Proceedings of the 56th Annual Convention of the American Association of Equine Practitioners - AAEP -

December 4-8, 2010
Baltimore, Maryland, USA

Next Meeting:

Nov. 18-22, 2011 - San Antonio, Texas, USA

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Control and Prevention of \textit{Rhodococcus equi} Foal Pneumonia

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Transfusion of hyperimmune plasma seems to reduce the cumulative incidence of \textit{Rhodococcus equi} pneumonia, but this procedure is far from completely effective and has attendant risks. Neither an acceptable chemoprophylactic agent nor an effective vaccine is currently available. Screening for early detection of disease may be the most effective approach for controlling \textit{R. equi} at farms, but approaches must be tailored to specific needs and resources of farms. Author’s address: Equine Infectious Disease Laboratory, Department of Large Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas 77843-4475; e-mail: ncohen@cvm.tamu.edu. © 2010 AAEP.

1. Introduction

Pneumonia caused by \textit{Rhodococcus equi} continues to be an important cause of disease and death in foals.\textsuperscript{1} Because case-fatality rates may be high and treatment may be prolonged and expensive,\textsuperscript{2} controlling and preventing disease is more desirable than relying solely on treating affected cases. The purpose of this article is to review evidence regarding preventing \textit{R. equi} foal pneumonia and using screening tests to control the disease.

2. Preventing \textit{R. equi} Foal Pneumonia

Three principal approaches to preventing \textit{R. equi} pneumonia have been examined: (1) altering management practices, (2) chemoprophylaxis, and (3) immunoprophylaxis. Management practices associated with \textit{R. equi} foal pneumonia are reviewed in the study regarding epidemiology of the disease in this section.\textsuperscript{3} To the author’s knowledge, only foaling at pasture has been evaluated in a prospective controlled manner.\textsuperscript{4} Chemoprophylaxis

The use of antimicrobial agents to prevent \textit{R. equi} pneumonia has been examined. Two studies have evaluated the use of azithromycin for chemoprophylaxis. In a randomized controlled study conducted in the United States among 338 foals at 10 farms, a cumulative relative risk reduction of approximately 76\% was observed when foals received azithromycin (10 mg/kg, q 48 h, PO) for the first 14 days of life beginning on the first day of life.\textsuperscript{5} In a study conducted at a large breeding farm in Germany, the incidence of abscessing pneumonia was not significantly different between foals that received azithromycin (10 mg/kg, q 24 h, PO for the first 28 days of life) for prevention of \textit{R. equi} pneumonia (cumulative incidence = 60\%) and foals that did not receive azithromycin for chemoprophylaxis (cumulative incidence = 69\%) among 70 foals; however, the age at onset of abscessing pneumonia was apparently delayed in treated foals.\textsuperscript{6} Neither study was fully blinded nor was a placebo used. The reason for the discrepancy between studies remains unknown but
does not seem to pertain to dosage or duration of azithromycin treatment. Possible explanations include differences in case definitions, selection bias, methods of randomization, incidence of disease/pressure(s) for disease development, and possibly drug formulation. Regardless, use of azithromycin is not considered an acceptable approach for chemoprophylaxis, because widespread use of this drug would create greater pressure for emergence of macrolide resistance among bacteria. Evidence exists that prognosis is worse for foals with *R. equi* pneumonia from which macrolide-resistant isolates have been recovered.

Gallium maltolate is a metal-based compound with antimicrobial properties that has been shown to reduce replication of *R. equi*, both in pure culture and within macrophages, to reduce tissue concentrations of *R. equi* in mice after experimental infection, to be bioavailable in foals, and to be safe in foals. Chemoprophylaxis with gallium maltolate (50 mg/kg, q 24 h, PO for the first 14 days of life) failed to reduce the incidence of *R. equi* pneumonia in a placebo-controlled trial of 438 foals at 12 farms in the United States. 

### Immunoprophylaxis

Both active and passive immunomodulation have been investigated to prevent *R. equi* pneumonia. To date, despite considerable and innovative effort, an effective vaccine is lacking. If the assumption that most foals become infected during the early perinatal period is correct, innate immune responses may play a dominant role in controlling infection. Active stimulation of innate immune responses using commercially available immunomodulators has been investigated by a number of groups, however, to date, no controlled clinical trials documenting efficacy of this approach in foals have been reported.

Transfusion of hyperimmune plasma has been shown to reduce either the severity or cumulative incidence of experimentally induced or spontaneous *R. equi* pneumonia. Although results of observational studies have not uniformly attained statistical significance, all but one study have shown a relative reduction in risk. Unfortunately, neither vaccination of the dam before parturition nor administration of hyperimmune colostrum to foals has proven to be effective, however, evaluation of these approaches has been somewhat limited.

In summary, evidence that chemoprophylaxis is effective is conflicting, and an acceptable chemoprophylactic agent is lacking. A vaccine also is lacking. Transfusion of hyperimmune plasma, the only method that is both acceptable clinically and proven to reduce the incidence of disease, is incompletely effective.

### 3. Screening for *R. equi* Foal Pneumonia

Pneumonia caused by *R. equi* pneumonia seems to be an insidious disease in which clinical signs may not be apparent until pathological changes are well-progressed. Thus, screening to detect foals in the early stages of disease is likely to improve therapeutic outcomes. A variety of screening techniques have been described, including visual inspection of foals, monitoring rectal temperatures, monitoring clinical signs of pneumonia or extrapulmonary disorders, checking hematological parameters, serological testing, and thoracic imaging using either radiography or ultrasonography. Serum concentrations of either antibodies against *R. equi* or serum amyloid A do not seem to be useful screening tests. Although blood fibrinogen concentration did not seem useful, white blood cell (WBC) concentrations seemed to have reasonable sensitivity and specificity for detecting *R. equi* pneumonia. The principal limitations of WBC are the time and effort required to collect blood samples from foals, the lag from time of submission, and the potential for false-positive results attributable to other infectious or inflammatory conditions or stress-associated leukocytosis.

Use of ultrasonography for screening has not been systematically evaluated. The procedure has adherents and detractors, resulting from the various advantages and limitations associated with this approach. Thoracic ultrasonography can be performed relatively rapidly, and competence with the procedure can be rapidly developed. Results of ultrasonography are immediately available and may be more sensitive than radiography for detecting lesions in their early stages of development. Results are specific for the presence of pulmonary pathology (as contrasted with, for example, results of WBC concentrations). Because treatment of advanced disease can be difficult, detection of disease should lead to reduced mortality, and there are some data that support this contention. Disadvantages of the procedure include the costs borne by the farm for repetitive sonographic examinations, the increased labor needed to handle foals on a repetitive basis, and an increased number of foals treated for presumptive *R. equi* pneumonia. There are anecdotal and observational data indicating that not all foals with evidence of pulmonary consolidation or abscessation will progress to develop clinical signs of pneumonia caused by *R. equi*. Although the probability of disease given evidence of sonographic evidence of consolidation or abscessation remains unknown, it is generally accepted that this probability is less than 1 (100%). Consequently, the apparent incidence—and thus, the number of foals requiring treatment—is increased as a result of sonographic screening. Greater numbers of treated foals result in higher costs, increased risk of adverse events associated with treatment, and further pressure for development of resistance to macrolides by bacteria. Systematic comparison of WBC versus ultrasonographic screening is both lacking and needed.
ease is an important tool for controlling disease at farms.

4. Conclusions
Transfusion of hyperimmune plasma and application of screening tests remain the most effective methods for controlling the incidence of *R. equi* foal pneumonia at breeding farms. There is tremendous need for development of a highly effective preventive strategy. Further evaluation and development of screening tests are greatly needed to address this important health problem of foals.

References