Evaluation of clinical characteristics, diagnostic test results, and outcome in horses with internal infection caused by *Corynebacterium pseudotuberculosis*: 30 cases (1995–2003)

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Objective—To determine clinical signs, results of diagnostic testing, and outcome in horses with internal *Corynebacterium pseudotuberculosis* infection.

Design—Retrospective study.

Animals—30 horses.

Procedure—Information pertaining to clinical data, results of diagnostic tests, and costs of hospitalization and treatment was extracted from medical records of affected horses.

Results—Internal *C pseudotuberculosis* infection was diagnosed on the basis of clinical signs, diagnostic imaging, and clinicopathologic data, including results of serologic tests and bacterial culture. The most common clinical signs were concurrent external abscesses, anorexia, fever, lethargy, weight loss, and signs of respiratory tract disease or abdominal pain. Clinicopathologic abnormalities included a geometric mean reciprocal serum synergistic hemolysin inhibition titer ≥ 512, leukocytosis with neutrophilia, hyperglobulinemia, hyperfibrinogenemia, and anemia. Specific organ involvement was diagnosed in 27 of 30 horses. Affected organs included the liver (18 horses), lungs (12), kidneys (7), and spleen (3); multiple organs were affected in 10 horses. Treatment with antimicrobials for a median of 36 days (range, 7 to 97 days) was usually successful, yielding an overall survival rate of 71%.

Conclusions and Clinical Relevance—Early diagnosis and long-term antimicrobial treatment were important for a successful outcome in horses with internal *C pseudotuberculosis* infection. Ultrasonographic imaging was an important technique for identifying specific organs affected, aiding in obtaining samples for a definitive diagnosis, and monitoring response to treatment. Pregnant mares with internal infections are at risk for fetal loss. Preexisting chronic organ disease may be associated with a poor prognosis. (*J Am Vet Med Assoc* 2005;227:441–448)

Corynebacterium pseudotuberculosis is a gram-positive facultative intracellular pleomorphic bacterium with a worldwide distribution. The bacterium causes 2 primary forms of disease in horses.[1] In most geographic regions, *C pseudotuberculosis* infection causes a diffuse infection of the limbs known as ulcerative lymphangitis, but in the western and southwestern United States, the predominant manifestation of infection is formation of external abscesses, most often in the pectoral and ventral abdominal regions. The latter form of the disease is most prevalent in California[2-6] and Texas,[7,8] where it is referred to as pigeon fever or dryland distemper. The mode of infection is speculative, but it is postulated that the organism enters the horse through abrasions in the skin. Insects are suspected to play a role as mechanical vectors; results of a recent study[9] support the hypothesis that insects such as *Haematobia irritans, Stomoxys calcitrans,* and *Musca domestica* act as vectors.

Development of internal abscesses, generalized infection, and abortion have been reported[2-7,10-13] in horses in areas where development of external abscesses from *C pseudotuberculosis* is prevalent. Although internal organ involvement is diagnosed in < 10% of horses with *C pseudotuberculosis* infection, a 40% mortality rate has been reported in association with such internal infections; the mortality rate increases to 100% among horses that receive no antimicrobial treatment.[6] Horses that develop internal infection require long-term antimicrobial treatment for resolution.[6,8,14] Early diagnosis of internal infection caused by *C pseudotuberculosis* is important for a successful outcome but is often difficult because of the insidious onset and nonspecific nature of accompanying clinical signs, which may include anorexia, fever, lethargy, and weight loss. In areas where infection is endemic, horses that have had an external *C pseudotuberculosis* abscess in the previous 6 months and develop signs of systemic illness should be suspected of having internal *C pseudotuberculosis* infection. Similarly, horses with compatible signs that reside on a property where other horses have had external abscesses should also be evaluated for internal infection.

In recent years, there has been an increase in the number of horses with internal *C pseudotuberculosis*

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infection at our hospital, and there have been reports of outbreaks of disease in Colorado, Wyoming, Utah, and Kentucky, geographic areas in which the disease has previously been rare.[15] In regions where the disease has not previously been endemic, recognition of clinical signs of internal *C pseudotuberculosis* infection and prompt initiation of appropriate treatment may be hampered by a low index of suspicion on the part of the veterinarian. The purposes of the study reported here were to determine the clinical findings of internal *C pseudotuberculosis* infection and the best diagnostic testing methods used to localize internal infection to specific organ systems. Additional aims of the study were to assess modes of treatment, treatment costs, outcome, and whether early diagnosis would be associated with reduced likelihood of death. We hypothesized that horses with involvement of multiple internal organs would have a higher mortality rate and more severe abnormalities in results of clinicopathologic testing than horses with involvement of a single organ.

Criteria for Selection of Cases

Medical records of all horses that were evaluated at the University of California, Davis **Veterinary Medical Teaching Hospital** (**VMTH**) between January 1995 and December 2003 and that had a history, clinical signs, and clinicopathologic data compatible with a diagnosis of internal *C pseudotuberculosis* infection were reviewed. Horses were included in the study if pure growth of *C pseudotuberculosis* was obtained via bacterial culture of specimens from an affected organ system or if the horse had a reciprocal serum antibody titer ≥ 512 as measured by the **synergistic hemolysin inhibition** (**SHI**) test.

Procedures

Data collected included breed, sex, age, date of initial examination at the VMTH, heart rate, respiratory rate, rectal temperature, and clinical signs as recorded at the time of initial physical examination. The duration of clinical signs prior to examination, housing information, and whether there were *C pseudotuberculosis* infections in other horses on the property were recorded when the information was available.

Clinicopathologic data collected included results of CBCs, serum and plasma biochemical analyses, serum SHI test, and coagulation tests. Results of cytologic evaluation of abscess fluid, pleural fluid, peritoneal fluid, and fluid obtained via transtracheal aspiration were recorded when available. Results of bacterial culture and histologic interpretations of biopsy specimens were also examined. Diagnostic images (radiographs and ultrasonographs) were reviewed for relevant findings.

Diagnoses—Data were analyzed, and cases were categorized by organ system affected. Infection of the lower portion of the respiratory tract (lungs) was diagnosed on the basis of findings from physical examination, thoracic radiography or ultrasonography, and positive results for pure growth of *C pseudotuberculosis* from pleural fluid or fluid obtained via transtracheal aspiration. Hepatic and renal involvement was diagnosed on the basis of results of serum biochemical analyses, abdominal ultrasonographic imaging, histologic interpretation of biopsy specimens, or positive results of bacterial culture of tissue aspirates. Splenic involvement was determined via ultrasonographic imaging. Horses were characterized as having a presumptive internal abdominal abscess if they met the inclusion criteria but no additional diagnostic testing was performed. One horse had a mesenteric abscess that was detected via rectal palpation.

Treatment—Medications prescribed, dose, frequency of administration, and duration of treatment were recorded. The total duration of medical treatment was estimated from the history, treatments administered during hospitalization, and medications prescribed at the time of discharge from the hospital.

Outcome—Clients or referring veterinarians were contacted to determine whether any complications had arisen after discharge from the hospital and follow-up outcome. The follow-up period after hospital discharge ranged from 6 months to 9 years. Complications associated with the disease or with medical treatments, costs incurred at the VMTH, and duration of hospitalization were reported.

Statistical analyses—Descriptive statistics and analyses were calculated by use of commercial statistical software.[a] Comparisons were made between survivors and nonsurvivors and between horses with single versus multiple organ involvement on the basis of specific organs involved, single or multiple organ involvement, serum SHI titer, leukocytosis, neutrophilia, hyperfibrinogenemia, and early versus late diagnosis. Diagnosis was considered early if it was rendered within 15 days of the onset of clinical signs of disease and late if rendered 20 to 30 days after onset. Discrete values were compared with χ^2 contingency analyses, and nondiscrete values were compared by use of a Wilcoxon rank sum test. For all comparisons, values of $P \leq 0.05$ were considered significant.

Results

Signalment—Thirty horses met the criteria for inclusion in the study. Seven breeds were represented, the most common being Quarter Horses (n = 12), Arabians (6), Thoroughbreds (4), and Warmbloods (3). Twenty-one (70%) horses were mares, 6 (20%) were geldings, and 3 (10%) were stallions. Of the 21 mares, 5 were pregnant at the time of infection. The median age of the horses was 8.5 years (range, 10 months to 22 years).

Seasonality—Cases were detected throughout the year, with the greatest frequency in November and January. More than half (16/30 [53.3%]) of the horses were first examined from November through January, and nearly three fourths (22/30 [73.3%]) were first examined from October through March.

History and clinical signs—Horses had clinical signs of illness for 1 to 30 days (median, 10 days) prior to being examined at the VMTH. Information regarding the incidence of *C pseudotuberculosis* infections on the property of origin was available for 14 horses. Thirteen

of those horses originated from premises where other horses had presumptive *C pseudotuberculosis* external abscesses in the previous 12 months. Housing data were available for 17 of 30 horses. Fourteen of those horses lived on pasture, and 3 were stabled.

The most common clinical signs at the time of initial examination at the VMTH were anorexia (19 horses), lethargy (14), weight loss (14), signs of respiratory tract disease (11), and signs of abdominal pain (10). Nineteen (63.3%) horses had a concurrent or recent history of external abscess formation, and of those, 13 had external abscesses at the time of admission, 5 had abscesses that had resolved within the 3 months preceding examination, and 1 had an external abscess that had resolved 6 months prior to examination. Of the 11 horses that did not have a history of external abscesses, 5 had resided on premises where there was a history of presumptive *C pseudotuberculosis* external abscesses affecting other horses. Eight horses had ventral or limb edema, with resultant lameness in 7 horses; 3 mares aborted their fetus. Clinical signs that were observed in 1 or 2 horses included bruxism, dehydration, diarrhea, edema, oral ulceration, mucous membrane petechiation, pigmenturia, polyuria-polydipsia, purpura hemorrhagica, synovitis, urticaria, and weakness or ataxia.

Vital signs (eg, rectal temperature, heart rate, and respiratory rate) were recorded at the time of initial physical examination. Fifteen (50%) horses were febrile (rectal temperature > 38.4°C [101.1°F]; mean, 38.3°C [100.9°F]; range, 36.8° to 39.6°C [98.2° to 103.3°F]). Twenty (66.7%) horses were tachycardic (heart rate > 48 beats/min; mean, 55 beats/min; range, 36 to 80 beats/min). Seven (23.3%) horses were tachypneic (respiratory rate > 24 breaths/min; mean, 25 breaths/min; range, 12 to 80 breaths/min). Of 15 horses with a rectal temperature in the reference range, 9 were being treated with antimicrobials, nonsteroidal anti-inflammatory drugs, or both.

Clinicopathologic data—Results of a CBC and serum and plasma biochemical analyses were available for all horses (**Table 1**). Twenty-eight horses had hyperglobulinemia (serum globulin concentration > 4.7 g/dL), 28 had neutrophilia (> 6,800 cells/µL), 24 had leukocytosis (> 11,600 cells/µL), 24 had hyperfibrinogenemia (plasma fibrinogen concentration > 400 mg/dL), and 20 had hyperproteinemia (plasma protein concentration > 7.7 g/dL). Thirteen horses had abnormal values for all 5 of those clinicopathologic variables, and 24 horses had abnormalities in 4 of the 5 variables. Seventeen horses had Hct values within the reference range (30% to 46%), and 11 were anemic (Hct < 30%). Two horses had thrombocytopenia (15,000 and 52,000 platelets/µL; reference range, 100,000 to 225,000 platelets/µL).

Table 1—Values of certain clinicopathologic variables in 30 horses with internal *Corynebacterium pseudotuberculosis* infection.

Variable	Mean ± SD	Range
Hct (%)	33.9 ± 7.2	23.4–50.0
Total WBC count (cells/µL)	19,297 ± 9,485	6,400–53,420
Neutrophil count (cells/µL)	16,080 ± 9,109	2,944–49,627
Platelet count (platelets/µL)	228,967 ± 86,280	15,000–449,000
Fibrinogen concentration (mg/dL)	670.0 ± 306.4	100–1,600
Total protein concentration (g/dL)	8.7 ± 1.5	6.3–12.1
Globulin concentration (g/dL)	6.7 ± 1.8	3.5–10.5
Geometric mean serum SHI titer	2,611	64–20,480

SHI = Synergistic hemolysin inhibition.

Coagulation tests (eg, prothrombin time, partial thromboplastin time, fibrin degradation products, and antithrombin III activity) were performed in 10 horses. Five horses were tested prior to undergoing a transcutaneous biopsy procedure, 2 were tested because of a subjective perception of prolonged bleeding at venipuncture sites, 2 because of petechiae on oral mucous membranes, and 1 because of hemorrhagic diarrhea. Results of coagulation tests were within reference ranges for 6 horses, whereas 4 horses had high concentrations of fibrin degradation products (> 10 to > 40 µg/mL; reference limit, < 10 µg/mL) and low antithrombin III activity (36% to 72%; reference value, 100%). Two horses had prolonged prothrombin times (17.7 and 23.8 seconds; reference range, 14 to 17 seconds), and 2 had results (16.4 and 16.7 seconds) near the upper limit of the reference range. No horses had prolonged partial thromboplastin times. On the basis of clinical signs, platelet counts, and coagulation test results, 4 horses had a diagnosis of **disseminated intravascular coagulation** (**DIC**).

Bacterial culture was attempted in 35 samples from 25 horses. Pure growth of *C pseudotuberculosis* was obtained in 19 samples from 17 horses. Positive results of bacterial culture were obtained from fluid from a transtracheal aspirate (10 horses), peritoneal fluid (3), pleural fluid (2), kidney aspirate (2), urine (1), and liver aspirate (1). Negative results for bacterial culture were obtained from peritoneal fluid (5 horses), liver biopsy specimens (5), urine (3), fluid from a transtracheal aspirate (2), and blood (1).

A serum SHI test was performed in 28 horses, 27 (96.4%) of which had a titer ≥ 512 (Table 1). One horse with pneumonia had no titer at admission and did not develop an SHI titer > 64 in the ensuing 30 days.

Diagnoses—Specific organ involvement was observed in 27 of 30 horses. Eighteen horses had hepatic involvement, 12 had infection of the lower portion of the respiratory tract, 7 had renal abnormalities, and 3 had splenic abscesses. Involvement of a single organ was most common, occurring in 17 of 27 (63.0%) horses. Involvement of multiple organs occurred in 10 of 27 (37.0%) horses, the majority (8/10) of which had 2 affected organ systems (in each instance, 1 abdominal organ plus pneumonia). Seven of the horses with multiorgan infection had concurrent pneumonia and hepatopathy. Three horses had clinical signs and clinicopathologic abnormalities consistent with internal infection as well as serum SHI titers ≥ 512, and additional diagnostic testing was not pursued in those horses. One of those horses had an abdominal abscess associated with the mesentery that was detected via rectal palpation. Transrectal ultrasonography revealed the

abscess to be 13 to 16 cm in diameter. Transabdominal ultrasonography revealed no evidence of hepatic, renal, or splenic involvement, and the abscess was not visible transabdominally.

Liver—Hepatopathy was diagnosed in 18 of 27 (66.7%) horses. Fifteen of those horses had high serum activity of one or more liver-derived enzymes. Fourteen horses had high activities for γ-glutamyltransferase (25 to 422 U/L; reference range, 8 to 22 U/L), 10 had high activities for sorbitol dehydrogenase (13 to 168 U/L; reference range, 0 to 8 U/L), 10 had high activities for alkaline phosphatase (305 to 2,472 U/L; reference range, 86 to 285 U/L), and 5 had high activities for aspartate aminotransferase (507 to 2,766 U/L; reference range, 138 to 494 U/L). Three horses with hepatopathy detected via abdominal ultrasonography had serum liver enzyme activities within reference ranges. Ultrasonographic imaging revealed abnormalities in the liver of 12 horses. The sonographic appearance suggested the formation of abscesses in 10 horses; multiple abscesses **(Figure 1)** were detected in 7 of those horses, whereas a single discrete area of hypoechogenicity **(Figure 2)** was detected in 3. In the other 2 horses, ultrasonography revealed hepatomegaly without evidence of abscess formation. Liver biopsy specimens were obtained with ultrasound guidance from 6 horses, 5 of which had histologic evidence of acute inflammation in addition to chronic liver disease. Changes associated with low-grade pyrrolizidine alkaloid toxicosis were detected in 2 horses, severe fibrosis in 2 horses, and chronic hepatitis in 1 horse. The liver biopsy specimen from 1 horse did not provide diagnostic information. Liver biopsy specimens from 5 of the 6 horses were submitted for bacterial culture but failed to yield bacterial growth. A transcutaneous ultrasound-guided aspirate of a presumptive liver abscess from another horse yielded a reddish-brown serosanguinous fluid that yielded pure growth of *C pseudotuberculosis*.

Abdominocentesis was performed in 15 horses with serum biochemical or ultrasonographic evidence of hepatopathy. The peritoneal fluid was characterized as a transudate in 3 horses, a modified transudate in 2 horses, a purulent exudate in 9 horses, and a lymphocytic exudate in 1 horse. The total protein concentration of the exudates ranged from 2.2 to 7.9 g/dL (median, 4.0 g/dL), and the total nucleated cell counts ranged from 7,300 to 193,600 cells/μL (median, 18,650 cells/μL). No organisms were seen during direct microscopic examination of any of the samples. Bacterial culture of peritoneal fluid was performed in 7 horses and yielded pure growth of *C pseudotuberculosis* in 3 horses.

Lower portion of the respiratory tract—Infection of the lower portion of the respiratory tract was diagnosed in 12 of 30 (40.0%) horses; 10 horses had pneumonia, and 2 had pleuropneumonia. All 12 horses had clinical signs referable to disease in the lower portion of the respiratory tract during physical examination at the time of admission. A definitive diagnosis of pneumonia was made on the basis of results of a transtracheal aspirate or thoracocentesis procedure and subsequent growth of *C pseudotuberculosis* on bacterial culture of the fluid. Thoracic radiography or ultrasonography examination was performed in all 12 horses, with the majority (8 horses) undergoing both procedures. Results of radiographic and ultrasonographic imaging were in agreement in all instances, except in 1 horse in which thoracic radiographs were interpreted as unremarkable but pleural irregularities were detected via ultrasonography. Pleural irregularities (eg, thickening and comet-tail artifacts) were the most common ultrasonographic finding (7 horses). In association with the pleural changes, 4 horses had small areas of subpleural pulmonary consolidation (4 horses) and 3 horses had larger areas of cranioventral pulmonary consolidation. Moderate to marked pleural effusion was observed in 2 horses. Mild pleural effusion was detected in 1 horse in which thoracocentesis was not performed because of the small volume of fluid. An additional horse with ultrasonographic findings of hepatopathy also had evidence of pneumonia (ie, pulmonary consolidation) on thoracic radiographs and sonograms; however, definitive diagnostic procedures were not performed in this

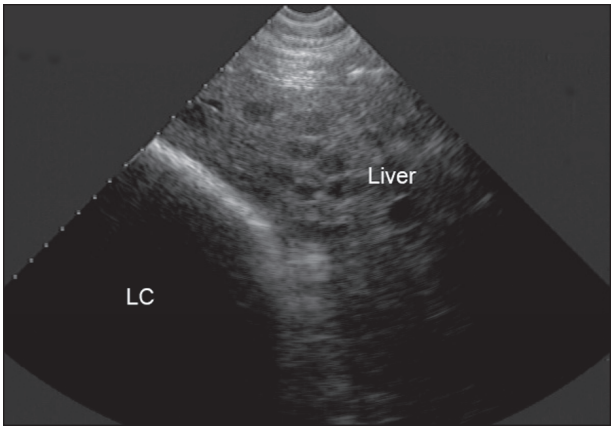

Figure 1—Ultrasonographic view of an abnormal right liver lobe in a 3-year-old horse with hepatopathy caused by *Corynebacterium pseudotuberculosis* infection. Notice the scattered hypoechoic areas that create a mottled or moth-eaten appearance. Image obtained from the right 11th intercostal space (ICS) with a 3.5-MHz sector transducer. Dorsal is to the right and ventral is to the left on all ultrasonographic images. LC = Large colon. Scanning depth = 14 cm.

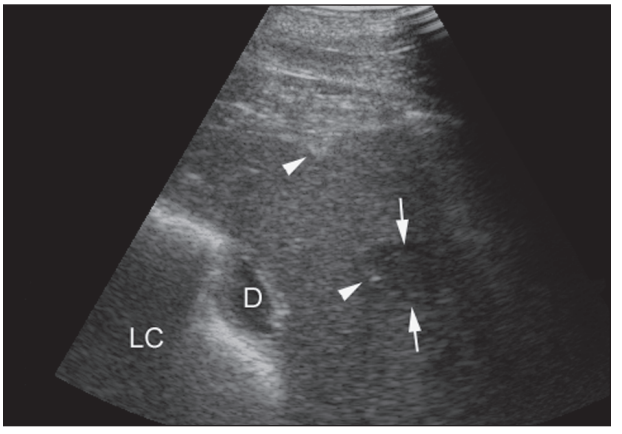

Figure 2—Ultrasonographic view of a solitary liver abscess (arrows) in the right liver lobe of a 4-year-old horse with hepatopathy caused by *C pseudotuberculosis* infection. Image obtained from the right 14th ICS with a 2.5-MHz curvilinear transducer. Arrowheads indicate areas of ultrasound-guided transcutaneous needle aspirations. D = Duodenum. Scanning depth = 13 cm. *See* Figure 1 for remainder of key.

horse to confirm that the pneumonia was caused by *C pseudotuberculosis*. Other organs were not involved in the 2 horses with pleuro-pneumonia. Pleural fluid samples from both horses were classified as exudates, with total protein concentrations of 5.7 and 6.5 g/dL and total nucleated cell counts of 38,000 and 27,500 cells/µL, respectively. In both of those horses, bacterial culture of the pleural fluid yielded pure growth of *C pseudotuberculosis*, whereas bacterial culture of fluid obtained via transtracheal aspiration yielded no bacterial growth.

Kidney—Seven horses had renal disease. Abdominal ultrasonographic imaging revealed abscess formation in 6 horses and bilateral renal enlargement in the seventh horse. Four horses had a single large renal abscess (**Figure 3**), and 2 had multiple small abscesses; abscesses were detected in both kidneys in 1 horse. In the horses with unilateral renal abscesses, the contralateral kidney was large. Ultrasound guidance was used to obtain transcutaneous renal aspirates from 2 of the horses with a single large abscess in the right kidney. Bacterial culture of the aspirates from both horses yielded pure growth of *C pseudotuberculosis*. Ultrasound-guided transcutaneous biopsy specimens were obtained in 3 horses. Histologic examination revealed chronic renal disease with fibrosis in 2 horses and bilateral nephritis and pyelonephritis in the third horse. Only 3 horses had high values for serum concentrations of BUN (32 to 67 mg/L; reference range, 12 to 27 mg/dL) and creatinine (2.1 to 6.2 mg/dL; reference range, 0.9 to 2.0 mg/dL). Two of those horses had underlying chronic renal disease confirmed via histologic evaluation, and the other had bilateral renal abscesses. Three horses with unilateral renal abscesses had serum BUN and creatinine concentrations within the reference range. Renal disease from *C pseudotuberculosis* infection was confirmed by bacterial culture of a urine sample in 1 horse, bacterial culture of a transcutaneous renal aspirate in 1 horse, and histologic evidence of nephritis and pyelonephritis coupled with other diagnostic criteria in the third horse. Abdominocentesis was performed in 2 horses in which the kidneys were the only organs involved. The peritoneal fluid was characterized as a modified transudate in 1 horse and as a mild purulent exudate in the other. No organisms were seen on direct microscopic examination, and there was no growth on bacterial culture.

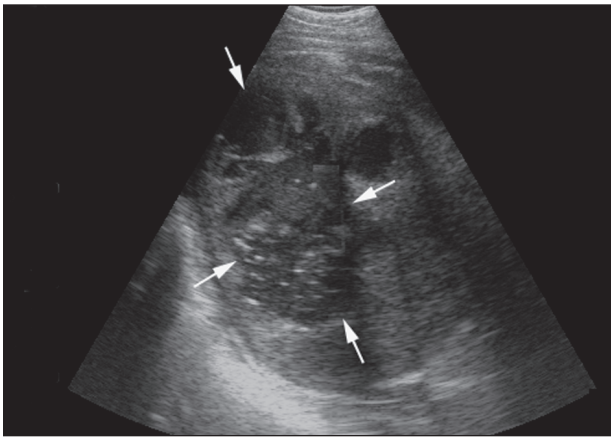

Figure 3—Ultrasonographic view of a solitary abscess in the right kidney of a 4-year-old horse with a 1-day history of pigmenturia. Notice that a portion of the renal medulla is obliterated by an accumulation of hypoechoic fluid with scattered hyperechoic foci (arrows). Scanning depth = 24 cm.

In contrast to the other organs, renal involvement was associated with greater changes in inflammatory indices. The 7 horses with renal involvement had significantly ($P = 0.02$) higher WBC counts (mean ± SD, 28,523 ± 12,841 cells/µL) than did the 20 horses without renal involvement (16,880 ± 6,462 cells/µL). Likewise, renal involvement was associated with significantly ($P = 0.02$) higher total neutrophil counts (25,054 ± 13,073 cells/µL vs 13,230 ± 5,888 cells/µL) and higher plasma fibrinogen concentrations (929 ± 431 mg/dL vs 595 ± 199 mg/dL [$P = 0.04$]) than in horses without renal involvement.

Spleen—Three horses had ultrasonographic evidence of abscesses in the spleen. In 1 horse, the spleen was the only involved organ detected; 1 horse had concurrent pneumonia and liver disease; and the other horse had concurrent pneumonia, liver disease, and renal involvement.

Treatment and complications—Antimicrobial drugs were used in the treatment protocols of 28 of 30 horses. The exceptions were 2 horses that had diarrhea at the time of initial examination in the absence of any history of recent antimicrobial treatment. Median duration of antimicrobial administration was 36 days (range, 7 to 97 days). A variety of antimicrobials to which *C pseudotuberculosis* is susceptible were used to treat internal infections. Erythromycin was used in 2 horses in 1995 but was not used in subsequent years. Rifampin was administered in combination with another antimicrobial in 19 of 28 (67.9%) horses. Rifampin alone was used for continued treatment in 7 horses after an initial period of treatment in combination with another antimicrobial. Thoracic or abdominal ultrasonographic imaging was used to monitor response to treatment in 6 horses. Five of 6 horses had improvement or resolution of the ultrasonographic findings in affected organs. Ultrasonographic findings, in addition to clinicopathologic data, aided in the decision-making process for continued antimicrobial treatment in those horses.

No horse developed severe diarrhea or life-threatening colitis as a complication of treatment. However, 5 (17.9%) horses treated with antimicrobials developed a transient change in fecal consistency 1 to 12 days after initiation of combination treatment that included rifampin. Two horses developed soft-formed feces that resolved within 9 days without modification of treatment. One of those horses was treated with rifampin and potassium penicillin G, the other with rifampin and ceftiofur. Three horses, all treated with rifampin and sodium ampicillin, developed loose feces within 2 days of initiation of administration of antimicrobials. Of those, 2 horses developed feces with a semiformed consistency but tolerated resumed treatment with ampicillin and rifampin after administration had been discontinued for several days. The third horse did not tolerate administration of ampicillin, developed signs of colic, and frequently had loose feces during IV admin-

istration. For that horse, administration of ampicillin and rifampin was discontinued for 7 days, during which time it was treated with gentamicin alone. Fecal consistency improved after 7 days and treatment with rifampin was resumed, followed by the addition of ceftiofur to the treatment regimen 2 days later. Jugular vein thrombosis associated with IV catheterization developed in 4 horses. In those instances, IV catheters were removed and the thromboses resolved without clinically important effects or interruption in treatment.

Outcome—Seventeen of 24 (71%) horses for which follow-up information was available survived and recovered. Five horses were euthanatized. One horse, with a 3-week history of illness without treatment, was euthanatized on the day of examination because of severe pleuritis, DIC, and hemorrhagic diarrhea. Two horses with histologic evidence of chronic hepatic disease responded poorly to treatment and were euthanatized after 1 week of hospitalization. Two horses were discharged and treated at home but were subsequently (within 8 weeks) euthanatized because of lack of response to treatment. One of those horses had a large abscess in the right kidney that was detected via ultrasonographically during the initial examination and had not decreased in size when rechecked 8 weeks later. Two horses died suddenly at home; 1 horse had histologic evidence of chronic renal disease, and 1 horse had histologic evidence of chronic hepatic disease. Only 1 of 4 horses with DIC at the time of initial examination survived.

The median age of nonsurvivors was 9 years (range, 5 to 16 years). Of the 17 surviving horses, clients or referring veterinarians reported that the horses made complete recoveries and returned to their original use. The horse with the greatest number of internal organs infected was a 22-year-old Arabian mare with concurrent abscesses on a hind limb and evidence of DIC at admission; that horse made a complete recovery. Horses with multiple organ involvement had a higher death rate than horses with involvement of a single internal organ system, although the difference was not significant ($P = 0.07$). There were no significant changes in clinicopathologic data that were strongly predictive of survival. Mortality rates for early versus late diagnosis were not significantly different.

Five mares were pregnant when internal infection with *C pseudotuberculosis* was diagnosed. One of the pregnant mares was euthanatized because of concurrent chronic renal failure, 3 mares aborted, and 1 gave birth to a foal that survived to discharge after being treated for failure of passive transfer. A postmortem examination was performed on an aborted fetus from a mare with pneumonia and revealed *C pseudotuberculosis* abscesses in the liver, lungs, spleen, diaphragm, kidney, and bladder. Bacterial culture of liver, spleen, and kidney tissue yielded pure growth of *C pseudotuberculosis*. The mare that gave birth to a live foal had severe pleuropneumonia with multiple loculated pleural abscesses but no apparent involvement of abdominal organs; however, abdominal ultrasonography was not performed.

Of the 30 horses, 27 were admitted to the VMTH for medical treatment, whereas the other 3 were managed by periodic outpatient visits or by visits from the Equine Field Service. For hospitalized patients, the median duration of hospitalization was 7 days (range, 2 to 35 days). The median cost of hospitalization for diagnostic evaluation and initial treatment was $2,419 (range, $477 to $6,489).

Discussion

The ages of horses with internal *C pseudotuberculosis* infections were consistent with findings from previous reports.[2,5,6,10-14] Previous studies[5,6] have not revealed a sex predilection, but mares constituted 70% of the horses in our study. This may be because of the relatively small number of horses (n = 30), compared with a report of 538 horses with internal and external infections by Aleman et al.[6] In that study, analyses of data regarding sex and internal versus external infections were not performed. The possibility that mares may be more susceptible to systemic disease should be considered. The number of mares affected in our study may also have been confounded by other variables; 11 of 14 horses kept at pasture were mares, and it is possible that pastured horses had increased exposure to flies or were not as closely observed as stabled horses.

Corynebacterium pseudotuberculosis infections typically have a seasonal occurrence in California, with most infections diagnosed during September, October, and November.[2,5,6] In our study, internal *C pseudotuberculosis* infections were most often diagnosed in November through January. This apparent 2-month difference in the occurrence of internal abscesses, compared with external abscesses, may represent a true delay in the development of internal infections, delayed owner recognition of illness, or owner delay in seeking veterinary care after development of clinical signs.

Clinical signs and clinicopathologic data associated with internal *C pseudotuberculosis* infections were not specific but were indicative of an infectious or inflammatory process. There were substantial similarities in data from horses with internal infections and data from horses with external *C pseudotuberculosis* infections[5,6] or other systemic illnesses.[14,16] Nineteen of 30 (63%) horses with internal infections in our study had concurrent or recent external abscesses, which may have masked evidence of internal infection and delayed further diagnostic investigation. Fever is not an uncommon clinical sign in horses with external abscesses and has been reported[6] in 23.5% of affected horses. Fever develops more frequently in horses with internal infection (45% to 50%); that percentage is likely an underestimate because many horses had already received treatment with antimicrobials, nonsteroidal anti-inflammatory drugs, or both prior to evaluation at the VMTH.[6] Data pertaining to clinicopathologic testing in horses in our study were similar to findings reported in other studies[6,14,16] of horses with internal abscesses caused by *C pseudotuberculosis* or other pathogens. The reason for the more marked changes in horses with renal disease is not known. Diffuse intravascular coagulation is a condition that develops secondary to many systemic disease condi-

tions and septic processes and is generally associated with a poor prognosis.[17] Three of 4 horses with DIC in our study died or were euthanatized. To the authors' knowledge, DIC has not previously been reported in association with *C pseudotuberculosis* infections.

Clinicians at our hospital have a high index of suspicion for *C pseudotuberculosis* infection in horses with histories or clinical signs that are consistent with an internal inflammatory focus and thus routinely use the serum SHI test to screen affected horses. In a previous report,[6] all horses with internal *C pseudotuberculosis* infection, and in which serum SHI titers were measured, had titers ≥ 512, leading the authors to conclude that the SHI test was a reliable aid in the diagnosis of internal abscesses. Horses with only external abscesses may also have re-ciprocal serum SHI titers ≥ 512, but 40% of those horses will not have a high titer,[6] and a complete clinical evaluation is necessary to distinguish horses with internal infection. In our study, the serum SHI titer was ≥ 512 in 27 of 28 horses. The horse that did not seroconvert was tested 3 times over a 30-day period and did not generate an antibody titer > 64. Although the findings of our study support the usefulness of the serum SHI test as a diagnostic aid for internal abscesses, they also indicate the possibility for false negatives.

Abdominal ultrasonography detected abnormalities in 18 of 22 horses in which the procedure was performed. Ultrasonography was useful not only for identifying affected internal organs but also for revealing the nature and extent of involvement (ie, whether abscesses were solitary or multiple and whether paired organs such as the kidneys were involved unilaterally or bilaterally). Importantly, abdominal ultrasonography detected involvement of specific organs in 3 horses with hepatopathy, 4 horses with renal disease, and 3 horses with splenic abscesses in the absence of clinicopathologic changes pointing to involvement of these organs. Abdominal ultrasonography also facilitated transcutaneous liver and kidney biopsy procedures and aspiration of abscess fluid, procedures that led to a definitive diagnosis. Our experience in obtaining positive results of bacteriologic culture from ultrasound-guided aspirate specimens (3/3 horses), compared with biopsy specimens (0/5), suggests that aspirate specimens of affected tissues are more likely to yield bacterial growth and hence a definitive diagnosis of *C pseudotuberculosis* infection. Serial abdominal ultrasonographic evaluations were performed in 4 horses with abdominal organ involvement. Ultrasonographic findings corresponded well with the clinical response to treatment in all 4 horses. Although recheck ultrasonographic evaluations appeared to be underutilized in this study, those 4 horses were evaluated in the last 2 years of the study. The use of abdominal ultrasonography has increased during this time, especially in horses with clinical signs that are suspicious for internal *C pseudotuberculosis* infection. Horses that were evaluated earlier in the study period were less likely to undergo follow-up ultrasonographic evaluation. Ultrasonography should be used in conjunction with hematologic and serum biochemical analyses to monitor response to treatment and may be the only available modality to monitor horses in which there is no clinicopathologic evidence of organ disease. Thoracic ultrasonographic imaging was also useful in determining the extent of involvement in horses with thoracic disease. Pleural roughening and small- to moderate-sized areas of consolidation were common findings in most horses. Pleural effusion did not appear to be a common feature of pneumonia caused by *C pseudotuberculosis* because effusion developed in only 3 of 12 horses. These ultrasonographic findings are not unique to *C pseudotuberculosis* pneumonia, but serial examination may be used to monitor response to treatment.

Corynebacterium pseudotuberculosis is susceptible in vitro to many of the antimicrobials commonly used in horses, including penicillin G, macrolides, tetracyclines, cephalosporins, fluoroquinolones, chloramphenicol, and rifampin, but it may be resistant to aminoglycosides.[18-20] Gentamicin was administered to 10 horses as part of a broad-spectrum antimicrobial treatment protocol initiated prior to definitive diagnosis. Antimicrobial treatment in horses has the attendant risk of development of diarrhea, which can be a life-threatening[21] complication. In an earlier study[6] from our hospital, 39% of horses developed diarrhea during antimicrobial treatment for internal abscesses. In our study, 5 of 28 (18%) horses treated with antimicrobials developed a change in fecal consistency and only 3 required interruption in treatment to facilitate resolution of the diarrhea. This decrease in frequency of antimicrobial-associated diarrhea is likely attributable to changes in clinician selection and use of antimicrobial drugs during the interval between the previous study (1982 to 1993) and this study. Since 2001, the preferred antimicrobial combination for long-term treatment for internal abscesses at our hospital has been rifampin with ceftiofur. Only 1 of 7 horses treated with the ceftiofur-rifampin combination in our study developed transient fecal softening. Fecal consistency returned to normal in that horse without interruption of the antimicrobial treatment regimen. In all 5 horses that developed changes in fecal consistency, treatment had commenced with 2 antimicrobials. Rifampin was one of the antimicrobials used in each of those instances; the drug was administered in combination with ampicillin (3 horses), potassium penicillin G (1), or ceftiofur (1).

To the authors' knowledge, costs of treatment of internal *C pseudotuberculosis* infections have not been reported. Mean costs of treatment for external *C pseudotuberculosis* abscesses in horses in Colorado[22] were $139 and 13 days' loss of use. In our study, because horses with internal infection often required hospitalization (median stay, 7 days) and long-term administration of antimicrobials (median, 36 days), costs associated with treatment of internal infections were substantially higher. Although the median cost of hospitalization was $2,419, the total costs to the client were probably greater because horses were usually discharged from the hospital before recovery was complete. Other costs incurred by clients that were not reflected in our estimates include non-VMTH pharmacy charges, referring veterinarian services, costs for housing affected horses at lay-up facilities with personnel that provide services such as administration of

medications and rehabilitation, and costs associated with temporary loss of use of the animal.

Internal *C pseudotuberculosis* infections have long been recognized to be associated with a poor prognosis and abortion in pregnant mares.[2-6,10-13] In our study, the overall fatality rate was 29%. Of 7 horses that died or were euthanatized, 4 had histologic evidence of underlying chronic disease in an infected organ system, most often the liver or kidneys. It is possible that chronic organ disease predisposes to infection of that organ, even though the condition was most likely subclinical and unknown to the clients.

There have been sporadic reports of *C pseudotuberculosis*–associated abortions in systemically ill[5,6,10-12] and apparently healthy pregnant mares,[7,13] which emphasizes the abortogenic potential of *C pseudotuberculosis* infection. The finding of disseminated *C pseudotuberculosis* infection in the fetus examined postmortem was consistent with findings from previous reports[7,11,13] and suggests that bacteremia in the fetus is an important mechanism of infection. Owners of pregnant mares should be informed of this potential, and efforts should be made to monitor fetal viability in pregnant mares with clinical signs consistent with internal abscesses.

a. SAS JMP, version 5.0.1.2, SAS Institute Inc, Cary, NC.

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