infection (time of diagnosis)	Antimicrobial therapy recommended	Interval between start of appropriate therapy and diagnosis	Complications, reference
3	Septicemic (primary)	Asthmatic attack, chronic obstructive pulmonary disease, sepsis (ER)	Bacterial culture (PM)	Gentamicin	8 h before death and PM diagnosis	Respiratory failure, acidosis, hypoxemia, and irreversible shock complicated by chronic obstructive pulmonary disease
4	Pneumonic (primary)	Urinary tract infection (outpatient, day 1 after onset); pneumonia (ER, day 3 after onset)	Bacterial culture (PM)	Tetracycline	3 d before death and PM diagnosis (during outpatient visit); might not have received proper doses because of vomiting	Severe hypoxemia, metabolic acidosis, and heart failure [10]
11	Bubonic (axillary)	Cellulitis	Bacterial culture (day 11 after onset; day 5 of hospitalization)	Tetracycline, gentamicin, streptomycin, chloramphenicol	2 d before correct diagnosis (tetracycline and gentamicin); day of correct diagnosis (streptomycin and chloramphenicol)	Thrombocytopenia, gastrointestinal bleeding, lactic acid acidosis, ARDS, and cardiac arrest
16	Pneumonic (primary)	Gastroenteritis (outpatient day 1 after onset); cyanosis and septic shock (ER, day 3 after onset)	Bacterial culture (PM)	None	Died before correct diagnosis	Cyanosis, septic shock, and right upper lobe pneumonia [11]
20	Bubonic (axillary)	Injury due to a fall (outpatient, day 3 after onset); septicemia, DIC, ARDS, and possible meningitis (ER, day 5 after onset)	Bacterial culture (PM)	None	Died before correct diagnosis	DIC, ARDS, and possible meningitis [12]

NOTE. ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulation; ER, emergency room; PM, postmortem.

medical care, complaining of vomiting as well as persistent fever (temperature, 40.6°C), myalgia, and malaise. Her leukocyte count was 15,600/mm³ with a left shift, and her blood pressure was 90/50 mm Hg. A chest radiogram revealed right lower lobe pneumonia. She was hospitalized, and treatment with cephalosporin antibiotics and supportive therapy were started; 7 hours later, she became hypotensive and hypoxic, requiring intubation, mechanical ventilation, and vasopressor therapy. On day 2 after the onset of illness, a diagnosis of plague was considered, and antibiotic therapy was changed to include gentamicin and doxycycline. On day 3, a bronchoscopic washing was positive for *Y. pestis* by fluorescent antibody assay, as was a sputum sample obtained on day 4. The patient remained intubated for 10 days; however, her condition gradually improved, and she was discharged from the hospital 17 days after the onset of illness. The right-sided pulmonary infiltrate was still present at discharge but resolved within the following 3 weeks, and the patient made a full recovery.

Eighty-five members of the hospital staff and 18 family members or friends were identified as having had significant contact with the patient; these contacts underwent either fever surveillance or prophylactic antibiotic treatment. Most of the contacts received prophylaxis with doxycycline, which is recommended for such use [8, 19]. Three of the contacts developed fever within 6 days of exposure to the patient, including the physician who had performed the intubation and the patient's 2 children. For postexposure prophylaxis, the physician received doxycycline, and the 2 children were given trimethoprim-sulfamethoxazole;

all were negative for antibodies to the F1 surface antigen of *Y. pestis* when tested 6–7 months after exposure. A bone marrow sample from the exhumed cat's carcass was positive for *Y. pestis* by fluorescent antibody assay. The carcass was not evaluated for evidence of pneumonia, but the veterinarian who acquired plague from this animal reported that it did not exhibit coughing or other symptoms of respiratory illness. An inspection of the site where the cat lived did not reveal any obvious signs of epizootic plague activity.

Fatal Cases of Cat-Associated Human Plague

Five (21.7%) of the 23 cases of cat-associated human plague were fatal (table 2). Two of these patients had primary pneumonic plague (cases 4 and 16), 1 had septicemic plague (case 3), and 2 had bubonic plague with axillary buboes (cases 11 and 20). Each of these patients initially was considered to have an illness other than plague (table 2). Four of the 5 decedents consulted physicians 1–3 days before being admitted to a hospital and were prescribed the following: tetracycline (case 4), an antibiotic considered effective for treatment of plague; antibiotics other than those recommended for treating human plague (dicloxacillin [case 11] and ciprofloxacin [case 16]); medications to relieve nausea and vomiting (case 4); and analgesics for relief of symptoms thought to be related to injury (case 20) [13–15, 19]. Although 1 patient (case 4) was prescribed treatment with an appropriate antibiotic (tetracycline) on the day after the onset of illness, her condition rapidly deteriorated,

and she died within 4.5 hours after being admitted to a hospital on day 2 after the onset of illness. Reportedly, she took only 2 of the 4 prescribed doses of tetracycline on her first day of illness, and these doses might not have been retained because of vomiting [13]. The admitting diagnosis for this patient was pneumonia, and she was treated with penicillin (not recommended as therapy for plague).

Only 1 of the patients who died (case 3) was admitted to a hospital during the first attempt to obtain medical assistance. This individual complained of difficulty in breathing and flulike symptoms on her second day of illness and was taken by ambulance to an emergency department. Physical examination revealed that in addition to dyspnea the patient had peripheral cyanosis and a WBC count of 21,800 cells/mm³. At admission, she was given supportive respiratory therapy, as well as a single dose of gentamicin for treatment of undiagnosed septicemia. Shortly before her death (8 hours after admission), the hospital laboratory reported observing bacilli on a peripheral blood smear, which is considered a grave prognostic sign [17].

Case 11 was the only fatal case to be correctly diagnosed before the patient died. During his first 2 days of hospitalization, the patient was treated with nafcillin, which is not recommended for treatment of plague. On the third day of hospitalization (day 9 after the onset of illness), gram-negative rods were noted in sputum samples from the patient, and he was treated with tetracycline, gentamicin, and cefotaxime. Two days later, a diagnosis of *Y. pestis* infection was confirmed by bacterial culture (day 11 after the onset of illness), resulting in treatment with streptomycin and chloramphenicol. Secondary complications associated with these cases included various sequelae of the systemic inflammatory response syndrome, such as metabolic acidosis, acute respiratory distress syndrome, disseminated intravascular coagulation and bleeding, hypoxemia, and cardiac arrest (table 2).

Discussion

Physicians in areas in the West where plague is enzootic should be informed of the risks of cat-associated human plague and consider plague as a possible diagnosis for persons who have handled sick or dead cats and present with fever and chills, myalgias, arthralgias, headache, or prostration. The presence of inguinal, femoral, axillary, or cervical lymphadenopathy should further increase the suspicion of plague, as should the identification of septicemia or pneumonia. Persons who acquire plague as a result of handling infected cats are most likely to develop axillary or cervical lymphadenopathy (table 1), while those infected through flea bites typically develop inguinal or femoral lymphadenopathy.

Misdiagnoses and delays in treatment often lead to fatalities, as demonstrated by the 5 cases summarized in table 2. As soon as plague is suspected, diagnostic samples should be obtained, and patients should receive appropriate antimicrobial therapy.

The drug of choice is streptomycin, although gentamicin is an acceptable alternative [19]. Tetracyclines and chloramphenicol also are considered to be effective. Because of its ability to penetrate tissues, chloramphenicol is recommended for cases involving plague meningitis, pleuritis, endophthalmitis, and myocarditis. Appropriate diagnostic samples include blood and other potentially infectious fluids or tissues. Isolation of *Y. pestis* from such samples by culture typically requires ≥ 2 days, but a presumptive diagnosis often can be made by using a fluorescent antibody assay to detect the F1 surface antigen of *Y. pestis*. Samples also should be obtained for serology, but detectable titers might not develop until many days after the onset of illness.

Since 1977, cases of cat-associated human plague have occurred almost every year in the western US, which emphasizes the importance of considering plague as a possible diagnosis for persons who have compatible symptoms and a history of exposure to cats. This diagnosis should especially be considered in the 4 states (Arizona, California, Colorado, and New Mexico) that reported 19 of the cat-associated cases and 89% of all cases occurring in the US from 1977 through 1998 [8, 20]. Populations in these states are increasing, and housing developments continue to expand into rural areas containing active plague foci. Furthermore, cat owners in these high-risk areas often allow their animals to roam freely, greatly increasing the likelihood that cats will encounter infectious fleas or eat *Y. pestis*-infected animals, particularly deer mice or other small rodents [21–23]. These factors suggest that human exposures to *Y. pestis*-infected cats in western states will increase.

The occurrences of vector-borne diseases are often highly seasonal because of annual variations in vector or host activity patterns that affect the likelihood of pathogen transmission. In the western US, most persons acquire plague through the bites of infectious fleas, and the risks of such exposures increase markedly during the summer months when epizootic transmission among rodents and their fleas also is at a peak [1, 20]. It is interesting that the occurrence of cases of cat-associated human plague did not appear to increase significantly during the summer months. Cat-associated cases also were less likely than other cases to be associated with epizootic activity. These observations are perhaps not surprising, as cats are likely to become infected as a result of eating native mice or voles (*Peromyscus* species or *Microtus* species), which have been proposed to be partially resistant to plague and are presumed to serve, along with their fleas, as reservoirs (maintenance or enzootic hosts) of *Y. pestis* infection during interepizootic periods. Cats that consume these animals might, therefore, become infected with *Y. pestis* at any time of year and then expose humans to plague. These observations suggest that a diagnosis of plague should be considered, regardless of season or levels of local epizootic plague activity, for persons who have compatible symptoms and a history of exposure to a sick or dead cat in the western US.

Persons who handle *Y. pestis*-infected cats can acquire plague through a variety of means (table 1). All patients in our study had a history of close physical contact with cats (handling), which resulted in these persons being bitten or scratched by teeth or claws believed to be contaminated with *Y. pestis* (8 cases), being exposed to presumably infectious body fluids while caring for, examining, or burying sick cats (10), or being exposed to presumably infectious respiratory droplets or other airborne infectious materials during face-to-face contact with the cats (5). The epidemiological investigations did not suggest that these persons acquired plague through infectious flea bites, although we cannot exclude the possibility that patients were exposed to wild rodent fleas as a result of handling flea-infested cats. If flea exposures did occur, it is highly unlikely that they were associated with the bites of cat fleas (*Ctenocephalides felis*), which infest cats in some regions of the US but are extremely rare or absent in the primarily semiarid regions where the cases in our study occurred. Repeated experimental studies also have demonstrated that cat fleas are very poor vectors of plague [24]. Cats that hunt are also likely to bring infected rodents into or near human habitations, which could pose a risk for persons who dispose of, or otherwise come into direct contact with, these animals.

The timely diagnosis of primary pneumonic plague in persons who have handled potentially infectious cats is extremely important because this form of the disease is associated with a high fatality rate and has potential for person-to-person spread [1, 17, 25]. Of the 23 patients described in our review, 5 developed primary pneumonic plague as a result of inhaling infectious respiratory droplets or airborne oral secretions during face-to-face contact with infected cats (table 1). These 5 cases are noteworthy because only 2 other cases (7 total) of primary pneumonic plague have been identified in the US since 1924. Sources of infection for the latter 2 cases could not be determined, but contact with infected cats cannot be ruled out, particularly for a fatal case that occurred in a California veterinarian in 1977 [26].

Persons who have close contact (<2 m) with infected cats or human patients with symptoms of pneumonic plague should be advised of the risk of airborne exposure to plague and given antibiotic prophylaxis. For prophylaxis, doxycycline or tetracycline is recommended for persons aged ≥ 9 years, and trimethoprim-sulfamethoxazole is preferred for children aged <9 years [8, 19]. Plague vaccine is no longer commercially available in the US and is not suitable for postexposure prophylaxis. Vaccination is recommended only for persons working in microbiological research laboratories or for certain individuals, such as mammalogists, who routinely handle the rodent hosts or flea vectors of plague [8].

Human exposures to *Y. pestis*-infected cats frequently occur during care for an ill cat (table 1). Infected cats have a spectrum of illness similar to that for people, with high rates of mortality among untreated animals (38% in 1 experimental study) [21,

22, 27, 28]. These animals typically present with fever, lethargy, anorexia, and an enlarged lymph node or bubo (frequently submandibular) that may be abscessed [22]. Pneumonic plague was described in 10% of *Y. pestis*-infected cats in a New Mexico study [22]. Because of the severity of cat plague, ill animals are often taken to a veterinary clinic for care, placing veterinarians and their staff at risk of exposure. Six (26.1%) of the 23 cases reported in this article occurred in veterinarians (4 cases) or their staff (2 cases). Two of these 6 patients developed primary pneumonic plague, and 4 had axillary buboes (which suggests inoculation of the hand or arm); none of these 6 cases was fatal. Kaufmann et al. [7] reported another likely case (culture confirmed; nonfatal) that occurred in 1936 in a California veterinarian who developed fever, chills, headache, myalgia, and an apparent axillary bubo 3 days after examining a cat with a submandibular abscess of unknown etiology.

Veterinarians often fail to consider plague as a diagnosis for cats because they are not aware that plague exists in the regions where they practice. The likelihood of misdiagnosis also is increased by the fact that most veterinarians lack experience in diagnosing *Y. pestis* infections in cats. Submandibular buboes in cats are easily confused with similar looking abscesses that commonly arise from various causes, including fights with other animals. Under such circumstances, veterinarians may fail to take appropriate precautionary measures and are likely to prescribe antibiotics, such as penicillins, that are useful for treating "cat fight" abscesses but are ineffective against *Y. pestis*. Misdiagnosis of *Y. pestis*-infected cats also can pose a further risk to their owners when they are sent home for additional care.

Persons working in veterinary practices where plague is enzootic should maintain an awareness that plague can occur in cats. In general, veterinary staff who follow standard operating procedures for handling potentially infectious animals or materials should be adequately protected from *Y. pestis* infection. Such procedures should include wearing a well-fitted surgical mask, gloves, and eye protection. Exudates should be considered infectious, and any material used for treating suspect cats should be disinfected, autoclaved, or incinerated. Veterinary clinic personnel should be advised of these risks and encouraged to consult their physician and local or state health department in the event of possible exposure to an infected cat. Vaccination is not recommended for veterinarians or their staff (none of the veterinary personnel with plague who were described in this article had received plague vaccine) [8].

In conclusion, *Y. pestis*-infected cats are expected to pose a continuing risk for persons living in those areas of the western US where *Y. pestis* exists in native rodent and flea populations. Prevention of cat-associated cases will require enhanced plague awareness among pet owners, veterinarians, health care providers, and the general public. These persons should be provided with appropriate information on the symptoms of plague in humans and cats, personal protective measures, and use of insecticidal agents to kill fleas on cats. Cat owners also should

prevent their cats from roaming freely in plague-affected areas [1, 8]. General preventive measures should be taken in areas where cats or other animals are found to be infected. These measures, which are designed to reduce the likelihood that humans will be exposed to infectious fleas or rodents, include avoiding sick or dead animals, avoiding areas where recent plague epizootics have occurred, modifying human environments to reduce the amount of food and shelter available to rodents, and, in certain situations, having trained personnel apply insecticides to control fleas or, rarely, rodenticides to reduce rodent populations. Finally, state and local health departments in areas where plague is enzootic in the western US should maintain adequate plague surveillance programs to detect increased human risks associated with plague epizootics in rodents and cases of plague in domestic cats.

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