Strangles: Portrait of an Equine Plague
Is there anything new?

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Strangles is a highly contagious disease, primarily of the equine upper respiratory tract, caused by *Streptococcus equi* subsp *equi.* It is categorized as a gram-positive β hemolytic cocci within Lancefield group C and has been the bane of horses for centuries. First reported by Jordanus Ruffus in 1251 it has remained relatively unchanged (genetically) and remains one of the most commonly diagnosed contagious diseases of horses worldwide. There is good evidence that *S.equi* evolved from a common ancestral strain of *S. equi* subsp. *Zooepidemicus.* Recent research has identified key features in the *S.equi* genome, which occurred during its evolution from an ancestral strain of *S.equi* spp *zooepidemicus*, which may enhance its ability to evade host innate immune responses and rapidly multiply in the diffuse tonsillare tissue of horses. The microbe can survive in water sources for over a month but recurrent infections are primarily due to asymptomatic carriers enabling *S. equi* to persist for years and continue to infect naïve horses. The economic impact of strangles on the equine industry is significant due to the high prevalence of the disease with estimates suggesting 30% of upper airway infections in horses worldwide are attributable to *S.equi*.

Natural infection results from direct contact with either an infected or asymptomatic carrier horse that has maintained the organism within chondroids in the guttural pouches. Fomite transmission may also occur when environmental conditions are suitable for maintaining the organism (nasal secretions) on contaminated clothing or cleaning gear. Typical morbidity rates will approach 100% in some cases with reported complications of < 10% of affected individuals. Recovering horses may continue to shed the organism for at least 6 weeks following clinical resolution and this is a major risk factor for disease transmission to naïve horses. Following recovery from disease, approximately 75% of horses develop solid immunity to further *S.equi* infection.

Key Features of *S.equi* Pathogenesis include:

- Shedding is not initiated until 1 or 2 days after the onset of pyrexia. New cases should be isolated immediately.
- Nasal shedding persists for 2 or 3 weeks in most horses. Persistent guttural pouch infection may result in shedding for years.
- Field and experimental data support the conclusion that disease severity is dependent on challenge load and duration.
  (Sweeney C, et al. ACVIM consensus statement. J Vet Intern Med 2005;19:123)

Clinically, *S. equi* infection is most common in horses less than 5 yrs of age as disease is very uncommon in young foals (< 3 months of age) born to mares previously exposed to the bacterium. Adequate passive transfer (colostral antibodies) will confer protection during the first several months of life. Milk from mares that have recovered from *S.equi* contains IgA and the IgG- isotype, IgGb that are likely protective for suckling foals. Strangles is characterized by an abrupt onset of fever (>101.5 F), mucopurulent nasal discharge and abscess formation in the submandibular and retropharyngeal lymph nodes. Pharyngitis will cause dysphagia, and affected horses may become anorexic and have signs of depression and listlessness. Mature abscesses typically rupture externally although retropharyngeal lymph nodes may ultimately rupture and potentially drain into the guttural pouches causing empyema. While generally limited to the lymph nodes of the upper airway, *S. equi* can spread (hematogenous) to distant sites including lungs, mesenteric lnn, and brain. Hematological abnormalities include leukocytosis with a neutrophil count of 25,000 cells/μL and a plasma fibrinogen concentration > 600 mg/dL. Nasal shedding of S equi usually begins 2 to 3 days after onset of fever and persists for 2 to 3 weeks in most animals. Some animals that remain asymptomatic and may have pre- existing immunity never exhibit detectable shedding. In others, shedding may persist much longer should infection persist in the guttural pouch or the sinus.

Systemic and mucosal immune responses are evident 2 to 3 weeks after infection and coincide with mucosal clearance.

Environmental persistence of S equi

S equi remains viable in water for 4 to 6 weeks, but not in feces or soil. Despite older literature claiming extended survival in the laboratory setting, recent studies using real world scenarios showed rapid death (1-3 days) of the bacteria on fencing and soil. S equi is sensitive to bacteriocins from environmental bacteria and does not readily survive in the presence of other soil borne flora.

Diagnostic Testing

Along with clinical signs and hematologic abnormalities, definitive diagnosis is based on aerobic culture of nasal secretions, preferably obtained from the guttural pouch or a pharyngeal wash or cytology brush. Detection of *S.equi* DNA utilizing PCR testing has proven beneficial. However, PCR cannot distinguish between dead or live organisms and a positive result must be considered presumptive until confirmed by bacterial culture. Quantitative PCR or other PCR formats are approximately three times more sensitive than culture. Generally, use of PCR testing of an endoscopically guided guttural pouch lavage for detection of S equi in subclinically infected carrier animals is ideal.

SeM Antibody Titer: Antibody titers to SeM minus its carboxy terminus (currently commercially available in the United States and Europe) peak about 5 weeks after exposure and remain high for at *least* 6 months. Given the possibility that antibodies directed against SzM of S *zooepidemicus* could cross-react with SeM., incubation of sera with heat-killed *S. zooepidemicus* to remove cross-reactive antibodies should be performed to enhance test specificity. SeM specific titers cannot be used to determine carrier status and a single determinate is not a measure of active infection. Titers will wane over time and horses that received antibiotic therapy during an outbreak appear to have a reduced immune response and may remain susceptible to reinfection.

Treatment

Management of horses suffering from strangles can be most challenging as morbidity in a naïve population is very high. Horses with overt clinical signs generally do not present a diagnostic dilemma. However, other horses on the premises should be very closely monitored and strict biosecurity measures implemented. Treatment strategies vary and generally depend on the stage and severity of the disease. Opinion as to whether or not to implement antibiotic therapy is controversial as the majority of cases will require only supportive therapy. If antibiotic treatment is indicated, *S.equi* is consistently sensitive to the B-lactam class (penicillins and cephalosporins). Other classes include the macrolides and trimethoprim-sulfadiazine, keeping in mind that antibiograms may not translate into in vivo efficacy.

I. Horses either exposed or with very early clinical signs (fever spike, anorexia); these horses should be treated with penicillin (22,000U/kg) according to manufacturer's instructions for a minimum of 5 days. If there is no clinical progression, antibiotic therapy may be discontinued.
II. Horses with lymph node abscessation; administration of penicillin in these cases may slow the progression and ultimate resolution of disease. Therapy should be directed toward enhancing maturation and drainage of the abscesses. The administration of NSAID's may improve the horse's demeanor and encourage eating and drinking.
III. Horses with complications; severe cases of *S.equi* infection generally require aggressive supportive therapy such a s IV fluids and penicillin.

Antibiotics may be indicated in some cases, although these are always at the discretion of the attending veterinarian including;

- acutely infected animals with very high fever and malaise prior to abscess formation
- horses with profound lymphadenopathy and respiratory distress
- horses with metastatic abscessation
- cases of purpura hemorrhagica treated with corticosteroids

- guttural pouch infections treated locally and systemically to eliminate the carrier state.
- Antibiotics should NOT be used as a preventative in animals that may have been exposed. Overuse of antibiotics, promotes resistance, provides a false sense of security, and convalescent immune responses may not be induced.

A recent study involving an outbreak on a large Standardbred farm was controlled by the use of CCFA (ceftiofur crystalline free acid). Other than this report of long acting ceftiofur use during a large strangles outbreak improving treatment compliance and resulting in final resolution, there are no data on its efficacy *in vivo*. The interested reader is referred to the 2005 ACVIM consensus statement for *Streptococcus equi* Infections in horses at http://www.acvim.org for a detailed description of treatment options.

Prophylaxis from *S.equi* infection

Management and biosecurity measures are critical for prevention and spread of *S.equi* infections. Segregation of new arrivals along with any history of recent respiratory disease carefully investigated. New arrivals should have a pharyngeal wash or guttural pouch lavage to obtain samples for PCR analysis. In cases where exposure to *S.equi* has possibly occurred it is recommended that serum titers against SeM protein be monitored. A recent study suggests the current recommendation by laboratories that provide SeM ELISA is not to vaccinate when the titer is $\geq$ 1:3,200 and not the previously recommended titer of 1:1,600. (Boyle A. Detection of S.equi in wash samples and SEM titers following strangles outbreaks. Proceeding of ACVIM forum. 2012)

Vaccination is indicated where disease transmission either has or is likely to occur. Subunit and attenuated live vaccines are commercially available for intramuscular and intranasal administration respectively. Recent studies have indicated commercially available attenuated live vaccine may be administered *Per Os*.

References available on request.