How to Prevent and Control Pneumonia Caused by Rhodococcus equi at Affected Farms

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Methods for control and prevention should entail a systematic plan for treating affected foals, screening for early detection of infected foals not manifesting clinical signs, and preventing new cases. Plans need to be tailored to the specific needs and resources of individual farms. Author's address: Department of Large Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4475. © 2002 AAEP.

1. Introduction

Pneumonia is an important cause of disease and death for foals. Although many different organisms have been associated causally with pneumonia in foals, Rhodococcus equi is considered the most common cause of severe pneumonia.1–3 The impact of this disease can be large because prevalence and case-fatality rates are often high; treatment is prolonged, expensive, associated with adverse effects, and not uniformly successful; the disease may diminish future performance; and farms reputed to have the disease can suffer loss of clients.1–4

Although treatment of R. equi pneumonia has been well reported, descriptions of methods for control and prevention are relatively rare. For most infectious diseases, control and prevention has a greater impact on the burden of disease than does treatment. This presentation describes an approach for controlling and preventing R. equi pneumonia at farms affected by this disease.

2. Methods

For farms with foals affected by R. equi pneumonia, we suggest an approach to control and prevent that addresses three considerations: 1) treating affected foals; 2) screening for early detection of infection or disease in foals without clinical signs; and 3) preventing infection or disease in foals.

Preliminary Considerations

This approach for control and prevention entails considering the farm as the unit for evaluation, rather than individual foals. It is important to consider that programs for control and prevention must be tailored to the specific needs and resources of a given farm. Resources that a farm is willing and able to commit will vary, and the duration and magnitude of the problem will influence how much money and resources the owners or managers of a farm are willing to dedicate. For example, the actions taken by a farm with three breeding mares that previously has not experienced problems with R. equi pneumonia may be different than those used by a large breeding farm with recurrent problems.
with the disease. Owners and farm managers should be advised that, as for treatments, programs for control and prevention cannot be expected to be 100% effective.

The farm history should be investigated. Some farms seem to have recurrent problems caused by \textit{R. equi} (endemic farms), some have sporadic problems, and many farms do not experience problems. Endemic farms are more likely to have need for, and be willing to expend resources to, control and prevent the problem. Nevertheless, the first occurrence of \textit{R. equi} pneumonia on a farm may represent the beginning of recurrent problems. Veterinarians should consider a foal with \textit{R. equi} pneumonia as an individual patient in need of care, a source of virulent organisms, and a signal that the farm of origin may experience problems with and recurrence of the disease.

Treatment of Affected Foals

Treatment of affected foals is not considered in detail here because it is not the principal focus of this report. Briefly, any affected foals should be treated for \textit{R. equi} pneumonia. Although control trials to evaluate optimal treatment are lacking, erythromycin and rifampin are considered standard for treatment. This protocol can be costly and can result in adverse reactions in treated foals (including diarrhea and hyperthermia) and their dams (severe, acute colitis). Some isolates of \textit{R. equi} may be resistant to erythromycin and rifampin. Another macrolide, azithromycin, is being studied for use in foals, but it is uncertain whether the frequency of adverse events or antimicrobial resistance will be lower with this newer macrolide.

Whether affected foals should be isolated from other foals and pregnant mares is unclear. Virulent isolates of the organism can be found in the soil of farms with or without history of \textit{R. equi} pneumonia, and the source of infection for foals remains uncertain. Exposure is likely widespread on affected farms and has probably occurred for many foals by the time cases of \textit{R. equi} pneumonia are identified. However, foals can amplify the organism in their intestinal tracts, thereby enhancing contamination of the environment with the organism. Because such environmental contamination may increase risk of exposure, it may be advisable to isolate affected foals. In the case of farms with resident and transient populations, it seems appropriate to minimize comingling so that affected transients do not contaminate the environment of resident horses and vice versa.

Screening for Earlier Detection of Infection or Disease

We describe various methods for screening foals at farms with history of \textit{R. equi} pneumonia to detect disease or infection at an earlier point in time. The rationale for screening is our belief that earlier initiation of specific treatment will improve the prognosis for recovery. The various methods for screening described often need to be applied repeatedly and can be considered either individually or collectively (Table 1). That is, the suggested methods can be employed sequentially, individually, or in parallel, depending on the needs and resources of the individual farm. For some farms, using a single screening test and initiating treatment on the basis of a positive result might be best (e.g., a farm with recurrent high prevalence of disease or one for which resources are limited). In contrast, farms with greater resources or more sporadic disease occurrence might use a sequence of screening tests to ensure a higher probability that a foal selected for treatment has the disease. It is impossible, however, to stipulate circumstances that dictate the approach to screening that is best for a particular farm; the plan for a farm must be determined on the basis of consideration of the specific needs and wishes of each farm, through consultations between the veterinarian, the farm owners, and the farm managers.

It is important to emphasize that screening tests are not synonymous with diagnostic tests. In the context of our approach, positive results of a screening test for early detection of \textit{R. equi} would be a basis for initiating treatment for \textit{R. equi}. However, positive results of a screening test do not represent a definitive diagnosis of \textit{R. equi} infection or disease. A useful screening test is one in which the probability of disease is very high among those with a positive test result (i.e., high positive predictive value) and very low among those with negative test results (i.e., high negative predictive value). The higher the prevalence of disease at a farm, the higher the positive predictive value of the screening test. Thus, a positive result for a screening test (e.g., an elevated concentration of fibrinogen in blood) for \textit{R. equi} pneumonia would need to be interpreted differently for a foal at a farm with recurrent history of pneumonia caused by \textit{R. equi} than it would be for a foal at a farm without history of \textit{R. equi} pneumonia. For the former, but not the latter, the result would be a reasonable basis for treating the foal. The distinction between a diagnosis based on a screening test (an epidemiologic diagnosis) and a diagnosis based on definitive diagnostic testing (a clinical diagnosis) should be explained to owners, animal caretakers, and veterinarians lacking familiarity with these principles.

<table>
<thead>
<tr>
<th>Table 1. Methods to Screen for Earlier Detection of Foals Infected with \textit{R. equi}</th>
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<tr>
<td>Visually inspecting foals for attitude, respiratory effort, etc.</td>
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<tr>
<td>Measuring rectal temperature twice daily</td>
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<tr>
<td>Thoracic auscultation (not very sensitive!)</td>
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<td>Performing thoracic radiography</td>
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<td>Performing thoracic ultrasonography</td>
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Further reading

Visual inspection of foals at an affected farm should be used as an initial screening test. Pneumonia caused by *R. equi* is insidious, and clinical signs are often absent in foals with early infection or disease; however, increased respiratory effort or lethargy can be used to select foals that should be further evaluated. Visual inspection also may reveal extrapulmonary disorders of infection with *R. equi* (e.g., polyarthritis). These extrapulmonary disorders are often the initial clinical signs detected in affected foals. Rectal temperatures of foals can be monitored twice daily, with febrile foals selected for either further testing or treatment. Performing physical examination (including thoracic auscultation) twice weekly has been demonstrated to be effective for early recognition and reduction of mortality attributed to *R. equi* pneumonia at an endemic farm. In our experience, thoracic auscultation alone is an insensitive tool for early detection of foals with *R. equi* pneumonia.

Results of complete blood counts (CBCs) can be used for screening purposes. Foals with elevated white blood cell counts (e.g., >13,000 WBC/ml) or increased concentration of fibrinogen (>400 mg/dl) should be considered for either further testing or receiving treatment. Radiography, ultrasonography, or both can be useful for screening to detect foals with early or subclinical *R. equi* pneumonia. Diagnostic imaging is relatively specific because it may reveal pulmonary lesions. Radiography of foals 1–3 mo of age can be performed in the field. The radiographic appearance of pulmonary lesions is often strongly suggestive of *R. equi* pneumonia, and antimicrobial therapy for *R. equi* pneumonia is generally effective for the other principal cause of apparent abscessing pneumonia, *Streptococcus* sp. Radiography can detect lesions that are either central (axial) or peripheral (abaxial). Disadvantages of radiography include the need for special equipment and adequate personnel, exposure of personnel to radiation, costs associated with the procedure, the time required to perform and evaluate the results, and the finding that early radiographic lesions can be subtle and less characteristic of *R. equi* pneumonia than more advanced cases.

Ultrasoundography may reveal abnormalities of the peripheral pulmonary parenchyma. With experience, thoracic ultrasonography of a foal can be performed in a matter of minutes, and when the peripheral lung is involved, ultrasonography may be more sensitive than radiography. Disadvantages of ultrasonography include the potential to miss central pulmonary lesions surrounded by normal aerated lung, the need for expertise in diagnostic ultrasonography, the need for special equipment and adequate personnel, costs associated with the procedure, and the time required to perform and evaluate the results.

We do not recommend use of serologic testing for screening. Serologic methods for detecting *R. equi* include enzyme-linked immunosorbent assays (ELISAs), an indirect hemagglutination inhibition test, agar gel immunodiffusion (AGID), and synergistic hemolysis inhibition tests. Although such tests are widely available, systematic evaluation of serologic tests to reliably detect infection with *R. equi* in the field in North America is lacking. Problems with serologic testing include the fact that some of the measured antibody will be of maternal origin, serologic evidence of exposure may not be equated with active infection, and exposure to either virulent or avirulent isolates may result in positive test results. Seroconversion can occur among foals that do not develop *R. equi* pneumonia at farms that do not have a history of the problem. Some foals that have *R. equi* pneumonia may fail to seroconvert. Because of these limitations and the absence of data from North America demonstrating the clinical accuracy of serologic testing for early detection of infection, we do not believe such testing can be recommended for screening at this time. Serology may be most useful for presumptive confirmation of a diagnosis (e.g., a relatively high titer or preferably an increasing titer in conjunction with clinical signs of pneumonia) or as a component of screening (e.g., further diagnostic evaluation of a seroconverting foal).

As mentioned previously, each of these screening tests can be used independently, in various sequences, or in combination, depending on the needs, resources, and conditions of individual farms. A positive result of a screening test would be interpreted as an indication for either further screening or initiating treatment. The decision to initiate treatment must include consideration of the aforementioned adverse effects of erythromycin. An example of a sequential screening program would be one in which foals were visually inspected and had rectal temperatures recorded twice daily; any foal that appeared abnormal or was febrile would have a CBC; and any foal with an increased white blood cell count or increased concentration of fibrinogen would be treated with antimicrobials (or subjected to radiography or ultrasonography).

Again, the aim of screening is not for definitive diagnosis of *R. equi*. Rather, the goal of screening is to reliably identify foals likely to have early infection. Definitive diagnosis might be obtained on the basis of further clinical and microbiologic evaluation, including microbiologic culture or polymerase chain reaction testing of fluid obtained by transtracheal aspiration. When submitting samples for microbiologic culture, it is helpful to request from the laboratory that selective media (e.g., nalidixic-acid-novobiocin-actidionel (cycloheximide)-potassium tellurite medium) be used and that cultures be maintained for at least 3 days. Some veterinarians may prefer to subject some or all foals that are identified as positive by screening tests to more definitive diagnostic testing to reduce the rate of false-positive results. It should be recognized, however,
that accurate diagnosis early in the course of infection remains elusive and false-negative results of more definitive diagnostic testing can be obtained. Consequently, we recommend that screening be adopted with consideration by all concerned parties of the limitations of screening tests.

Preventing Disease
To date, the only method proven to prevent pneumonia caused by *R. equi* is transfusion of hyperimmune plasma.\(^{10,11}\) Despite its effectiveness, transfusion of hyperimmune plasma is not without limitations. Plasma is costly, labor-intensive to administer, is associated on rare occasion with transfusion reactions, and is not universally successful. The amount of plasma that should be administered and the time(s) of administration for optimal protection are unknown. We recommend administration of 1 l of hyperimmune plasma to a foal during the first few days of life and again during the third week of life. The rationale for this approach is that we believe exposure and infection occur early in life and that younger foals are more susceptible to infection than older foals. The basis for our beliefs include the finding that experimental infection resulted in more severe disease in foals infected at \(\geq 2\) wk of age than in foals infected at \(>2\) wk of age\(^{10}\) and the distribution of age of onset of foals with *R. equi* pneumonia.\(^{12}\) The constituents of plasma-administered IV that confer protection are not known.

Costs for IV administration of plasma are high. Costs of prevention, however, often outweigh costs of treatment and loss of commercial value of foals that succumb to the disease. It may be useful to conduct a cost-benefit analysis for implementing plasma transfusions for prevention, using decision-tree methods. Such an analysis requires estimating the average value of foals produced, the expected prevalence of disease, the case-fatality rate, and the average cost of treating *R. equi* pneumonia. Farms with a high prevalence of disease, high case fatality rate, or both will generally benefit financially from administration of 1–2 l of hyperimmune plasma to all foals. A sample decision-tree will be presented and has been published.\(^1\) Values in the decision-tree can be substituted by individuals to examine the cost-benefit of administration of hyperimmune plasma for circumstances of farms in their practices.

Vaccination of mares or oral administration of colostrum from *R. equi*-immunized mares to foals capable of absorbing immunoglobulin is not effective. A product containing concentrated serum that was developed to prevent failure of passive transfer was reported to increase serum antibody titers against *R. equi* and to delay by 2–3 wk the time of seroconversion to *R. equi* among foals.\(^{13}\) Controlled trials demonstrating the efficacy of this product have not been reported; in light of the failure of colostrum from immunized mares to be protective, claims of efficacy for this product should be viewed with considerable caution. Vaccination of foals or dams has not been demonstrated in control trials to be effective for preventing *R. equi* pneumonia. Novel strategies for vaccination, such as development of DNA vaccines to promote mucosal immunity, may eventually prove to be effective.

Environmental factors often influence the risk of infectious diseases. Although systematic evaluation of management factors associated with *R. equi* pneumonia has not been reported, many putative risk factors exist. In Texas, the disease is not associated with poor health management practices. Rather, the disease often occurs on farms that provide exemplary health management.\(^{14}\)

Removing manure from foaling stalls, pens, and paddocks could decrease environmental contamination and the level of exposure of susceptible foals, because *R. equi* is shed in feces of mares and foals and multiplies within feces. Frequent cleaning of foaling stalls may help to decrease contamination and opportunity for infection. However, the organism is a soil saprophyte that can be found at farms affected with the disease or farms not affected with the disease. The organism is seldom recovered from soil at a depth greater than 12 in. Removal and replacement of top soil in stalls and pens seems impractical and is unproven as a method of prevention, but we know of one farm in Texas that successfully used this strategy in conjunction with other approaches to control and prevention. Avoiding dirt-floored foaling stalls should be considered because the organism is a soil saprophyte, and it is possible that foaling stalls with dirt floors pose a greater risk than foaling stalls that have concrete or other synthetic flooring.\(^{14}\)

Methods used for disposal of manure might reduce exposure to *R. equi*. Directly spreading feces containing virulent *R. equi* on pastures may increase contamination of the environment. Composting manure before spreading it on pastures or disposing of manure without any application to pastures is recommended. However, solid evidence to support this recommendation is lacking.

We believe that density of horses, particularly the density of foaling mares and foals, is likely to increase the risk of *R. equi* pneumonia.\(^{14}\) Efforts to reduce the density of mares and foals should be considered on farms that have a high density of breeding horses and endemic *R. equi* pneumonia. A systematic cost-benefit analysis would have to be conducted to evaluate whether financial benefits of decreased disease and death outweigh the costs of lost revenue associated with fewer horses.

Keeping resident and transient populations separated may help to diminish transmission. Although evidence that this approach specifically prevents transmission and spread of *R. equi* pneumonia is lacking, it is a useful principle for general control of infectious diseases at farms with resident and transient populations. Whether there is benefit in isolating mares and foals returning to unaffected farms from *R. equi*-endemic farms is unclear.
Virulent isolates of this organism can be found in the soil of unaffected farms, and duration or pattern of shedding by infected horses is ill-defined. As a general principle for control of infectious diseases, the practice of isolating mares and foals returning from facilities where horses of diverse origins and ages seems advisable.

Inhalation is regarded as a principal mode of transmission. Thus, improving ventilation may decrease the risk of infectious respiratory diseases, including *Rhodococcus equi* pneumonia. A dusty environment has been anecdotally associated with *R. equi* infections. Diminishing dust in the environment may help to reduce the risk of *R. equi* pneumonia. Applying water sprinklers to pens and small paddocks can reduce dust. Rotation of paddocks to avoid overgrazing, reducing the density of horses (and foals) in paddocks or pens, and reseeding paddocks or pens may diminish dustiness of a horse’s environment by promoting adequate growth of grass.

3. Results

Expected results from implementing a program for screening and control will be a reduction in the prevalence of disease and a decrease in the mortality rate for affected farms. It is often possible to document the financial benefit to farm owners and managers of implementing such a program. As previously mentioned, no program for control and prevention (or treatment) can be expected to be 100% effective. The finding that the prevalence of *R. equi* at a farm can vary from year to year must be considered because it may lead one to over- or underestimate the effectiveness of a program for control or prevention.

4. Discussion

Diagnosis of *R. equi* pneumonia in a foal should alert the attending clinician to consider not only the medical needs of the affected foal but also to the need to consider the possibility of a herd/farm problem. Methods for control and prevention should be directed at treating affected foals, screening for earlier detection of infected foals, and implementing methods for preventing subsequent cases. Further research is needed to identify and substantiate evidence of effective methods for control and prevention of this important problem.

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References