Predictor variables for and complications associated with *Streptococcus equi* subsp *equi* infection in horses

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**Objective**—To evaluate predictor variables for and complications associated with *Streptococcus equi* subsp *equi* infection (strangles) in horses.

**Design**—Retrospective case-control study.

**Animals**—108 horses with strangles (cases) and 215 horses without strangles (controls).

**Procedures**—Medical records from January 2005 through July 2012 were reviewed. Cases were defined as horses with clinical signs of strangles (pyrexia, retropharyngeal lymphadenopathy, and mucopurulent nasal discharge) that were associated with a confirmed strangles outbreak or had positive results for *S equi* on PCR assay or bacteriologic culture. Controls were defined as horses with pyrexia that did not meet the other criteria for cases. Data compared between cases and controls included signalment, clinical signs, diagnostic test results, and disease complications and outcome. Logistic regression was used to identify variables associated with strangles and its complications.

**Results**—Clinical signs of strangles were not evident in 12 of 25 cases classified as *S equi* carriers (infected > 40 days). Predictor variables associated with strangles included mucopurulent nasal discharge and external abscesses in the pharyngeal region. Strangles was more likely to be diagnosed in the spring than in the summer. Cases with anemia were more likely to develop purpura hemorrhagica than were cases without anemia. No risk factors were identified for the development of guttural pouch empyema or metastatic abscesses.

**Conclusions and Clinical Relevance**—Results indicated that not all horses infected with *S equi* develop clinical signs of strangles. We recommend that guttural pouch endoscopy and lavage with PCR assay of lavage fluid samples be performed to identify *S equi* carrier horses. (J Am Vet Med Assoc 2015;247:1161–1168)

Strangles is an acute infection of the upper portion of the respiratory tract and regional lymph nodes of horses caused by *Streptococcus equi* subsp *equi*. The disease is generally characterized by pyrexia, purulent nasal discharge, and abscessed lymph nodes. The infection is contagious, and once strangles has been diagnosed in a horse, intensive biosecurity measures must be implemented to prevent rapid spread of the disease to other horses. Although complications associated with *S equi* such as purpura hemorrhagica, bastard strangles (metastatic abscesses or culture of *S equi* from abscesses located in internal organs not associated with the upper portion of the respiratory tract), guttural pouch empyema, and streptococcal myositis have been described, the prevalence of those complications is rarely reported.1,2 During a strangles outbreak on a Standardbred breeding farm, 4 of 205 (2%) horses developed purpura hemorrhagica,3 and investigators estimate that approximately 20% of *S equi*-infected horses develop bastard strangles.4

Strangles is maintained in a population by carrier horses that are subclinically infected with and shed *S equi*. Identification of those carrier horses is important because they can reinfect their cohorts or transmit the infection to naïve horses. Although the identification and treatment of *S equi* carriers have been described,5 information regarding the prevalence of carriers is lacking. Six of 1,850 (0.3%) horses were identified as *S equi* carriers during a strangles outbreak on a farm in the United Kingdom6; however, the investigators of that outbreak acknowledged that the true prevalence of *S equi* carriers on that farm was likely underestimated.7 The aims of the study reported here were to evaluate predictor variables for strangles in horses; determine the prevalence of *S equi* carriers and strangles-associated complications such as guttural pouch empyema, purpura hemorrhagica, and metastatic abscesses; and identify variables associated with the development of those complications.

**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>CI</th>
<th>IQR</th>
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<tr>
<td>Confidence interval</td>
<td>Interquartile range</td>
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Materials and Methods

Animals—The study had a retrospective case-control design and involved review of medical records of horses examined by the William H. Boucher Field Service Section of the George D. Widener Hospital for Large Animals at the University of Pennsylvania New Bolton Center from January 2005 through July 2012, and as such, the study did not require review by the university’s animal care and use committee. A board-certified large animal internist (AGB), a board-certified equine veterinary practitioner, or a clinician mentored by those specialists was the primary care veterinarian for all horses enrolled in the study. Therefore, the investigators had access to all medical records prior to, during, and after strangles outbreaks as well as client records that included information such as descriptions of clinical signs and results of rectal temperature monitoring. Cases were defined as horses in which strangles was definitively diagnosed on the basis of positive results for S equi as determined by PCR assay or aerobic bacteriologic culture or horses with classic clinical signs of strangles (pyrexia, submandibular or retropharyngeal lymphadenopathy, and bilateral mucopurulent nasal discharge) that were housed on the same premises as an S equi test-positive horse during the study observation period. Controls were defined as horses examined during the observation period that had a rectal temperature ≥ 38.6°C (101.5°F) but did not otherwise meet the criteria for a case.

Data collection and analysis—For each horse enrolled in the study, information extracted from the medical record included owner, farm of residence, signalment, clinical signs, season of onset of clinical signs (spring [March through May], summer [June through August], fall [September through November], or winter [December through February]), diagnostic test results (when available), treatments administered, complications, whether the disease recurred (clinical signs recurred after a period of complete absence), and S equi vaccination status. Age was recorded as both a continuous and categorical variable (< 2 years, 2 to 7 years, or > 7 years). Rectal temperature was recorded as both a binary (pyrexic [≥ 38.6°C] or normal) and categorical variables (normal [37.2 to 38.5°C (99.0 to 101.4°F)], mild pyrexia [38.6 to 39.3°C (101.5 to 102.7°F)], moderate pyrexia [39.4 to 40.5°C (102.8 to 104.9°F)], or severe pyrexia [≥ 40.6°C (≥ 105°F)]). Clinical signs such as mucopurulent nasal discharge, submandibular and retropharyngeal lymphadenopathy or abscesses (with or without rupture), neurologic deficits (change in mentation, ataxia, cranial nerve deficits, or seizure activity), lethargy, and edema (palpable or visual swelling in the distal portion of the limbs or dependent areas of the abdomen, udder, prepuce, pectoral region, or head) were recorded as either present or absent. Hematologic and biochemical abnormalities were likewise recorded as present or absent. Anemia was defined as an Hct < 30%, hemoglobin concentration < 11.6 g/dL, or BRC count < 6.2 × 10^6 RBCs/µL. Hyperfibrinogenemia and severe hyperfibrinogenemia were defined as fibrinogen concentration ≥ 400 mg/dL and ≥ 700 mg/dL, respectively. Leukocytosis and severe leukocytosis were defined as a WBC count ≥ 10.3 × 10^3 WBCs/µL and ≥ 12 × 10^3 WBCs/µL, respectively. Thrombocytopenia was defined as a platelet count < 72 × 10^3 platelets/µL. Hyperbilirubinemia was defined as a bilirubin concentration > 1.9 mg/dL. Horses were considered vaccinated against strangles if they had received an intranasal S equi vaccine within 24 months before the onset of clinical signs.

Aerobic bacteriologic culture and PCR assay results were recorded when available. Also recorded were data regarding the sample type (nasal swab specimen or fluid obtained during nasopharyngeal or guttural pouch lavage) and collection time relative to the onset of clinical signs and initiation of antimicrobial administration.

For each horse, information recorded regarding treatment included the class of systemic antimicrobials administered and whether penicillin was infused into the guttural pouch. Duration of hospitalization (when applicable) and survival time were also recorded. Long-term follow-up data were recorded from primary care records and telephone conversations with the owner when available. Complications such as metastatic abscesses (culture of S equi from abscesses located in internal organs not associated with the upper portion of the respiratory tract), purpura hemorrhagica (defined as substantial edema in the limbs with concurrent petechiation or ecchymoses with or without histologic evidence of vasculitis), guttural pouch empyema with or without chondroids as determined by endoscopy, streptococcal myositis, and respiratory distress were recorded as present or absent. The S equi status of each horse was also recorded. For the purpose of the study, an asymptomatic positive was defined as a horse with positive results for S equi as determined by PCR assay or bacteriologic culture that did not have clinical signs of strangles when the tested sample was acquired. A carrier was defined as a horse that still had positive results for S equi as determined by PCR assay or bacteriologic culture ≥ 40 days after strangles was initially diagnosed. Serial PCR assays for S equi were performed on carrier horses until a negative result was obtained on 1 guttural pouch lavage fluid sample or 3 consecutive nasopharyngeal lavage fluid samples. The duration of the carrier status was defined as the number of days from the onset of clinical signs or first positive test result for S equi (whichever was first) until the criteria for discontinuing serial testing were met.

Descriptive data were generated for both cases and controls. For some variables, information was not available for all study horses; therefore, the number of horses assessed varied among variables and is reported when necessary. The distribution of the data for continuous variables was evaluated for normality with the Shapiro-Wilk test. Results for continuous variables were reported as the median (IQR [25th to 75th percentiles]). Percentages were used to describe the results for binary and categorical variables. Univariate logistic regression was used to evaluate associations between potential predictor variables and the presence of strangles (ie, probability of being a case). Variables with P < 0.10 on univariate analysis were included in a multivariable logistic regression model. Because many of the predictor variables included in the multivariable logistic regression model had complete separation (the outcome var-
able completely separates the predictor variable [eg, the predictor variable was present in all cases but was not present in any of the controls)]. Firth logistic regression was used as described. Firth logistic regression was also used to identify variables associated with the development of purpura hemorrhagica, guttural pouch empyema, metastatic abscesses, and carrier status. Case status (case or control) was considered a confounder for each of those models and therefore was maintained as an independent variable in the respective final models. For each outcome of interest, the final multivariable regression model included only variables with \( P \leq 0.05 \), and the ORs and associated 95% CIs were calculated for those variables. Examination for confounding at the owner, farm of residence, and outbreak level was attempted, but there were too many owners and farms with too few horses represented in the study for it to be adequately assessed. All analyses were performed with commercially available statistical software.

**Results**

**Horses**—From January 2005 through July 2012, the ambulatory service examined 8,308 horses, of which 108 (1.3%) had strangles (cases) and 215 (2.6%) had pyrexia without clinical signs of strangles (controls) and met the criteria for study enrollment. The cases were owned by 65 individual owners and were housed at 37 farms. None of the cases were involved in >1 strangles outbreak. Long-term (range, 2 months to 9 years after the end of a strangles outbreak) follow-up information was available for 71 cases, and no additional complications associated with strangles such as purpura hemorrhagica or metastatic abscesses were recorded. The controls were owned by 157 individual owners and were housed at 103 farms. Twenty-three distinct conditions were diagnosed in the controls, with the most common being external abscesses (n = 35 [16%]), pneumonia (33 [15%]), equine granulocytic anaplasmosis (31 [14%]), and fever of unknown origin (most likely undiagnosed viral infections; 27 [13%]). Descriptive statistics for both cases and controls were summarized (Table 1).

**Clinical findings**—The clinical signs most frequently observed in cases were pyrexia (78/108 [72%]) and mucopurulent nasal discharge (66/106 [62%]). External abscesses in the retropharyngeal region were reported in only 23 of 105 (22%) cases. Less commonly observed clinical signs in cases included lethargy (28/104 [27%]), edema (9/104 [9%]), and neurologic deficits (3/104 [3%]; 1 horse had generalized weakness and 2 had dysphagia). Ten of 108 (9%) cases did not have any clinical signs of strangles.

The median rectal temperature was 39.4°C (102.9°F; IQR, 38.9° to 40°C [102° to 104°F]) for cases and 39.4°C (102.9°F; IQR, 39° to 40°C [102.2° to 104°F]) for controls. The median duration of clinical signs was 15 days (IQR, 8 to 30 days) for cases and 6 days (IQR, 3 to 18 days) for controls.

**Diagnostic test results**—Results for select hematologic and serum biochemical variables were summarized for both cases and controls (Table 2). None of the variables differed significantly between cases and controls except hemoglobin concentration. The median hemoglobin concentration for cases (9.2 g/dL [IQR, 9.3 to 9.6 g/dL]) was significantly (\( P < 0.001 \)) lower than that for controls (11.8 g/dL [IQR, 10.8 to 13.4 g/dL]). The frequency distributions of cases and controls with select hematologic and biochemical abnormalities were summarized (Table 3).

**Treatment**—Sixty-three of the 108 (58%) cases were treated with systemic antimicrobials. The majority (34/63 [54%]) of cases were treated with procaine penicillin; 26 (41%) horses were treated with trimethoprim sulfamethoxazole, and the remaining 3 (5%) horses were treated with chloramphenicol. Fifty-five of the 108 (51%) cases received bilateral guttural pouch infusion of penicillin. Twenty-one (19%) cases were treated with systemic antimicrobials and bilateral gut-
EQUINE
with oxytetracycline.

### Table 2—Results for select hematologic and serum biochemical variables for the horses of Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count (×10³ WBCs/µL)</td>
<td>No. evaluated</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Segmented neutrophil count (×10³ neutrophils/µL)</td>
<td>30</td>
<td>9.9 (7.8–12.2)</td>
</tr>
<tr>
<td>Lymphocyte count (×10³ lymphocytes/µL)</td>
<td>28</td>
<td>7.2 (4.6–9.1)</td>
</tr>
<tr>
<td>Platelet count (×10³ platelets/µL)</td>
<td>26</td>
<td>170 (104–192)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>28</td>
<td>30 (26–33)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>27</td>
<td>9.2 (8.3–9.8)</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>35</td>
<td>750 (500–1,002)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>11</td>
<td>2.8 (2.46–2.91)</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>12</td>
<td>1.3 (1.2–1.7)</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>11</td>
<td>112.4 (102.0–131.9)</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>11</td>
<td>2.3 (1.8–3.4)</td>
</tr>
</tbody>
</table>

### Table 3—Frequency distribution of horses from Table 1 with select hematologic or serum biochemical abnormalities.

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Definition</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>Hematocrit &lt; 30%, hemoglobin concentration &lt; 11.6 g/dL or RBC count &lt; 6.2 × 10⁶ RBCs/µL</td>
<td>27</td>
<td>18 (67)</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>WBC count &gt; 10.3 × 10³ WBCs/µL</td>
<td>30</td>
<td>11 (37)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>WBC count &lt; 4.3 × 10³ WBCs/µL</td>
<td>28</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neutrophilia</td>
<td>Neutrophil count &gt; 8.1 × 10³ neutrophils/µL</td>
<td>28</td>
<td>13 (46)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Neutrophil count &lt; 2.2 × 10³ neutrophils/µL</td>
<td>27</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lymphocytosis</td>
<td>Lymphocyte count &gt; 5.8 × 10³ lymphocytes/µL</td>
<td>27</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>Lymphocyte count &lt; 1.7 × 10³ lymphocytes/µL</td>
<td>29</td>
<td>13 (45)</td>
</tr>
<tr>
<td>Hyperfibrinogenemia</td>
<td>Fibrinogen concentration ≥ 400 mg/dL</td>
<td>35</td>
<td>31 (89)</td>
</tr>
<tr>
<td>Severe hyperfibrinogenemia</td>
<td>Fibrinogen concentration ≥ 700 mg/dL</td>
<td>29</td>
<td>19 (66)</td>
</tr>
<tr>
<td>Hyperproteinemia</td>
<td>Total protein concentration &gt; 6.9 g/dL</td>
<td>23</td>
<td>20 (67)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Platelet count &lt; 72 × 10³ platelets/µL</td>
<td>26</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

All variables were not determined for all horses.

### Complications—Case status was considered a confounder and was controlled (ie, included as an independent variable) in all multivariable Firth logistic regression models constructed to identify variables associated with the development of complications. Variables with too few observations (ie, variables for which over half of the horses had missing results) were not evaluated. Fifty of the 108 cases had guttural pouch endoscopy performed; of those 50 cases, 32 (64%) had empyema, and 3 (6%) had chondroids. All 3 horses with guttural pouch chondroids had clinical signs of strangles at the time an S equi test-positive nasopharyngeal or gut-
tural pouch lavage fluid sample was collected for bacterial culture or PCR analysis. Two of the 3 controls that had guttural pouch endoscopy performed had guttural pouch empyema. Multivariable Firth logistic regression did not identify any predictor variables for the development of empyema.

Seven of 107 (6.5%) cases and 1 of 206 (0.5%) controls developed purpura hemorrhagica. Cases were 38.66 times (95% CI, 1.05 to 1,420.67; \( P = 0.047 \)) as likely to develop purpura hemorrhagica as were controls. Horses with anemia were 22.9 times (95% CI, 0.94 to 556.91; \( P = 0.05 \)) as likely to develop purpura hemorrhagica as were horses without anemia. There was not a positive association between leukocytosis and the development of purpura hemorrhagica (OR, 1.49; 95% CI, 0.23 to 8.34; \( P = 0.83 \)). The median duration of clinical signs was 22 days (IQR, 8.25 to 38.75 days) for the 7 cases that developed purpura hemorrhagica. Three of those horses were treated with corticosteroids, and 1 horse was euthanized because of the severity of the condition and financial constraints of the owner.

Two of 107 (2%) cases developed metastatic abscesses (or bastard strangles), and the duration of clinical signs for those horses was 43 and 46 days, respectively. Multivariable Firth logistic regression did not identify any predictor variables for the development of metastatic abscesses.

One case (a yearling) had a tracheotomy performed on the farm because of concerns about potential asphyxia owing to retropharyngeal lymphadenopathy. That yearling subsequently developed pneumonia caused by \( \text{S} \text{ equi} \), which was presumably aspirated into the lungs. Two other cases were referred for hospitalization at the veterinary teaching hospital; 1 of those cases developed purpura hemorrhagica and bastard strangles. Fifteen control horses were referred to the veterinary teaching hospital. Seven controls were euthanized, 2 had systemic lymphoma, 2 had colic, 2 had diarrhea, and 1 had an uncharacterized neoplasia of the upper portion of the respiratory tract.

**Asymptomatic positives and \( \text{S} \text{ equi} \) carriers**—For 46 cases, sufficient information was provided in the medical record to determine whether clinical signs of strangles were present or absent at the time \( \text{S} \text{ equi} \) was identified by bacteriologic culture or PCR assay. Of those 46 cases, 14 (30%) had positive PCR results without clinical signs and were classified as asymptomatic positives. Six of those horses were culture positive for \( \text{S} \text{ equi} \). 6 horses were culture negative for \( \text{S} \text{ equi} \), and bacteriologic culture results were unavailable for the remaining 2 horses. None of the asymptomatic positives were vaccinated against strangles. Guttural pouch endoscopy was performed on 9 of the asymptomatic positives, and 6 had guttural pouch empyema.

Twenty-five of 62 (40%) cases evaluated for \( \text{S} \text{ equi} \) ≥ 40 days after strangles was initially diagnosed had positive test results on bacteriologic culture or PCR assay and were classified as carriers. Of those 25 carriers, 12 were also classified as asymptomatic positives, and 5 were thought to be index cases for strangles outbreaks. The median duration that carriers tested positive for \( \text{S} \text{ equi} \) was 60 days (IQR, 40 to 75 days). In a strangles outbreak involving 22 horses, results of serial testing led to 7 horses being classified as \( \text{S} \text{ equi} \) carriers. Endoscopic evaluation of the guttural pouch was performed on all 22 horses, and 5 of the 7 carriers had guttural pouch empyema. Results of multivariable Firth logistic regression suggested that horses with guttural pouch empyema were 5.01 times (95% CI, 0.86 to 29.10) as likely to be classified as carriers as were horses without guttural pouch empyema, but that association was not significant (\( P = 0.073 \)).

**Discussion**

In the present study, the presence of a mucopurulent nasal discharge and external abscesses in the pharyngeal region were identified as predictor variables for strangles in horses. Those findings were similar to results of other studies.\(^4\)\(^,\)\(^10\)\(^,\)\(^11\) Historically, external abscesses in the pharyngeal region were considered a common clinical sign of strangles.\(^6\)\(^,\)\(^11\) Only 23 of 105 (22%) horses with strangles (cases) in the present study had external abscesses in the pharyngeal region; however, none of the horses without strangles (controls) had external abscesses in the pharyngeal region. Results of the present study also indicated that strangles was more likely to be diagnosed in the spring than in the summer, a finding that was consistent with findings of other studies.\(^2\)\(^,\)\(^13\) That suggest that diseases of the respiratory tract in horses and humans are less likely to be diagnosed in the summer, compared with the other seasons.

Although pyrexia is considered a hallmark of strangles,\(^14\) only 78 of 108 (72%) cases in the present study had pyrexia. The remaining 30 cases either never developed pyrexia in response to the \( \text{S} \text{ equi} \) infection or an abnormally increased rectal temperature was never recorded in the medical or client records. Pyrexia caused by \( \text{S} \text{ equi} \) may be transient or cyclical and might have been missed by infrequent (once daily or every other day) rectal temperature monitoring of the horses in this study. Regardless, failure to detect pyrexia in 30 horses with strangles suggested that use of rectal temperature monitoring alone may not be sufficient to accurately identify all \( \text{S} \text{ equi} \)-infected horses. We chose to use horses with pyrexia not caused by strangles as controls in the present study because pyrexia was considered a hallmark of strangles and those horses originated from the same source population and therefore had similar risk for \( \text{S} \text{ equi} \) exposure as the cases. The use of pyrexia as a criterion for selection of controls precluded it from being assessed in the statistical models.

Results of the univariate analysis revealed that horses with severe hyperfibrinogenemia (fibrinogen concentration, ≥ 700 mg/dL) or anemia (Hct, < 30%; hemoglobin concentration, < 11.6 g/dL; or RBC count, < 6.2 × 10\(^6\) RBCs/µL) were more likely to be cases than controls. Results of other studies\(^15\)\(^,\)\(^16\) indicate that the mean fibrinogen concentration and WBC count for \( \text{S} \text{ equi} \)-naïve foals that subsequently developed strangles were significantly greater at 2 and 4 weeks after infection, compared with those of foals that had been previously infected with \( \text{S} \text{ equi} \), whereas the mean hemoglobin concentration, PCV, and RBC count did not differ significantly between the 2 groups of foals. Fi-
brinogen is an acute-phase protein and an indicator of active inflammation. The presence of transient anemia concurrently with hyperfibrinogenemia is congruent with anemia of inflammatory disease, which is caused by iron sequestration during an infection that results in impaired erythropoiesis. 17 Although the presence of anemia and hyperfibrinogenemia are not pathognomonic for strangles, determination of fibrinogen concentration and determination of hematologic variables are efficient and cost-effective diagnostic tests that can be used to provide evidence to support a diagnosis of strangles, particularly when trying to identify an index case and convince clients to perform additional strangles-specific testing such as the S. equi PCR assay.

In the present study, 40 of 50 (80%; ie, apparent sensitivity) nasopharyngeal or guttural pouch lavage fluid samples obtained prior to antimicrobial administration yielded positive results for S. equi as determined by a PCR assay. Findings of another study 10 indicate that up to 40% of horses with strangles may have negative test results for S. equi on nasal or nasopharyngeal swab specimens obtained during the early stages of the disease (ie, apparent sensitivity, 60%), which delays the initiation of appropriate treatment and biosecurity measures and necessitates additional testing. This difference in the apparent sensitivity between the diagnostic test protocols used in the present study and that other study 10 for identification of horses with strangles may be the result of the specimens tested. Test sensitivity is better for fluid samples obtained during nasopharyngeal or guttural pouch lavage than that for nasal or nasopharyngeal swab specimens. 10 Additionally, in the present study, a real-time PCR assay with seel primers was used, 10 and that assay has a higher sensitivity for identification of S. equi than does aerobic bacteriologic culture. 10,10

An asymptomatic positive was defined as a horse without clinical signs of strangles that had a positive result for S. equi on bacteriologic culture or PCR assay. Identification of asymptomatic positives is important because those animals are often the index case for a strangles outbreak. Unfortunately, a description of clinical signs present at the time test specimens were obtained was not available for all study horses; however, of the 46 cases for which a description of clinical signs at the time of specimen acquisition was available, 14 (30%) were classified as asymptomatic positives. Six of those horses had positive results for S. equi on both PCR assay and bacteriologic culture, 6 had positive results for S. equi on PCR assay but negative results on bacteriologic culture, and bacteriologic culture results were unavailable for the remaining 2 horses. It is likely that the 6 horses with S. equi–positive results on the PCR assay and negative culture results represented true asymptomatic positives instead of false-positive PCR results; the conflicting test results were probably a function of differences in the sensitivity between the PCR assay and bacteriologic culture and differences in the amount of S. equi in the samples tested. In another study, 10 the lower detection limit for S. equi was 30 CFUs/mL for bacteriologic culture and 1 CFU/mL for a PCR assay, and the lower detection limit for consistent identification of S. equi, or test reproducibility, was 100 CFUs/mL for bacteriologic culture and 30 CFUs/mL for a PCR assay. We believe that the samples that yielded a positive PCR result and negative culture result likely contained a low number of S. equi and did not reflect false-positive PCR results. 19

A carrier was defined as a horse that had positive test results for S. equi ≥ 40 days after strangles was initially diagnosed. Identification of S. equi carriers is imperative during a strangles outbreak because those horses frequently do not have obvious clinical signs of the disease and can perpetuate the outbreak within a population. In the present study, 25 of 62 (40%) cases were classified as carriers, which was higher than the prevalence (0.3% to 10%) of S. equi carriers reported in other studies. 3,7,20 Although none of the farms represented in the present study had more than 1 strangles outbreak during the observation period, compliance with recommended biosecurity measures varied among the farms and might have affected the prevalence of carriers. However, the prevalence of S. equi carriers in the present study should be interpreted with caution because, owing to the retrospective nature of the study, test results for samples collected > 40 days after strangles was initially diagnosed were available for only 62 of the 108 (57%) cases. A prospective study in which samples from horses with naturally occurring strangles are obtained at standard intervals is necessary to more accurately estimate the prevalence of S. equi carriers.

The presence of guttural pouch empyema was not positively associated with S. equi carrier status in the present study. However, the P value was close to our cutoff for significance. Thus, endoscopy of the guttural pouch may be a valuable tool for managing a strangles outbreak. In this study, endoscopy of the upper portion of the respiratory tract was performed on 9 of the 14 horses classified as asymptomatic positives, and 6 of those horses had guttural pouch empyema. This finding was consistent with results of other studies, 1,3,21 which suggest that horses without clinical signs of strangles can harbor S. equi in their guttural pouches for a prolonged period (> 40 days). During a strangles outbreak investigated by our ambulatory practice in which endoscopy was performed on all 22 horses on the affected farm, 7 horses were classified as S. equi carriers, of which 5 had guttural pouch empyema; 3 of those had no clinical signs and were classified as asymptomatic positives. This finding emphasizes the importance of performing video endoscopy on all horses on an affected farm during a strangles outbreak in conjunction with a PCR assay on guttural pouch lavage fluid samples to identify S. equi carriers. 8 This is in contrast to the 2005 American College of Veterinary Internal Medicine Strangles Consensus Statement, 14 which recommends that PCR assay or bacteriologic culture be performed on nasopharyngeal lavage fluid samples obtained from individual horses on 3 separate occasions. When compared with nasopharyngeal lavage, an advantage of endoscopy is that it allows clinicians to visually examine the guttural pouches of horses suspected of having strangles. From a cost standpoint, in our ambulatory practice, nasopharyngeal lavage with bacteriologic culture and PCR assay on the resulting fluid sample costs $75/horse plus the farm call fee, and guttural pouch lavage via endoscopy
with bacteriologic culture and PCR assay on the resulting fluid sample costs $220/horse plus the farm call fee. If the 2005 Strangles Consensus Statement\textsuperscript{14} protocol is followed, the cost would be tripled for the nasopharyngeal lavage and testing procedure to be performed on 3 separate occasions ($225 plus 3 farm call fees). Thus, in our practice, it is more cost and time effective for clients to have endoscopy and guttural pouch lavage performed on each horse once, compared with nasopharyngeal lavage performed on each horse on 3 separate occasions.

In the present study, 7 of 107 (6.5\%) cases developed purpura hemorrhagica subsequent to strangles, which was slightly higher than the prevalence of purpura hemorrhagica (4/74 [5.4\%]) in \textit{S equi}-infected horses during a previous strangles outbreak.\textsuperscript{3} The reason the prevalence of purpura hemorrhagica was higher in the present study than that in the other study\textsuperscript{3} might have been because the strain of \textit{S equi} involved in the present study was more pathogenic, the number of horses that had been previously exposed to \textit{S equi} and were therefore predisposed to developing purpura hemorrhagica was greater in the present study, or a more inclusive definition for the condition was used in the present study. Regardless, purpura hemorrhagica is an important complication associated with strangles, and horses with strangles should be closely monitored for this condition. In the present study, the only case that died did so after developing purpura hemorrhagica. The only predictor variable significantly associated with the development of purpura hemorrhagica in the present study was anemia; cases with anemia were almost 23 times as likely to develop purpura hemorrhagica, compared with cases without anemia. This significant association between anemia and purpura hemorrhagica seems biologically plausible because, in our experience, the horses most severely affected by strangles are the most likely to develop purpura hemorrhagica.

The prevalence of cases that developed metastatic abscesses, or bastard strangles, in the present study (2/107 [1.9\%]) was similar to that (2/74 [2.7\%]) reported in another study.\textsuperscript{3} The low number of cases that developed metastatic abscesses in the present study may be a reflection of the clinical management of those cases; however, the study lacked the power to definitively determine that. Although the management of most cases was guided by a board-certified large animal internist (AGB) and a board-certified equine veterinary practitioner, a variety of treatment regimens were implemented because of client financial limitations or lack of patient compliance for drug administration. It has been theorized that horses with strangles that are treated with antimicrobials are at an increased risk for developing metastatic abscesses, compared with affected horses that are not treated with antimicrobials. However, evidence to support that theory was not found during a review of the literature\textsuperscript{22} or in the present study. In fact, no predictor variables were identified for the development of metastatic abscesses in the present study.

Interestingly, vaccination of horses against strangles did not appear to protect them against developing the disease. Although the strangles vaccination history was available for only 65 cases in the present study, 10 (15\%) horses that were vaccinated with an intranasal vaccine against \textit{S equi} developed strangles within 24 months after vaccination. In another study,\textsuperscript{23} horses that received a component or live vaccine against \textit{S equi} developed clinical signs of strangles following experimental inoculation with the organism. Results of yet another study\textsuperscript{24} indicate that adult ponies with a low concentration of antibodies against \textit{S equi} developed less severe disease following experimental inoculation with the organism than did \textit{S equi}–naïve adult ponies. Collectively, these findings suggest there is a need for more efficacious vaccines against \textit{S equi}.

Even though the retrospective investigation of strangles outbreaks on multiple farms allowed for a comprehensive evaluation of the factors associated with strangles, the present study had multiple limitations, many of which are inherent in any retrospective study. Variability in the extent of owner compliance in the implementation of appropriate biosecurity measures to limit the horizontal transmission of \textit{S equi} among horses might have affected the duration of the outbreak and number of cases per farm that was enrolled in the study. Similarly, variable client and patient compliance with drug administration could have affected disease recurrence and duration in individual horses. The prevalence of complications associated with strangles among outbreaks or farms might have been affected by differences in the pathogenicity of the infecting strains of \textit{S equi}. However, because horses from several strangles outbreaks were represented in this study, the results likely represented disease caused by multiple \textit{S equi} strains and should be externally valid. The prevalence of horses with strangles and guttural pouch empyema and chondroids was likely underestimated in this study because video endoscopy was not performed on all horses. Finally, for owners that had multiple horses affected with strangles, the financial burden of treatment likely affected the frequency of diagnostic testing.

Results of the present study indicated that not all horses infected with \textit{S equi} develop pyrexia or other clinical signs of strangles. We recommend that horses suspected of having strangles be initially screened with a CBC and determination of fibrinogen concentration. Once strangles has been diagnosed on a farm, we recommend that all horses on the farm undergo video endoscopy of the upper portion of the respiratory tract, guttural pouch lavage, and PCR analysis of lavage fluid samples for \textit{S equi} so that carrier horses can be identified and properly treated and managed. A large prospective study in which all horses with strangles undergo standardized examinations, testing intervals, and treatment protocols is necessary to better elucidate the risk factors associated with clinical disease and \textit{S equi} carriers and the role of systemic and local antimicrobial administration on the duration and outcome of \textit{S equi} infections.

\textsuperscript{a.} Pinnacle, Zoetis Inc, Kalamazoo, Mich.
\textsuperscript{b.} Quartermaster, Pharmacia & Upjohn Co, Kalamazoo, Mich.
\textsuperscript{c.} STA TAC, version 12.1, StaTaCorp LP, College Station, Tex.
\textsuperscript{d.} Trimethoprim sulfamethoxazole, Armell Pharmaceuticals, Glasgow, Ky.
\textsuperscript{e.} Chloramphenicol, Wedgewood Pharmacy, Swedesboro, NJ.
\textsuperscript{f.} Lixiquimycin LA-200, Zoetis Inc, Kalamazoo, Mich.
\textsuperscript{g.} Smith PA. How to eliminate strangles infections caused by \textit{S equi}\textsuperscript{12} and the role of sentinel carriers (asbtr), in \textit{Proceedings}. 52nd Annu Conv Am Assoc Equine Pract 2006;P5315.1206.
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