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Clinical Features and Outcomes of *Pasteurella multocida* Infection

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Abstract: *Pasteurella multocida*, a zoonotic infectious organism, has most often been described in patients after an animal bite. Here, we characterize the clinical features and outcomes of *P multocida* infection in a large cohort of patients according to the presence or absence of an animal bite.

We retrospectively searched MUSC's laboratory information system for all patients with positive *P multocida* cultures from 2000 to 2014. Extensive data were abstracted, including clinical and outcome data. The Charlson comorbidity index (CCI) was used to assess comorbidities among patients.

We identified 44 patients with *P multocida* infections, including 25 with an animal bite. The average age was 64 years and the majority of patients were women (N = 30). There was no difference in age and sex distribution among those with and without a bite ($P = 0.38$ and 0.75, respectively). A CCI ≥ 1 was significantly associated with the absence of a bite ($P = 0.006$). Patients presenting without a bite were more frequently bacteremic (37% vs 4%, respectively, $P = 0.001$), and were hospitalized more often (84% vs 44%, respectively, $P = 0.012$). Of the 8 patients who required intensive care unit (ICU)-based care, 7 were non-bite-related. There were 4 deaths, all occurring in patients not bitten.

P multocida infections not associated with an animal bite were often associated with bacteremia, severe comorbidity(ies), immune-incompetent states, the need for ICU management, and were associated with substantial mortality.

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Abbreviations: CCI = Charlson comorbidity index, COPD = chronic obstructive pulmonary disease, ICU = intensive care unit, LOS = length of stay, MELD = Model for End-stage Liver Disease.

INTRODUCTION

Pasteurella multocida is a facultative anaerobic, fermentative Gram-negative coccobacillus found in the oropharynx of healthy animals, particularly cats, dogs, and pigs, as well as various wild animals.[1,2] Cats and dogs have the highest carriage rates, at 70% to 90% and 20% to 50%, respectively.[3] Human infections due to *P multocida* have been tightly associated with animal exposure and usually involve soft-tissue sites after animal bites or scratches.[4,5] Estimation of the prevalence of *P multocida* infection in the United States is difficult. Roughly 300,000 (1%) annual visits to the emergency rooms in the United States are due to animal bites or scratch wounds. Although not all of these lead to clinically relevant infections, when an infection occurs, *Pasteurella* species are isolated from some 50% of dog bites and 75% of cat bites.[6] Thus, although serious infections and death from *P multocida* infection in the United States are uncommon, this disease is important because of the pervasive nature of animal bites in the United States.

Of note, *P multocida* can be isolated from the respiratory tract of humans, presumably as commensal organism. Serious respiratory tract infections including pneumonia, empyema, and lung abscesses are typically found in patients with underlying pulmonary disease. Despite the apparent commensal relationship between *P multocida* and the respiratory tract, most patients with respiratory tract infection have a history of animal exposure.[1,2,7–11] An additional and not very commonly reported infection is of the bloodstream. *P multocida* bacteremia can occur by spread from a localized bite wound or from another localized source of infection, such as pneumonia, meningitis, or arthritis.[1] A variety of other serious invasive infections, such as meningitis, endocarditis, and peritonitis, have also been reported, but are rare.[1,8,12–18] *P multocida* appears to act as an opportunistic pathogen with a predilection for causing bacteremia in patients with liver dysfunction or in immunosuppressed patients.[1,2,8,9,12,19–21]

Broad-spectrum antibiotics that target *Pasteurella*, as well as other Gram-negative and Gram-positive bacteria, are the preferred prophylaxis for animal bites, which tend to be polymicrobial in nature. A combination of amoxicillin and the β-lactamase inhibitor clavulanic acid, doxycycline plus metronidazole for patients with penicillin allergies, or clindamycin plus a fluoroquinolone (ciprofloxacin), or clindamycin plus trimethoprim-sulfamethoxazole for children, or clindamycin plus ceftriaxone for pregnant women are the recommended treatment regimens.[6,22–24] Although there are a limited number of single case reports in the literature describing the clinical features and outcomes of patients presenting with systemic infection due to *P multocida*, larger studies are lacking. We therefore examined patients at our institution with *P multocida* infection, according to presence or absence of an animal bite.

METHODS

Study Design and Patients

This retrospective study was approved by the MUSC IRB (Pro00034870) and adhered to guidelines as set forth in the

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Declaration of Helsinki. We searched MUSC's microbiology laboratory information system for any patient with a positive *P multocida* culture (reports from blood, sputum, urine, subcutaneous tissue, and other biologic tissue culture) from 2000 to 2014. We also performed an ICD-9 search for ''*Pasteurella multocida*'' and/or ''animal bite'' through MUSC's Clinical Data Warehouse to identify additional potential subjects. We collected demographic, extensive clinical data (history of present illness, whether an animal bite occurred or not, medical history, physical examination, days spent in the intensive care unit [ICU], laboratory and radiologic findings, respiratory therapy, length of stay [LOS], and outcome data), bacteriologic (see below) data, and type and duration of antibiotics from the medical record. An animal bite was defined as breaking of the skin by the teeth of an animal. Other traumatic exposures of humans to animals, such as a scratch, were also included in the group animal bite.

The validated Charlson comorbidity index (CCI) and the age-adjusted CCI were used to classify prognostic comorbidities among patients.[25–28]

Microbiology

Specimens other than blood were routinely inoculated directly onto chocolate agar, trypticase soy agar with 5% sheep blood, MacConkey agar, and trypticase soy agar with 5% sheep blood, colistin, and nalidixic acid and streaked for isolation. Plates were incubated for 36 to 48 hours at 37°C in CO_2. Organisms that were Gram-negative bacilli/coccobacilli that grew only on chocolate agar and sheep blood agar and were oxidase positive, catalase positive, and indole positive were further characterized using conventional biochemical methods. Beta lactamase testing was performed according to the manufacturer's (BBL cefinase, BD Diagnostics, Sparks, MD) package insert.

Statistics

Demographic and clinical data were extracted and analyzed. Descriptive statistics including means, medians, frequencies, and percentages were used to summarize the data. A nonparametric test or χ^2 (Fisher exact test in the case of small sample) was used to compare groups of continuous and categorical variables, respectively. All *P* values reported are 2-sided; a level of 0.05 was considered statistically significant. All data were analyzed with IBM SPSS Statistics v22.

RESULTS

We identified a total of 44 patients with *P multocida* infections, 25 who had an animal bite (Table 1). The animals implicated included cats and dogs. The average age of patients in the cohort was 64 years and the majority of patients were women (n = 30, 68%). There was no difference in the age or sex distribution among those with and without an animal bite ($P = 0.38$ and 0.75, respectively). The most common source of infection was the skin, although in those without an animal bite, the bloodstream was the most common site of infection (Table 1). Isolation of *P multocida* from the bloodstream and respiratory tract was more frequently associated with absence of animal bite; conversely, skin infections were strongly associated with an animal bite ($P = 0.001$).

Among patients who presented with an animal bite, there was no correlation among comorbidity, source of infection, and inpatient hospital requirement. Patients presenting with a cat versus a dog bite were more frequently hospitalized ($P = 0.029$, Table 2). Patients presenting without an animal bite were more frequently hospitalized and had a longer LOS compared with patients who had a bite (84% vs 44% and 19.7 vs 5.1 days, respectively, $P = 0.012$). Of the 8 patients who required ICU care, 7 were non-bite-related ($P = 0.014$).

P multocida culture results were available for 39 of 44 patients. It was the sole organism recovered from blood or muscle cultures. In 3 of 4 (75%) respiratory cultures, *P multocida* grew abundantly as the sole isolate; in the fourth culture, *P multocida* was grown in equal abundance with usual oral flora. Eleven of 20 (55%) skin cultures—3 non-bite-related, 8 bite-related—grew *P multocida* as the sole isolate. Not unexpectedly, 7 (35%) skin cultures grew *P multocida* with organisms consistent with usual skin flora in varying concentrations. Of these, 2 were non-bite-related, whereas 5 were in animal bites. Interestingly, 1 non-bite-related skin culture grew equal amounts of *P multocida* and methicillin-susceptible *Staphylococcus aureus*, whereas another non-bite-related skin culture grew equal amounts of *P multocida* and methicillin-resistant *S aureus* and a lesser amount of a mixture of Gram-positive and Gram-negative flora.

As Gram stains are not typically useful in identifying *Pasteurella* infection, Gram stains were not ordered in all patients. For specimens that were subjected to routine Gram stains, 7 of 32 Gram stains showed only Gram-negative bacilli, whereas 3 additional stains showed Gram-negative bacilli mixed with Gram-positive cocci. Only 4 specimens with Gram stains showing Gram-negative bacilli were from patients with animal bite. Sixteen Gram stains showed no microorganisms an at all.

Pasteurella sp susceptibility testing, including the recommendation for beta lactamase testing, became standardized in 2006. Thus, beta lactamase results were available for 32 of 39 cultures; 69% were beta lactamase-negative and 13% were beta lactamase-positive. There was no apparent difference between beta lactamase positivity and the type or severity of infection ($P = 0.99$, Table 1).

Sixty-three percent of patients were affected by at least 1 disease that could lead to an immunocompromised status. Notably, a CCI $\geq$1 was significantly associated with the absence of bite ($P = 0.006$). The most common comorbidity was chronic lung disease (N = 7), followed by malignancy (N = 6). Patients without an animal bite presenting with CCI $\geq$1 and non soft-tissue infections required hospitalization more frequently (Table 3). In the 2 patients presenting with cirrhosis, Model for End-stage Liver Disease (MELD) scores were 29 and 33, respectively, and were both Child-Pugh score C, signifying advanced decompensated chronic liver disease; these patients are well known to be susceptible to infection. In patients with bloodstream infections, cancer was the most common comorbidity (4/8), followed by respiratory diseases and cerebrovascular disease (2/8 for both categories). Chronic obstructive pulmonary disease (COPD) was present in 3 of 4 patients presenting with *P multocida* pneumonia and no animal bite. Interestingly, 3 of 4 patients with a deep muscle abscess were affected by diabetes.

Patients with a non-animal bite *P multocida* infection were more often cared for in an ICU setting (1/25 [4%] for animal bite vs 7/19 [37%] for non-animal bite, Table 1). Among those who were treated in the ICU, the most common comorbidities were cerebrovascular disease (3), cirrhosis (2), malignancy (2), COPD (2), end-stage renal disease (1), and dementia (1). For those patients, bloodstream and respiratory tract infections were the most common source of infection (Table 3).

TABLE 1. Patient Clinic Characteristics According to the Presence or Absence of an Animal Bite

Patient Characteristics	Total (n = 44)	Animal Bite (n = 25)	No Animal Bite (n = 19)	*P*
Median age in years (25th and 75th percentiles)	64 (52–75)	66 (50–77)	64 (50–77)	0.38
Sex				0.75
Female	30 (68%)	18 (72%)	12 (63%)	
Male	14 (32%)	7 (28%)	7 (37%)	
CCI				0.006
0	20 (45%)	16 (64%)	4 (21%)	
≥1	24 (55%)	9 (36%)	15 (79%)	
Age adjusted CCI				0.22
0–2	22 (50%)	15 (60%)	7 (37%)	
≥3	22 (50%)	10 (40%)	12 (63%)	
Specimen source				0.001
Blood	8 (18%)	1 (4%)	7 (37%)	
Peritoneal fluid	1 (2%)	—	1 (5%)	
Muscle abscess	4 (9%)	2 (8%)	2 (11%)	
Synovial fluid	2 (5%)	1 (4%)	1 (5%)	
Respiratory	4 (9%)	—	4 (21%)	
Skin	24 (55%)	21 (84%)	3 (16%)	
n/r	1 (2%)	—	1 (5%)	
Beta-lactamase test				0.99
Positive	5 (11%)	3 (12%)	2 (11%)	
Negative	27 (61%)	15 (60%)	12 (63%)	
n/r	7 (17%)	4 (16%)	3 (15%)	
n/a	5 (11%)	3 (12%)	2 (11%)	
Hospital setting				0.012
Outpatient	17 (39%)	14 (56%)	3 (16%)	
Inpatient	27 (61%)	11 (44%)	16 (84%)	
Required ICU	8 (18%)	1 (4%)	7 (37%)	0.014
Antibiotic regimen				0.14
Oral antibiotic only	13 (30%)	8 (32%)	5 (26%)	
IV antibiotic	21 (48%)	9 (36%)	12 (63%)	
n/r	10 (22%)	8 (32%)	2 (11%)	
Surgical intervention	19 (43%)	12 (48%)	7 (37%)	0.55
LOS, days				0.012
Mean, SD (range)	13.5, 34.2 (2–180)	5.1, 2.8 (2–11)	19.7, 44.6 (3–180)	
Mortality	4 (9%)	0	4 (21%)	0.001

CCI = combined comorbidity index, ICU = intensive care unit, LOS = length of stay, n/a = not available, n/r = not reported, SD = standard deviation.

The mean LOS for patients presenting with an animal bite was 5.1 days (2–11, range), and the mean LOS in absence of an animal bite was 19.7 days (3–180, range). There were 4 deaths, all occurring in patients without animal bite. The mortality rate for patients with *P multocida* infection in absence of animal bite was 21%, and all deceased patients presented with serious and multiple comorbidities (at least a CCI of 3, or an age-adjusted CCI of 4) and often an immune-incompetent state. Either cirrhosis or metastatic cancer was found in all fatal cases (Table 3).

Most of an the patients presenting with soft-tissue infection secondary to animal bite received amoxicillin with the β-lactamase inhibitor clavulanic acid oral therapy for 10 to 14 days. In patients with a penicillin allergy, an alternative regimen with clindamycin or sulfamethoxazole trimethoprim was chosen (Table 2). Almost all patients requiring hospitalization, regardless of presence or absence of an animal bite, received intravenous antibiotics. Antibiotics given varied, although for those presenting without an animal bite, a more aggressive approach was preferred (typically double coverage with vancomycin and 3rd-generation cephalosporin). The duration of treatment for a patients without an animal bite tended to be longer than those with an animal bite (Table 3).

DISCUSSION

In this single-institution study, we have reported on the clinical features and outcomes of a large cohort of patients presenting with *P multocida* infection. Of the 44 patients identified, 19 (43%) presented without a documented animal bite or scratch. Although many of the infections associated with animal bites were confined to soft tissues, isolation of *P multocida* from the bloodstream and respiratory tract was more frequently associated with absence of animal bite. A key finding of our study was that infections without a bite history seemed to occur in patients with serious comorbidities who often had an immune-compromised state. This group of patients were also more frequently hospitalized, more often required ICU-based

TABLE 2. Clinical Characteristics and Antibiotic Regimens in Patients With *Pasteurella multocida* Infection With Animal Bite (n = 25)

Age	Comorbidities	CCI	Animal Bite*	Location of Infection	Hospital Days	Required Surgery†	IV Antibiotic Regimen	Oral Antibiotic Regimen	Antibiotic Duration
52	None	0	Cat	Skin	4	Skin	Vancomycin + Ampicillin sulbactam	Amoxicillin clavulanate + Sulfamethoxazole trimethoprim	4 + 10
78	None	0	Cat	Skin	2	Skin	Ampicillin sulbactam	Amoxicillin clavulanate	1 + 10
75	Diabetes, colon cancer, lupus	5	Dog	Skin	5	Skin	Ampicillin sulbactam	Amoxicillin clavulanate	5 + 14
53	None	0	Dog	Skin	4	Skin	Ampicillin sulbactam	Amoxicillin clavulanate + Ciprofloxacin	4 + 10
85	Diabetes, peripheral vascular disease	2	Cat	Skin	11	None	Ceftriaxone	Amoxicillin clavulanate	11 + 7
66	Diabetes, myocardial infarction	2	Dog	Skin	4	Skin	Clindamycin	Clindamycin	4 + 10
41	None	0	Dog	Skin	0	None	No IV antibiotics	Amoxicillin clavulanate + sulfamethoxazole trimethoprim	14
68	None	0	Cat	Skin	4	Skin	No IV antibiotics	Amoxicillin clavulanate + moxifloxacin	14
81	COPD	1	Dog	Skin	0	Skin	No IV antibiotics	Amoxicillin clavulanate	10
53	COPD	1	Cat	Skin	0	None	No IV antibiotics	Amoxicillin clavulanate	10
63	None	0	Cat	Skin	0	None	No IV antibiotics	Amoxicillin clavulanate	7
19	Asthma	1	Cat	Skin	2	Skin	No IV antibiotics	Amoxicillin clavulanate	14
76	None	0	Cat	Skin	0	Skin	No IV antibiotics	Sulfamethoxazole trimethoprim	10
30	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
45	None	0	Cat	Skin	0	None	No IV antibiotics	n/a	n/a
57	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
67	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
67	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
60	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
77	None	0	n/r	Skin	0	None	No IV antibiotics	n/a	n/a
86	Diabetes, chronic kidney disease	2	Dog	Deep muscle abscess	0	Abscess drainage	No IV antibiotics	Clindamycin	14
48	Peripheral vascular disease	1	Cat	Deep muscle abscess	4	Abscess drainage	Carbapenem	Amoxicillin clavulanate + ciprofloxacin	14 + 14
78	None	0	Cat‡	Synovial (knee) fluid	9	Arthrotomies and joint debridement	Ceftriaxone	Doxycycline	42 + indefinite
92	Dementia	1	Cat‡	Blood and synovial (shoulder and knee) fluid	7*	Arthrotomies and joint debridement	Ceftriaxone	Amoxicillin	28 + 180
35	None	0	Dog	Skin	0	None	n/r	n/r	n/r

aa = age-adjusted, CCI = combined comorbidity index, COPD = chronic obstructive pulmonary disease, IV = intravenous, n/a = not available, n/r = not reported, Skin = incision and drainage; *Required ICU.

* Species of animal bite.

† All skin surgeries were incision and drainage procedures.

‡ Skin scratch.

TABLE 3. Clinical Characteristics and Antibiotic Regimens in Patients With *Pasteurella multocida* Infection Without an Animal Bite (n = 19)

Age	Comorbidities	CCI	Location of Infection	Hospital Days	ICU	Death	Required Surgery	IV Antibiotic Regimen	Oral Antibiotic Regimen	Antibiotic Duration
66	Multiple myeloma, COPD	3	Blood	6	0	No	None	Piperacillin tazobactam	Amoxicillin	4 + 14
73	Metastatic ovarian cancer, pulmonary embolism	7	Blood	5	0	Yes	None	Piperacillin tazobactam	No oral antibiotics	3
54	Cirrhosis (MELD 33)	3	Blood	7	7	Yes	None	Ampicillin sulbactam	No oral antibiotics	7
64	Myelodysplastic syndrome, Burkitt lymphoma	4	Blood	8	0	No	None	Ceftriaxone	No oral antibiotics	14
55	Subdural hematoma	1	Blood/subdural empyema	17	13	No	Subdural drainage	Ampicillin	No oral antibiotics	14
36	ESRD, SLE, cerebrovascular disease	4	Blood/peritoneal dialysis fluid	15	8	No	Peritoneal catheter removal	Ciprofloxacin	Ciprofloxacin	7 + 14
81	Melanoma	2	Blood	n/r	n/r	n/r	n/r	n/r	n/r	n/r
41	COPD	1	Respiratory	8	6	No	None	Vancomycin	Moxifloxacin	5 + 10
73	COPD	1	Respiratory	5	0	No	None	Vancomycin + cefepime	Moxifloxacin	2 + 14
54	Subarachnoid hemorrhage	1	Respiratory	180	40	No	None	Vancomycin + carbapenem	No oral antibiotics	14
68	Myelodysplastic syndrome, COPD	3	Respiratory	16	16	Yes	None	No IV antibiotics	Amoxicillin clavulanate	14
64	Cirrhosis (MELD 29)	3	Synovial (knee) fluid	8	7	Yes	Arthrotomies and joint debridement	Meropenem + cefazolin	No oral antibiotics	8
51	Diabetes with ESRD	2	Deep muscle abscess	4	0	No	Abscess drainage	Vancomycin	No oral antibiotics	2
56	Diabetes	1	Deep muscle abscess	7	0	No	Abscess drainage	Vancomycin + cefepime	Doxycycline	4 + 56
44	Pulmonary embolism	1	Peritoneal fluid	6	0	No	Pancreatic cyst drainage	No IV antibiotics	Sulfamethoxazole trimethoprim	14
87	None	0	Skin	3	0	No	Skin ID	No IV antibiotics	Amoxicillin clavulanate	14
83	None	0	Skin	0	0	No	None	No IV antibiotics	Sulfamethoxazole trimethoprim	10
65	None	0	Skin	0	0	No	None	No IV antibiotics	Cephalexin	10
57	None	0	n/a	0	0	No	None	n/a	n/a	n/a

CCI = combined comorbidity index, COPD = chronic obstructive pulmonary disease, ESRD = end-stage renal disease, ID = incision and drainage, IV = intravenous, MELD = model for end-stage liver disease, n/a = not available, n/r = not reported, SLE = systemic lupus erythematosus.

care, had longer LOSs, and had a higher mortality rate than patients with non-bite-associated infections. In our study, the mortality rate for patients with *P multocida* in the absence of an animal bite was 4 of 19 patients (21%) and all of these patients appeared to have an underlying disease that could lead to being immunocompromised (2 cirrhosis or 2 widespread malignancy). Finally, our study was consistent with previous work in which a high mortality has been reported for patients with *P multocida* infections and bacteremia, pneumonia, arthritis, or peritonitis.[10,20]

Based on our data, we conclude that comorbidities are likely to be an important risk factor for development of non-bite *P multocida* infection. Further, we speculate that the presence of comorbidities may have contributed to poorer outcomes in this group. In contrast, the presence of comorbid conditions, as measured using the CCI, did not appear to influence the clinical outcome in patients presenting with animal bite-associated infections. Malignancies, pulmonary and cerebrovascular diseases were common among patients presenting with bloodstream infection. COPD was associated with most lung infections. Indeed, our data are consistent with several case reports that have described bacteremia occurring predominantly in patients with preexisting liver disease or in immunosuppressed patients.[1,2,8,9,14,17,19–21]

Our data have important implications for primary care and generalist care providers. This is because it is estimated that there are some 70 million dogs and 74 million cats in the United States, and approximately 37% of all households in the United States have a dog, and 30% have a cat.[29] Although it has been proposed dogs and cats are safe overall, physicians should be particularly attuned to the possibility of Pasteurella multocida infection leading to life-threatening complications in patients with significant co-morbidities and advise against unnecessary pet exposure.[30] Not unexpectedly, most of the patients presenting with *Pasteurella multocida* infection without an animal bite had contact with pets. In these patients, either a skin tear or a percutaneous catheter was reported as the source of infection. Interestingly, the majority of patients who presented without an animal bite had severe comorbid conditions such as cirrhosis, malignancy, renal insufficiency, autoimmune disease, and diabetes - all associated with secondary immunodeficiency.[31] Thus, based on our findings, we speculate that an immunocompromised state may predispose to *P multocida* infection without an animal bite.

The treatment of choice for *P multocida* infections has typically been with penicillin.[1,32] However, rare penicillin-resistant *P multocida* strains in human infections have been described.[33,34] In these cases, second- and third-generation cephalosporins, fluoroquinolones, and tetracyclines are recommended for treatment.[1] Antimicrobial resistance cannot be determined for our study because susceptibility testing other than beta lactamase testing has not been performed in our institution except upon request. In addition, beta lactamase data were not available for 18% of patients.

Although this study was able to capture detailed clinical data on an extremely large cohort, we recognize several limitations. First, it was retrospective and follow-up information is unavailable after hospital discharge. Thus, it could potentially be subject to recall bias, and it is possible that we could have missed patients with *P multocida* infection in our databases. However, we doubt this possibility because we used 2 different methods to identify patients. Further, even if such a bias was present, we do not believe that it would alter the conclusions of our study. Additionally, the study was performed at a single center and reflected patients in South Carolina and the greater Charleston area, which could limit its generalizability to the United States. Further, the single-center nature of the study could create a bias related to either a high or low number of pet owners in our clinical catchment area. We tend to doubt this potential bias since to the best of our knowledge, the demographics of pet owners in South Carolina and Charleston reflect those of the entire United States.[29]

In conclusion, compared with animal bite-associated *P multocida* infections, non-animal-bite-associated infections were found primarily in patients with severe comorbidities and immunodeficient states, were often associated with systemic infections, the need for ICU management, longer hospital LOS, and an increased mortality rate. In particular, the high mortality rate in patients with non-animal bite *P multocida* infection suggests that aggressive treatment approaches are warranted in immunocompromised patients.

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