EQUINE STRANGLING:
An update on recommendations for diagnosis, treatment, and prevention including long-term local eradication

Emily A. Graves, VMD, MS, Dipl. ACVIM

One of the most important challenges facing equine practitioners is to effectively control and help prevent highly contagious Streptococcus equi ssp equi infections, or strangles. Strangles is not only one of the most frequently diagnosed infectious diseases of horses worldwide,1-3 but it also has a number of potentially fatal complications and the capability of persistent infection in populations of asymptomatic carrier horses.4-10 In fact, it is estimated that half of all strangles outbreaks produce at least one carrier horse, creating a reservoir of chronically infected animals that perpetuate the disease in the highly mobile equine population.6,11 When complications occur, strangles changes from a self-resolving upper respiratory infection to a disseminated disease with a mortality rate as high as 40%.10 As one expert has noted, strangles is "a highly dangerous disease" and detection of S. equi ssp equi in any horse is significant.6

While our understanding of S. equi ssp equi and the pathogenesis of strangles has grown, the typical approaches to controlling the disease have not advanced appreciably in the past decade. As a result, strangles continues to be widespread, clinically significant, and economically damaging to the equine industry. The National Animal Health Monitoring System (NAHMS) compiled epidemiologic data from more than 1,000 farms in all regions of the U.S. This extensive survey found that strangles was the cause of approximately 20% of infectious upper respiratory disease in horses, the obligatory host species.12 Other studies have reported much higher morbidity rates in susceptible populations. For example, University of Pennsylvania investigators identified a 1-year old horse as the index case in a strangles outbreak that resulted in confirmed S. equi ssp equi infections in 61% (31/51) of horses with clinical strangles.9 A European study of three protracted strangles outbreaks found that between 29 and 52% of horses had laboratory confirmed S. equi ssp equi infections.11 S. equi ssp equi has an estimated 80% contact attack rate in susceptible horses.6 In addition, morbidity of >90% and mortality of 10% of clinical cases have been reported.4,13

Given the imposing epidemiology and pathology of strangles, it is advisable to have a clearly defined strategy for diagnosing the disease, managing outbreaks, and helping prevent their recurrence. Recognizing this, the American College of Veterinary Internal Medicine (ACVIM) developed a definitive Consensus Statement in 2005 that the American Association of Equine Practitioners (AAEP) considers to be the principal guideline document for managing strangles.10 Some of the key aspects of the ACVIM Consensus Statement are summarized in this report. These include a suggested protocol for identifying carrier horses, the all-important source of endemic disease and acute outbreaks. Also discussed is an approach for strangles eradication at the local level, a realistic option that can help curtail the widespread economic loss that this disease inflicts on the equine industry.

RECOGNIZING STRANGLING

In susceptible horses, abrupt onset of fever of 103°F or higher is usually the first sign of strangles, occurring 2 or 3 days after exposure and initial infection with S. equi ssp equi. This is followed several days later by serous nasal discharge that turns purulent. Suppurative lymphadenopathy is the most prominent feature of uncomplicated strangles. Swollen, painful lymph nodes appear about a week after infection. The submandibular, retropharyngeal, and parotid lymph nodes are most commonly affected, often asymmetrically. As the lymph nodes enlarge, upper respiratory obstruction accompanied by dyspnea and dysphagia may develop (hence the name “strangles”) along with a resulting loss of appetite. Tracheostomy may be required in severe cases. As the lymph node abscesses increase in size, they may rupture and drain either externally through the skin or internally into the guttural pouches, offering the horse some relief. Recovery from uncomplicated strangles usually takes 3 to 6 weeks; previously exposed horses generally have a milder, catarrhal form of strangles limited to upper respiratory signs, minimal if any lymph node abscessation, and a rapid recovery. However, the host’s immune status and virulence of the infective S. equi ssp equi strain, rather than the horse’s age, are the determinants of susceptibility. Despite experiencing an attenuated disease, infected horses with some residual immunity will still shed S. equi ssp equi, contaminating the environment or infecting susceptible contact horses.10 An estimated 70-75% of horses develop a durable, post-convalvescent S. equi ssp equi immunity lasting 5 years or longer.10 Horses with a less complete immune responses may become susceptible within a few months.3,10

COMPLICATIONS OF S. EQUI SSP EQUI INFECTION: SOURCE OF INCREASED MORTALITY

Strangles is often characterized as a high-morbidity, low-mortality disease. This description is somewhat misleading because of the impact of the estimated 20% rate of non-respiratory complications. These include disseminated or metastatic ("bastard") strangles, purpura hemorrhagica, and myopathies, including muscle infarctions and rhabdomyolysis with progressive atrophy. Horses that develop these sequelae have a much less favorable prognosis. For example, an outbreak described in the ACVIM Consensus Statement resulted in metastatic strangles in 28% (7/25) of the sick horses, 5 of which had to be euthanized.10,15 Metastatic strangles, which involves S. equi ssp equi ab-
scesses that develop in lymphoid tissue at sites other than the respiratory tract, can cause gastrointestinal pain and complications when the mesenteric lymph nodes are affected. Purpura hemorrhagica is perhaps the most dramatic non-respiratory complication of strangles. This immune-mediated sequela is a necrotizing vasculitis characterized by edema and localized hemorrhage caused by deposition of S. equi ssp equi M-protein immune complexes in blood vessel walls. A retrospective case analysis of 53 horses with purpura hemorrhagica determined that 17 were infected with or exposed to S. equi ssp equi.16 Among the assortment of profound clinical and pathological effects were subcutaneous edema of all four limbs, reluctance to move, hemorrhages on visible mucous membranes, anorexia, fever, tachycardia, colic, lymph node drainage, hematologic and biochemical abnormalities, and 13.6% mortality in S. equi-associated cases.10,16 The horses involved in this study were aged <1 to 19 years of age. Although horses >5 years old tend to be more resistant to strangles,4 the age range in this study indicates that prior exposure or immune status is not protective once S. equi ssp equi complications occur.

Muscle infarction is a rare complication which can be associated with purpura hemorrhagica. A severe vasculopathy results in infarction of skeletal muscle, necrosis, muscle stiffness, and a guarded prognosis. S. equi ssp equi-associated rhabdomyolysis can produce rapid onset of progressive muscle atrophy, lymphocytic vasculitis, and perivascular fibrosis.10 When recumbency occurs in such cases, rapid deterioration can be expected despite aggressive antimicrobial and anti-inflammatory treatment.17

WHEN TO USE ANTI-INFECTIVE TREATMENT

Systemic treatment of acute-phase and metastatic strangles

Systemic anti-infective (AIF) treatment of uncomplicated, acute-phase strangles is somewhat controversial because it can conceivably limit the affected horse’s post-infection immune response, leaving it at risk for re-infection. It should be noted that this is not an evidence-based contraindication supported by experimental or clinical data. The ACVIM Consensus Statement recommends that treatment in these cases be limited to rest and supportive care until the disease runs its course.22 Horses should be monitored to ensure that they are sufficiently pain-free to continue eating and drinking. The Consensus Statement adds that AIF treatment may be of benefit (1) in new cases immediately after onset of fever by preventing abscessation and limiting the spread of strangles to other horses on the premises, and (2) to decrease abscess size and relieve airway obstruction in horses with lymphadenopathy-associated respiratory distress. Systemic penicillin treatment of horses with metastatic strangles, perhaps with other AIFs to increase the spectrum of activity, has been recommended.21

Anti-infective treatment of carrier horses

Treatment of guttural pouch empyema with saline or polyionic fluids and a local penicillin-gelatin mixture is described in the ACVIM Consensus Statement.18 An alternative protocol consists of penicillin administered locally into the guttural pouch followed by systemic treatment with procaine penicillin G for 7 days, then oral trimethoprim-sulfadiazine (TMS) for 14 days.13 Treatment of infected guttural pouches should be combined with physical removal of chondroids, which if left in place, will maintain infection and defeat the effects of AIF treatment.

Which anti-infective agent to use

S. equi ssp equi is consistently sensitive to penicillin. Although penicillin is generally acknowledged to be the drug of choice for systemic AIF treatment of strangles, ceftiofur’s activity against a broad range of S. equi ssp equi strains has also been confirmed.22 Most S. equi ssp equi isolates are also sensitive to TMS, although exceptions have been noted.4,18,19 One report noted that initial TMS treatment of guttural pouch carriers of S. equi ssp equi was unsuccessful in 33% (5/15) of cases.19 When these horses were then treated with penicillin and ceftiofur, guttural pouch infection and inflammation were eliminated. Antimicrobial sensitivity data for North American equine S. equi ssp equi isolates found that susceptibility was 100%, 97%, and 72% to ceftiofur, penicillin, and TMS, respectively.21 Widely accepted guidelines list penicillin, ceftiofur, and TMS as the first, second, and third choices respectively for AIF treatment of strangles caused by S. equi ssp equi.23 Although not specifically recommended in the ACVIM Consensus Statement, ampicillin is a member of the beta-lactam antimicrobial class along with penicillin and ceftiofur, and has been shown to have activity against S. equi ssp equi comparable to the other two drugs.23

LOCAL ERADICATION & CONTROL

When strangles outbreaks occur at multi-horse sites, the task of eradicating the disease and reestablishing biosecurity is invariably difficult and lengthy. Acutely infected and carrier horses need to be identified, isolated, and in some cases treated, followed by diagnostic monitoring of affected and suspect horses for extended periods. This process becomes more difficult as the mobility and the size of the on-site horse population increase, with premises of >100 horses being at substantially greater risk.3 Despite these hurdles, local eradication is a realistic possibility.

Observation & screening of newly arriving horses

Routine screening of horses that are introduced onto a farm can be difficult, especially at sites with a large, transient population. The ACVIM Consensus Statement recommends quarantining newly arriving horses for 3 weeks and screening them for S. equi ssp equi by multiple nasopharyngeal swabs, measures that many horse owners would consider to be onerous.39 However, to the extent possible, horses entering the premises should be observed for signs of strangles for at least 2 weeks before being mingled with resident horses.3 Horses that remain clinically asymptomatic after this period are at low risk of transmitting disease. A useful screening method short of diagnostic testing is to take daily (twice-daily is better) rectal temperatures of newly arriving horses for the 2-week holding period. Horses with temperature elevations ≥101.5°F should be considered suspect. Because fever usually precedes S. equi ssp equi shedding by 24-48 hours, prompt isolation of horses after pyrexia is detected will help prevent transmission to other horses.
Prompt identification and isolation of clinically affected or suspect horses
Clinically affected or S. equi ssp equi-positive horses should be quarantined and movement of horses on and off the premises should be stopped until all infected and contact horses are found to be diagnostically negative.

Diagnostic monitoring of convalescent or contact horses
At least 3 post-recovery nasopharyngeal swabs or lavages should be obtained at weekly intervals from convalescent horses for culturing and PCR testing. Horses that test negative on consecutive tests may be safely returned to the non-quarantine area.

Detection and monitoring of carrier status
Asymptomatic convalescent horses should be evaluated by guttural pouch endoscopy and testing of nasopharyngeal or guttural pouch lavage samples to determine if they are S. equi ssp equi carriers. As noted earlier in this report, a minimum of 3 consecutive weekly samples should be tested. Additional, subsequent tests will help provide added assurance of negative carrier status.

Treatment of guttural pouch infections and carrier horses
Topical and systemic AIF treatment should be administered to S. equi ssp equi carriers to eliminate guttural pouch infection, and guttural pouch chondroids should be removed.

Vaccination
The AAEP classifies strangles vaccination as risk-based, rather than a core, equine vaccination, meaning that vaccination should be based on a risk-benefit assessment by the attending veterinarian in conjunction with the horse owner. AAEP guidelines recommend vaccination against S. equi ssp equi on premises where (1) strangles is a persistent, endemic problem or (2) a high risk of exposure is anticipated. Risks for strangles exposure include high stocking density, frequency of travel, comingling with horses from other locations, and susceptibility due to lack of prior vaccination or natural exposure to S. equi ssp equi. Given the prevalence of strangles, its potential for causing debilitating clinical disease and costly treatment, and the presumed benefits of herd immunity, vaccination is advisable for all healthy horses that meet these risk criteria.

Two types of equine S. equi ssp equi vaccines are available in the U.S. A parenteral, inactivated S. equi ssp equi extract vaccine given in 3 primary doses has been shown to reduce the clinical attack rate by 50% in vaccinated horses. A modified-live S. equi ssp equi vaccine given by the intranasal (IN) route (Pinnacle® I.N., Zoetis Inc.) is administered in two primary doses 2-3 weeks apart followed by annual revaccination. The IN vaccine stimulates mucosal immunity in the nasopharyngeal tract, mimicking the immune response to natural infection.

Sanitation, hygiene, and pasture management on contaminated premises
Organic material that infected horses came in contact with should be removed from stables. Contaminated facilities, equipment, and vehicles should be cleaned and disinfected. To effectively disinfect, organic debris should be removed first, followed by washing with mild soap and rinsing. Several types of disinfectants are appropriate for use on S. equi ssp equi contaminated premises, including dilute bleach solutions, iodophors (povidone iodine), quaternary ammonium compounds (such Roccal-D), and Virkon. Cost and efficacy will guide the choice of disinfectant. Disinfectant labels will list those bacteria against which it is effective. Water troughs, a common site of S. equi ssp equi transmission, should receive special attention during an outbreak, including once daily cleaning and disinfection. Pastures where infected horses grazed should be rested for 4-6 weeks.

Personnel handling sick horses should observe barrier precautions, including use of disposable gloves, washing or disposal of outer garments, and use of foot baths. Handlers should perform frequent hand-washing or use of sanitizer before contact with individual horses. Handlers should also work with sick horses after all work with healthy horses has been completed.

SUMMARY
Equine veterinarians and horse owners should be vigilant for outbreaks of strangles due to the disease’s high prevalence, potentially fatal complications, and the difficulty and cost of recovery, site clean-up, and eradication. Because uncomplicated strangles is self-limiting, AIF treatment is generally reserved for horses immediately following onset of clinical signs to preempt abscessation and S. equi ssp equi transmission to other horses, horses with severe lymphadenopathy that restricts breathing, and horses with guttural pouch infections that are the source of a persistent carrier state.

Effective prevention and control of strangles is heavily dependent on physical isolation and restricted movement of sick or at-risk horses in order to limit S. equi ssp equi exposure and transmission. Isolation of affected horses should be accompanied by diagnostic monitoring of infection status based on culturing and PCR testing of nasopharyngeal swabs or lavage samples.

Recovering, asymptomatic horses infected with S. equi ssp equi are the source of long-term shedding and endemic disease. Identification of persistently infected horses is accomplished by testing of nasopharyngeal or, preferably, guttural pouch lavage samples for a minimum of 3 weeks after clinical signs have resolved. Endoscopy will further reveal S. equi ssp equi-associated guttural-pouch abnormalities such as empyema and chondroids.

Vaccination can be an important component of a strangles control program for horses in an endemic area or in frequent contact with horses of unknown S. equi ssp equi-infection status. PINNACLE I.N., a modified-live vaccine given by the IN route, has the advantage of helping confer systemic immunity, as well as mucosal immunity at the nasopharyngeal site of natural infection. IN vaccination also avoids local injection-site reactions.

Long-term eradication of strangles on premises where outbreaks have occurred can be made feasible by implementing a program of diagnostic monitoring to detect and treat S. equi ssp equi carrier horses, careful sanitation to eliminate environmental S. equi ssp equi contamination, and vaccination of susceptible, at-risk horses.
PROTECTION INDUCED BY PINNACLE I.N. HELPS PREVENT DISEASE CAUSED BY S. EQUI SSP EQUI

S. equi ssp equi produces a surface virulence factor known as the M protein (SeM), unique to streptococci. SeM inhibits phagocytosis by lymphocytes of the host's innate immune system. Horses that recover from S. equi ssp equi infection develop both serum and mucosal SeM immunoglobulins. However, mucosal SeM immunoglobulins appear to play a prominent role in protection at the local, nasopharyngeal site of initial S. equi ssp equi infection.10,24 Inactivated, intramuscular S. equi ssp equi vaccines stimulate a serum SeM immunoglobulin response but appears not to induce mucosal SeM immunoglobulins.3,25 This may explain why injectable, inactivated S. equi ssp equi vaccines help reduce the S. equi ssp equi attack rate by only an estimated 50%.10 In contrast, IN vaccination with PINNACLE I.N. has been shown to produce both serum and mucosal SeM immunoglobulins,3 an immune response that mimics what occurs following natural infection.10,24

Because it is given intranasally, PINNACLE I.N. avoids local, injection-site reactions that can occur with parenteral S. equi ssp equi vaccines.10 A field study of 582 horses given 2 primary doses of PINNACLE I.N. found that 5 of 582 first-time vaccinates had mild local or systemic reactions, and 0 of 582 second-time vaccinates had post-vaccination reactions, a 0.43% incidence (Data on file, Study Report No. 22741, Zoetis Inc.).29

After aseptic rehydration, PINNACLE I.N. is instilled into one nostril with a specially designed cannula. Proper placement of the cannula is important to ensure that vaccine is delivered to the pharyngeal area, where it can elicit a mucosal immune response at the site of natural infection.

REFERENCES