

## PIGEON FEVER AND STRANGLES

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### Introduction

Pigeon Fever and Strangles are two common abscesses that form in horses. They are a significant source of morbidity in horses in the state of Texas with a recent increase in the number of Pigeon Fever cases (2009-2012). This paper will review what is known about both infections. Readers are directed to the text *Equine Infectious Disease* by Sellon and Long and to the 2005 ACVIM consensus statement on Strangles as two excellent additional resources.

### Pigeon Fever

Pigeon Fever is the common term for an infectious disease caused by the bacteria *Corynebacterium pseudotuberculosis*. The bacteria lives in the soil and survives best in drought conditions. The organism enters the skin through fly bites, abrasions, or lacerations where it then spreads via lymphatics to local lymph nodes. External abscess formation with or without lameness is the most common clinical presentation (91% of cases), with cases of internal abscesses (8%), and ulcerative lymphangitis (1%) seen less frequently. The disease is not new to Texas; however, its incidence appears to fluctuate in our state rather than being a commonplace diagnosis in states such as California, Nevada, and Utah. Equine veterinarians are challenged with providing the best care while also easing the minds of worried owners. The many presentations of *Corynebacterium pseudotuberculosis* infection, methods of diagnosis, treatment, and prevention of outbreaks are reviewed.

### *Etiology and Pathogenesis*

*Corynebacterium pseudotuberculosis* infection occurs as caseous lymphadenitis in small ruminants and granulomatous or visceral infection in cattle. Strains appear to be species-specific based upon biotyping, with nitrate positive isolates identified in equine infections, nitrate negative isolated involved in small ruminant infections, and both positive and negative isolates identified in cattle. As such, cross transmission from small ruminants to horses does not appear to occur and transmission between cattle and horses is theoretically possible but not confirmed.

The organism enters the horse through the skin via biting insects, mucous membranes, or abrasions although the exact mechanism is unknown. Direct transmission (horse to horse) does not appear to occur as consistently as with strangles, and horses kept in stalls are at a decreased risk of disease. The organism produces a variety of exotoxins, the most clinically significant of which is phospholipase D and sphingomyelinase. These toxins degrade the endothelial cell wall, increasing vascular permeability resulting in the significant edema observed with external abscesses. Phospholipase D and corynomycolic acid activity contribute to the inflammation, pain and edema observed during abscess formation. The synergistic hemolysis action of sphingomyelinase with *R. equi* exotoxin is the basis for diagnostic serology using the synergistic hemolysis inhibition test (SHIT). Incidence of disease can vary year to year on a single property, but once a single case is observed, the property is considered to be at risk for years as the organism survives in the soil. Horses present at any time of year with both external and internal abscess.

### *External Abscess*

The vast majority of horses infected (91%) will present with abscesses involving the peripheral lymph nodes, with the cervical and ventral chains being the most commonly affected. Infection of the lymph nodes deep to the pectoral muscles or at the thoracic inlet will lead to significant swelling of the soft tissues in the pectoral region and proximal forelimb. Some horses may present for lameness in the case of abscesses of the pectorals and especially with abscesses deep to the triceps muscles. Others may present for suspected trauma, as initial symptoms may go unobserved and the ruptured abscess is the first sign noticed. Abscesses along the ventral abdomen may resemble *Culicoides* hypersensitivity and abscesses of the inguinal lymph nodes may present with swelling of the sheath or around the mammary gland.

### Diagnosis

Diagnosis of pigeon fever abscesses is often made based upon swellings in specific areas of the body and the presence of characteristic thick, green-tan, purulent exudate. Culture of the discharge will confirm nitrate positive *Corynebacterium pseudotuberculosis*. Use of serology for the diagnosis of external abscesses is unreliable, as some horses do not mount an antibody response to external infection. The typical progression of an external abscess will involve soft tissue inflammation and edema surrounding the lymph node. This stage may be

accompanied by a significant amount of discomfort as the swelling becomes firm as it enlarges. About a quarter of infected horses will develop fevers up to 104°F. The abscess generally matures, resulting in hair loss and rupture of the skin allowing the abscess to drain; however, many times veterinarians will be asked to intervene and open the abscess prior to full maturation.

#### Treatment

As with Strangles, lancing and drainage is often the only treatment required for external abscesses. Many Pigeon Fever abscesses are deep to muscles (pectoral and triceps) and use of ultrasound to guide lancing is beneficial. Daily flushing of the wound with saline or water for a period of 3-5 days will often result in resolution of the infection. Care should be taken to prevent excessive contamination of the environment during lancing and flushing of the wound, and owners should attempt fly control to prevent both further infection of the wound and transmission of the organism to other horses. Systemic administration of antimicrobials is generally not recommended as it does not shorten the course of the disease and in some cases may actually prolong the clinical course; however, persistence of active drainage beyond two weeks or repeated occurrence of infection may indicate a need for antibiotics. The organism is sensitive to most antimicrobials, and duration of administration will vary depending on the severity of the infection. A period of 10 to 28 days is generally effective for the treatment of complicated cases of external abscessation.

#### ***Internal Abscess***

Internal infection and abscess formation can be significant and should be included in the differential list for any horse presenting to equine veterinarians for weight loss and general malaise, with or without fever. Many cases of internal infection will be identified in horses that have either had external abscesses (63% of cases) in the preceding months or reside on premises where external abscesses have been diagnosed in other horses; however, there will be some horses that present without this history. The organism appears to have a predilection for the spleen, liver, and kidney. Reports of pneumonia, pericarditis, pleuritis, peritonitis, osteitis, otitis and meningitis are also described. As with bastard Strangles, solitary abscesses of mesenteric lymph nodes may also occur.

#### Diagnosis

The diagnosis of internal infection with *Corynebacterium pseudotuberculosis* is best determined by use of serology by synergistic hemolysis inhibition. Titers  $\geq 1:512$  combined with appropriate clinical signs, leukocytosis, and hyperfibrinogenemia is considered diagnostic for the presence of internal abscesses. Serial monitoring of titers is not useful in evaluating response to therapy as titers can remain elevated for months to years following resolution of infection. Other abnormalities on biochemical profiles may be present depending on the site of infection, with elevations in hepatic enzymes frequently observed with liver involvement. Imaging of the infected tissue by ultrasound in organ involvement or radiography in bone involvement is very useful in the diagnosis and monitoring of response to therapy. Resolution of abnormalities in architecture based on ultrasound combined with improvement in blood cell counts and biochemistry values is useful in determining when to stop treatment.

#### Treatment

Therapy for internal infection requires long term antimicrobial therapy using site of infection and penetration requirements to guide antimicrobial selection, as the organism is susceptible to most antibiotics. A combination of broad-spectrum antimicrobial with rifampin appears to be effective in the vast majority of cases. Duration of antibiotic administration should be a minimum of 28 days and in the author's experience averages approximately 2-4 months. In one retrospective study, median duration of antimicrobial administration was 34-42 days (range 28-97 days).

Mortality is reported to be high in cases of internal infections (40% with treatment); however, this number is based upon an older study in which cases evaluated had advanced disease at the time of diagnosis. Clinical experience is that most cases will respond to appropriate antimicrobial and supportive therapy; however, this comes with a large financial and time commitment on the part of the owners. Left untreated, cases of infection within the abdominal cavity are 100% fatal.

#### ***Ulcerative Lymphangitis***

Horses with ulcerative lymphangitis usually have a concurrent external abscess and present with significant swelling of the distal limbs with multiple areas of drainage along lymphatics. Differentials include cellulitis of other causes and purpura hemorrhagica. This is the rarest presentation of *C. pseudotuberculosis* infection in horses, observed in less than 1% of cases.

## Diagnosis

Diagnosis is based upon concurrent external abscessation, compatible clinical signs, and identification of the organism by culture of exudative material. Biopsy of the skin and subcutaneous tissues may be performed as well and Strep M titers performed to rule out purpura hemorrhagica resulting from *Streptococcus equi* var *equi*.

## Treatment

Therapy for ulcerative lymphangitis is similar to that of any other bacterial cellulitis and includes supportive care, bandaging, cleaning of draining abscesses, and antibiotic administration.

## Prevention

Currently there is no vaccine available for the control and prevention of *C. pseudotuberculosis* infection. As such, the best method of prevention is good sanitation, removal of waste, and fly control. Use of a feed-through insect regulator seems to be effective in reducing the number of biting insects on individual properties, and it's important that all horses on the property receive the feed through. While treating pigeon fever abscesses, it is recommended that environmental contamination be reduced by either treating in areas easily disinfected with concrete or rubber flooring or collected purulent material from the initial lancing in a waste container rather than letting it hit the ground. Further, some large boarding facilities may consider requiring infected horses be kept in individual stalls until the drainage has ceased. As with other infectious diseases, practicing some light biosecurity may be beneficial in terms of cleaning infected stalls last, sanitizing grooming equipment, and thoroughly disinfecting stalls where infected horses are kept.

## Strangles

Strangles is the common term for an infectious disease caused by the bacteria *Streptococcus equi* var *equi*. It causes abscessation of lymph nodes, most commonly of the upper respiratory tract.

## Etiology and Pathogenesis

As a member of group C streptococcus, *Strep equi* is a gram positive cocci that can be differentiated from *Streptococcus equi* zoepidemicus by the lack of fermentation of lactose and sorbitol. *Strep equi* has a variety of virulence factors including a nonantigenic hyaluronic acid capsule, streptolysin S, streptokinase, IgG, Fc-receptor protein, pyrogenic exotoxins, peptidoglycan, and the antiphagocytic M protein (SeM). The capsule inhibits the phagocytic ability of neutrophils. Additionally the M protein also has antiphagocytic properties which inhibit complement function. The M protein is highly conserved across *Strep equi* species, except for some chronic guttural pouch infections. The organism is transmitted directly and indirectly from horse to horse. Once ingested or inhaled, *Strep equi* attaches to cells in the crypt of pharyngeal tonsils and quickly moves intracellular. Translocation occurs to the lymph nodes draining the head where abscesses develop. Most abscesses occur in the pharyngeal region but metastasis to other lymph nodes can occur via hematogenous and lymphatic spread. Development of abscess outside of the pharyngeal tissue is a condition known as "bastard strangles".

Bacteremia occurs on day 6 to 12 in horses inoculated with intra-nasal virulent *Strep equi*. The first clinical sign of infection is a fever on day 3 to 14 after exposure associated with release of the pyrogenic exotoxins. Lymph node abscess develop rapidly which is frequently accompanied by lymph edema. Nasal shedding begins 4 to 14 days after exposure and can persist for years, although most cease after resolution of the clinical disease in 3 to 7 weeks. 75% of horses will develop immunity after a *Strep equi* infection, leaving 25% susceptible to reinfection within months of resolution. Local mucosal and humoral immunity develops against M protein although the development of local and serum antibody responses are independent of each other. Foals are protected when colostrum IgA and IgG recirculate to the nasal mucosa.

## Epidemiology

Purulent discharge is an easily recognizable source of contamination and transmission. Indirect transmission occurs through sharing of contaminated husbandry equipment, especially water. There are limited studies on environmental persistence of *Strep equi*, with some studies showing up to 60 days in some laboratory conditions, although recent reports (CVJ 2009) show a limited survival (< 3 days) in outdoor environments. As such the most important source of *Strep equi* exposure is other horses. Transmission of *Strep equi* can occur from asymptomatic carrier horses. These cases are occasionally early in the course of a clinical disease, but more commonly are horses harboring the organism in the upper respiratory tract after resolution of the clinical disease. Some horses may harbor *Strep equi* for years in the sinus and guttural pouch. These horses continue to shed low

levels of bacteria in the normal nasal secretions. Identification of these animals can be challenging, and can be accomplished with nasopharyngeal lavage with PCR testing. Surface bacteria in the pharynx turnover rapidly and identification of DNA in this location is indication of an active infection or colonization. A carrier state has been proposed to occur in 10% of horse who develop guttural pouch empyema as a consequence of a Strep equi infection.

### ***Clinical Signs***

The severity of clinical signs is dependent on the horse's immunity, challenge load, and duration of exposure. The classic clinical signs include abrupt pyrexia, lethargy, and lymph node swelling. The fever may present prior to any other noticeable change. As lymphadenopathy develops horses may develop significant pharyngitis with dysphagia.

Other clinical signs affecting local neurologic function may develop depending on where in the pharynx the abscess develops. Squeezing of the larynx will often cause marked pain, retching, and elicit a cough. The abscesses will then mature and rupture. The observation of large quantities of purulent exudate from the nostrils when the horse has its head down, when the horse is eating, or when the horse is coughing is a strong indicator of guttural pouch empyema.

20% of horses with strangles experience some type of complication which can significantly increase mortality. Complications include pupura hemorrhagica, immune mediated myositis, ulcerative lymphangitis, glomerulitis, myocarditis, metastasis, airway obstruction, and dysphagia. While not impacting mortality, development of a carrier state is a frustrating and expensive complication.

### ***Diagnosis***

Definitive diagnosis of typical Strangles case is straightforward and is based on culture of nasal swabs, nasal lavages, guttural pouch lavages, and samples aspirated from abscesses. Occasionally other beta hemolytic streptococcus or the live attenuated vaccine strain may complicate identification of *Streptococcus equi equi*. Additionally cultures from lavages early in the clinical course of the disease may not grow a positive bacteria. Nasal lavages are preferred over nasal swabs as it will sample a larger area.

Serologic tests for multiple antigens is possible, and the major serologic test is for SeM. Serology will identify horses with previous exposure to Strep equi, but not necessarily a current infection.

Testing of samples by PCR for the SeM can detect very small levels of Strep equi DNA. PCR will identify both living and dead DNA and should be confirmed with culture. In a single individual case, culture is most likely adequate for diagnosis. In a herd situation, identification of animals shedding Strep equi is important to limit the outbreak. In such cases PCR is critical to identifying the asymptomatic carrier, determining Strep equi status prior to transport or comingling, and to evaluate the effectiveness of clearing Strep equi from the guttural pouches.

### ***Treatment***

Treatment depends on the stage of disease and use of antibiotics remains controversial. Most typical cases require no treatment other than anti-inflammatories and supportive care. During an outbreak treatment of a horse with an acute fever for 5 days may be curative and prevent focal abscessation. Horses successfully treated in this manner will not develop an anamnestic immune response and will remain susceptible to subsequent infection. No experimental or clinical data exists to support the belief that use of antibiotics will increase the risk of bacteremia or "bastard strangles" Treatment of horses showing the earliest signs is an effective way to limit an outbreak in stables and barns.

Once lymphadenopathy is identified there is limited use for antibiotic therapy. Treatment will improve the initial symptoms, but delays the ultimate maturation and rupture of the abscess. Therapy in horses with lymphadenopathy is directed at maturing the abscess and improving comfort.

In cases where life threatening complications have developed (severe pyrexia, dyspnea, ect) antibiotics are indicated to reduce abscess size and inflammation. Horses that have resolved all clinical signs, but continue to test positive on nasal lavage culture or PCR may benefit from a course of systemic antibiotics and local treatment of the guttural pouch.

### ***Prevention***

Measurable immunity develops in 75% of cases recovered from Strangles for 5+ years. Multiple vaccines for Strep equi exist including adjuvant extracts of Strep equi containing SeM and attenuated live strains of Strep equi. Occasional contamination of an injection site occurs when live vaccine is given at the same time as other IM vaccines. Vaccinating in the face of an outbreak with the attenuated live strain has not been shown to increase complications. However protective immunity takes up to 2 weeks to develop and DNA from the vaccine will lead to

a false positive on subsequent PCR testing for 4 to 6 weeks. Prevention of additional cases is an important aspect of treatment in a herd. Shedding does not typically begin for 1 to 2 days after a fever is identified allowing for quarantine of pending cases. One method of handling a herd outbreak is to isolate clinical cases and segregate additional horses into test positive, pending, and test negative groups. It is important to not contaminate twitches or other equipment when doing nasal lavages and use of sedation and lip chains enhances this process. This method will identify carrier horses allowing for treatment and potentially eliminating Strep equi from an endemic herd.