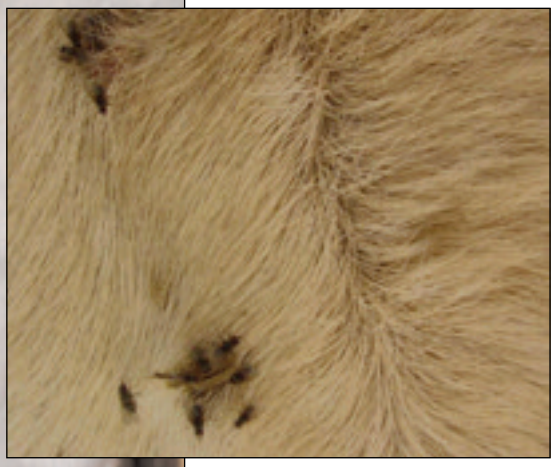
# DRYLAND DISTEMPER

## *Corynebacterium pseudotuberculosis infections in horses*

*By Sharon J. Spier, DVM, Ph.D., Dipl. ACVIM*
*Professor, Dept. of Medicine and Epidemiology, UC Davis School of Veterinary Medicine*



Deep intramuscular abscesses in horses caused by Corynebacterium pseudotuberculosis were first reported in San Mateo County in 1915.[1] Since that time, disease caused by these bacteria can be considered one of the most frequent infectious diseases in the Western United States, particularly California. Infections tend to occur both as sporadic cases on a farm or as outbreaks involving hundreds to thousands of horses in a region. The most common clinical form of the disease, characterized by external abscesses in the pectoral or ventral abdomen, is often called "pigeon fever" due to the swelling of the horse's pectoral region resembling a pigeon's breast (Figure 1), or "dryland distemper," reflecting the prevalence in arid regions of the Western United States. Two other clinical forms of the disease include internal organ involvement such as hepatic, renal, or splenic abscesses and infection of the limbs, termed "ulcerative lymphangitis."

### Etiology

*Corynebacterium pseudotuberculosis* is a gram-positive pleomorphic rod-shaped, intracellular, facultative anaerobe with worldwide distribution. In North America, cases have been reported throughout the United States. Infection has been reported in sheep, goats, cattle, buffalo, camelids, equids, and humans. Corynebacterium pseudotuberculosis grows well at 36°C on blood agar in 24 to 48 hours, and it forms small, pinpoint in diameter, whitish, opaque colonies that are surrounded by a weak zone of hemolysis.[2]

The high content of lipids may facilitate survival of the organism in macrophages.[3] Two species-specific biotypes of C. pseudotuberculosis have been identified based on differences in nitrate reduction[4], and DNA fingerprinting techniques have revealed multiple strains.[5-8] Biotypes isolated from small ruminants are nitrate negative, while those from horses are nitrate positive. Natural cross-species transmission does not seem to occur between sheep and horses, however cattle can have infection from either biotype.[4]

Corynebacterium. pseudotuberculosis produces various extracellular exotoxins, which play a role in virulence; the most studied is phospholipase D (PLD). Phospholipases are a group of enzymes that share the ability to hydrolyze one or more ester linkage in glycerophospholipids. Phospholipase D is important in the pathogenesis of the disease by its action on cell membranes causing hydrolysis and degradation of sphingomyelin in endothelial cells and increasing vascular permeability, facilitating the spread of the bacteria and persistence in the host. The bacterial phospholipase D is similar to the PLD of the brown recluse spider, which explains the presence of pain and edema at the site of infection.[9,10] The synergistic activity of C. pseudotuberculosis exotoxins with the exotoxins of Rhodococcus equi in lysing red blood cells in agar forms the basis for the synergistic hemolysis inhibition (SHI) test.[11] The SHI test is presently the most useful serologic test available to detect IgG antibody to C. pseudotuberculosis in horses with internal infections.

### Epidemiology

Three forms have been described in horses: ulcerative lymphangitis or limb infection, external abscesses, and internal infection. Ulcerative lymphangitis appears as a severe cellulitis, where the lymphatics are affected in 1 or more limbs with multiple draining ulcerative lesions. In a retrospective study of C. *pseudotuberculosis infection* in horses from California, horses with ulcerative lymphangitis comprised only 1% of the cases, whereas external abscesses occurred in 91%,

**Typical pectoral abscess (left). Horn flies on ventral midline of horse (inset).**

and internal abscesses in 8% of the cases.[12] There appears to be no breed or sex predilection for the development of the infection or for any of the three forms of disease.

The portal of entry of this soil-borne organism is thought to be through abrasions or wounds in the skin or mucous membranes. Many insects have been incriminated as vectors for the transmission of the disease to horses, and recent studies have shown that *Haematobia irritans, Musca domestica, Stomoxys calcitrans* can act as vectors of this disease.[13] The regional location of abscesses suggests that ventral midline dermatitis is a predisposing cause of infection. (Figure 2) Due to the variable incubation period, ventral midline dermatitis may not be present at the time of maturation of the abscesses.

Temporal and special analysis indicated an incubation period of 3 to 4 weeks. Within a geographic area, the disease appeared to be transmitted between 7 and 56 days throughout a 4.3 to 6.5 km distance, strongly suggesting that the disease could be transmitted through horse-to-horse contact or from infected to susceptible horses via insects, other vectors, or contaminated soil.[14] The organism has been shown to survive for up to 2 months in hay and shavings, and more than 8 months in soil samples at environmental temperatures.[15,16] The incidence of disease fluctuates considerably from year to year, presumably due to herd immunity and such environmental factors as rainfall and temperature.To date, the definitive environmental factors supporting the spread of infection have not been proven.[17] Disease incidence is seasonal, with highest number of cases occurring during the dry months of the year, which is late summer and fall in the Southwestern United States, although cases may be seen all year. Horses with internal infection are more frequently seen one to two months following the peak number of cases with external abscesses.[18]

Horses of all ages may be affected, although the low incidence of disease in foals less than 6 months of age suggests that passive transfer of immunoglobins offer protection in foals born in endemic areas. A case-control study in an endemic area revealed young adults (less than 5 years) and horses in contact with other horses on summer pasture had increased risk of infection.[19] Horses housed outside or with access to an outside paddock appeared to be at higher risk than stabled horses.[19]

## Clinical Findings

External abscesses may occur anywhere on the body, but most frequently develop in the pectoral region and along the ventral midline of the abdomen. Abscesses contain tan, odor-free pus and are usually well encapsulated. Additional sites for abscess formation are the prepuce, mammary gland, axilla, limbs, and head. Other less common areas are the thorax, neck, parotid gland, guttural pouches, larynx, flanks, umbilicus, tail, and rectum. Septic joints and osteomyelitis have been reported.[12] Horses may have an abscess involving a single site or involving multiple regions of the body. Generally, horses with external abscesses do not usually develop signs of systemic illness; however, one-quarter will develop fever.[12]

If signs of systemic illness are present, further diagnostics to rule out internal infection are warranted. The case fatality for horses with external abscesses is very low (0.8%).[12]

Clinical pathologic abnormalities that may be observed include anemia of chronic disease, leukocytosis with neutrophilia, hyperfibrinogenemia, and hyperproteinemia. These hematological parameters can occur with either internal or external abscesses but are more consistently observed with internal abscesses.

Internal infection occurs in approximately 8% of affected horses, which is associated with a case fatality rate of 30 to 40%.[12] Diagnosis can be challenging, and long-term antimicrobial therapy is imperative for successful outcome. In a retrospective study, the organs most commonly involved were liver and lungs, with kidney and spleen being affected less often. Abdominal ultrasound was a useful diagnostic technique to specifically identify affected abdominal organs[18,21] (Figures 3).

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A diagnosis of internal infection is based on clinical signs, clinicopathologic data, serology, diagnostic imaging, and bacterial culture.The most common clinical signs are concurrent external abscesses, decreased appetite, fever, lethargy, weight loss, and signs of respiratory disease or abdominal pain. Other signs observed in horses with internal abscesses include ventral edema, ventral dermatitis, ataxia, hematuria (due to renal abscesses), and uncommonly, abortion.

Serologic testing using the Synergistic Hemolysis Inhibition (SHI) test can be useful in aiding the diagnosis of internal abscesses.[11,12,21] The SHI test measures IgG to the exotoxin of C. pseudotuberculosis and is available through the California Animal Health and Food Safety Laboratory System in Davis, California. Serology is generally not helpful for diagnosis of external abscesses and may be negative early in the course of disease and even the time of abscess drainage. Positive SHI titers must be interpreted carefully and combined with clinical signs to distinguish active infection from exposure or convalescence. Both published and unpublished data from the University of California suggests a reciprocal titer of =256 is indicative of active infection. Horses with internal abscesses generally have SHI titers =512. Titers = 16 are considered negative, while titers between 16 and 128 are considered suspicious or indicative of exposure.[22] These are rough guidelines, however, as there is considerable overlap in results from horses with active disease, exposure and recovery from infection.

Ulcerative lymphangitis is the least common form seen in North America, although this form of disease has been reported worldwide. Limb swelling, cellulitis, and draining tracts following lymphatics are seen. Horses often develop a severe lameness, fever, lethargy, and anorexia. Aggressive medical therapy (antimicrobial and anti-inflammatory) is necessary or the disease often becomes chronic, resulting in limb edema, lameness, weakness, and weight loss.[2]

## Therapy

The treatment regimen for external abscesses must be individualized for each horse depending on the severity of disease, including the presence of systemic illness such as fever or anorexia, the extent of soft tissue inflammation, the maturity of the abscess, and the ability to successfully establish drainage of pus. Establishing drainage is the most important treatment and ultimately leads to faster resolution and return to athletic performance. The proximity of the fibrous abscess capsule to the skin varies, often being <1 cm deep for ventral midline abscesses, to greater than 10 cm deep underlying muscle for some pectoral, axillary, triceps or inguinal abscesses. Aspiration and drainage of superficial abscesses is easily performed; however, the use of diagnostic ultrasound is helpful for localization of deeper abscesses and to judge maturity of the abscess and proximity to the skin. The abscess contents and lavage solutions such as saline with or without antiseptic should be retrieved and disposed of to prevent further contamination of the immediate environment.

## Antimicrobial Therapy

Antimicrobials are indicated for horses with ulcerative lymphangitis and for horses with internal abscesses. The use of antimicrobials for external abscesses is not necessary in most horses and may prolong the time to

resolution.[12] Antimicrobial therapy may be justified when signs of systemic illness are present—such as fever, depression, and anorexia—or when extensive cellulitis is present. Horses with deep intramuscular abscesses that are lanced and draining through healthy tissue may also benefit from antimicrobial therapy.

*Corynebacterium pseudotuberculosis* is susceptible in vitro to many antimicrobials commonly used in horses, including penicillin G, macrolides, tetracyclines, cephalosporins, chloramphenicol fluoroquinolones, and rifampin, but some isolates may be resistant to aminoglycosides.[8,23,24]

Several factors should be considered when choosing an antimicrobial. The intracellular location of the organism, the presence of exudates and a thick abscess capsule, and the duration of therapy are important as are the cost of the drug and the convenience of administration. Despite in vitro susceptibility, the nature of the bacteria and the copious exudate render certain antimicrobials ineffective for some cases. Trimethoprim-sulfa (5 mg/kg based on the trimethoprim fraction, twice daily orally) or procaine penicillin (20,000 U/kg twice daily intramuscularly) are effective for external abscesses especially on the ventral midline. Rifampin (2.5-5 mg/kg twice daily orally) in combination with ceftiofur (2.5 – 5 mg/kg twice daily intravenously or intramuscularly) appears highly effective for treatment of internal abscesses. Internal abscesses have reportedly responded to procaine penicillin (dose as above), trimethoprim-sulfa (dose as above), and potassium penicillin (20,000 to 40,000 U/kg four times daily intravenously).[21]

Horses with ulcerative lymphangitis or cellulitis should be treated early and aggressively with antimicrobials or residual lameness or limb swelling may occur. Typically intravenous antimicrobials (ceftiofur or penicillin G) alone or in combination with rifampin (orally) are used until lameness and swelling improves, and then therapy with orally administered antimicrobials such as trimethoprim sulfamethoxazole or rifampin are continued to prevent relapse. The time to resolution reported in one study was approximately 35 days.[12] Physical therapy, including hydrotherapy, hand walking, and wraps, as well as NSAIDs are also recommended.

## Prevention

Until a protective bacterin or toxoid is developed for horses, we can only suggest that horse owners in endemic areas practice good sanitation and fly control and avoid unnecessary environmental contamination from diseased horses. Oil-based fly repellents provide longer lasting protection than aqueous products. Presently there is no evidence that diseased horses within a stable should be quarantined, other than paying strict attention to insect control. The feed through products containing cyromazinea (a chitin inhibitor) are safer than organophosphate products and may reduce the incidence of disease by controlling vector populations. Proper sanitation, disposal of contaminated bedding, and disinfection may reduce the incidence of new cases. Proper wound care is also important to prevent infection from a contaminated environment.

Research is being performed to develop a protective vaccine for horses. A commercial bacterin-toxoid has been used in small ruminants with success and is approved in some countries.[25,b,c] The safety and effectiveness of this product has not been tested in horses. Use of an experimental bacterin-toxoid demonstrated increased SHI titers following two injections; however, the protection remains to be established. The lack of experimental challenge models to reproduce the disease, and the sporadic incidence of disease complicates research efforts.



Footnotes

a. Solitude Insect Growth Regulator, Pfizer Animal Health, USA

b. Caseous D-T, Colorado Serum Co., Denver, CO 80206

c. Glanvac 6™, Pfizer Animal Health, Australia

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