Proceedings of the American Association of Equine Practitioners

Focus on the First Year if Life
Phoenix, AZ, USA – Sept. 11-14, 2014

Next Meetings:
Focus on Ambulatory - Jul. 26-28, 2015
Focus on Poor Performance - Sep. 10-12, 2015

Reprinted in IVIS with the permission of the AAEP
Prevention and Control of *Rhodococcus equi* Foal Pneumonia

Noah D. Cohen, VMD, MPH, PhD, DACVIM

*Take Home Message*—Effective prevention of *R. equi* pneumonia is currently lacking. Screening may be an effective tool, but most available tests lack adequate combinations of sensitivity and specificity.

**Author's address**—Equine Infectious Disease Laboratory, Department of Large Animal Clinical Sciences, College of Veterinary Medicine & Biomedical Sciences, Texas A&M University, College Station, TX 77843-4475; e-mail: ncohen@cvm.tamu.edu.

I. INTRODUCTION

Pneumonia caused by *R. equi* remains an important cause of disease and death in foals. This presentation will review current knowledge regarding prevention and control of *R. equi* pneumonia, with an emphasis on practical and novel information from research findings.

II. PREVENTION

Preventing infectious diseases is generally a preferable strategy to treating active cases, particularly for an insidious disease like *R. equi* pneumonia where lung lesions are well advanced by the time clinical signs are manifested in foals. Three general strategies have been advanced for preventing *R. equi* pneumonia: 1) management practices; 2) chemoprophylaxis; and, 3) immunological manipulation.

**Management Practices**

As mentioned in the preceding presentation, management strategies such as reducing density of mares and foals, foaling in paddocks or pastures, or reducing airborne concentrations of *R. equi* might reduce the incidence of *R. equi* pneumonia;\(^1\)\(^-\)\(^3\) however, controlled studies evaluating such interventions are lacking or importantly flawed. Recently, it was demonstrated that administration of gallium nitrate orally to mares peripartum reduced airborne concentrations of *R. equi*.\(^4\) Given that mare feces is an important source of virulent *R. equi*, this strategy merits further investigation; however, safety and environmental impact of this practice are unknown although not anticipated. Some management suggestions (e.g., foaling in paddocks) may be impractical or unacceptable to some farm owners or managers.

**Chemoprophylaxis**

Although evidence exists that chemoprophylaxis with azithromycin during the first 2 weeks of life is highly effective,\(^5\) this practice is **NOT** recommended for the following reasons. First, conflicting evidence exists regarding efficacy.\(^6\) Moreover, many foals with pulmonary lesions and few or no clinical signs of disease may recover spontaneously.\(^7\)\(^-\)\(^11\) Most importantly, widespread use of macrolides may contribute to resistance to this class of antimicrobials.\(^12\)

**Immunological Modification**

The first successful method for preventing *R. equi* pneumonia reported was the transfusion of hyperimmune plasma.\(^13\)\(^,\)\(^14\) This approach, however, is not uniformly effective, carries some risk for foals, and is expensive and labor-intensive.\(^15\)\(^-\)\(^18\) Nevertheless, it remains the only licensed product for helping to reduce the burden of disease caused by *R. equi* at breeding farms. At farms that elect to use plasma transfusion for controlling *R. equi* pneumonia, transfusion of all foals on the first or second day of life is strongly recommended. The most common dose is 1 liter per foal (approximately 4 ml/kg). Anecdotally, some veterinarians will transfuse 2 liters (about 8 ml/kg) to foals on the first or second day of life. Evidence that this practice reduces the incidence of pneumonia or increases risk of adverse effects of transfusion to the foal is lacking. Because the nadir of waning maternally-transferred antibody occurs at approximately 4 to 6 weeks of age, some veterinarians transfuse a second liter at 4 weeks of age. There are no data to indicate whether this practice of transfusing a second liter further reduces the severity of pneumonia or increases the risk of adverse transfusion reactions.

Transfusion of plasma is a method for transferring immunity. An alternative approach to transferring immunity is to stimulate either non-specific or specific immune responses. Unfortunately, evidence exists that foals are infected during early life.\(^5\)\(^,\)\(^19\) Responses to live agents or adjuvanted killed vaccines are diminished in foals during early life.\(^20\)\(^,\)\(^21\) Moreover, adaptive immune responses require days or weeks to
develop, and infection with *R. equi* could be well established in foals before these responses develop. Consequently, it is plausible that innate immune responses are critical for protecting foals. Evidence exists that innate immune responses in foals are diminished.22-26 Thus, it is plausible that stimulating innate immune responses might provide (some) protection against *R. equi* and other infectious diseases of neonates. Several innate immunomodulatory agents have been investigated in horses.22,24,27,28 Although inactivated parapox virus improved phagocytic capacity and oxidative burst of neutrophils from foals,27 this product failed to protect foals against disease when administered 3 times during the first 10 days after birth.29 Synthetic cytosine-phosphate-guanine oligodeoxynucleotides (CpG ODNs) have been demonstrated to enhance cytokine expression by peripheral blood mononuclear cells (PBMCs) and neutrophils of foals ex vivo,22,24,25 and in vivo administration of a CPG ODN has been demonstrated to increase interferon-gamma expression by neutrophils of neonatal foals.7 Controlled studies of CpG ODN administration to foals to prevent disease, however, are lacking.

The “holy grail” of *R. equi* prevention remains an effective vaccine. Despite several decades of effort using a variety of strategies including inactivated vaccines, sub-unit vaccines, DNA vaccines, and genetically-engineered modified live bacteria, no licensed vaccines are available in North America to prevent clinical *R. equi* infection.30-39 The only method that has been documented to protect foals against experimental intrabronchial *R. equi* infection has been intra-gastric administration of live, virulent *R. equi*.30,41 Although this approach will not be acceptable for commercial application because of concerns for environmental dissemination and contamination and potential to cause disease in foals, it indicates that intra-gastric vaccination can be protective. Recently, a reduced-virulence mutant of *R. equi* was demonstrated to protect 2 of 4 foals against subsequent intrabronchial challenge with virulent *R. equi*.42 Although encouraging, effectiveness > 50% will likely be necessary for commercial success. An effective vaccine would be a boon to the equine breeding industry and foal health.

**III. CONTROL**

The absence of highly effective prevention has caused farm managers and veterinarians to seek other approaches for controlling *R. equi* pneumonia. Screening foals for earlier recognition of disease and therefore earlier intervention has gained considerable traction because of the insidious progression of the disease. A variety of screening tests have been proposed, including physical inspection, physical examination, white blood cell (WBC) or fibrinogen concentrations, serology or serum biochemical testing, and thoracic imaging.13 Few of these tests have been systematically evaluated. Serological testing for anti-*R. equi* antibodies and serum amyloid A concentrations have been demonstrated to be ineffective as screening tests because of unacceptable combinations of sensitivity and specificity.13,44 Although WBC concentration was demonstrated to have good sensitivity and reasonably good specificity in 1 study,45 it was not an accurate test in another.10 Both studies found that fibrinogen concentrations were not accurate for screening for *R. equi* pneumonia.10,45 Thoracic ultrasonography (TU) to detect pulmonary abscesses or consolidated lung tissue has been widely adopted. This procedure has the advantage of being specific for the presence of lung lesions which may be detected before foals develop clinical signs of pneumonia, thereby allowing for earlier intervention to improve outcomes. The results are available in real-time and lesions can be sequentially monitored for progression and response to treatment. With experience, the procedure can be performed relatively rapidly. Sensitivity of TU is very high.11,46 The procedure has been described as reducing mortality from *R. equi* pneumonia at farms with affected foals.46 Despite these advantages, there are some limitations of TU screening. First, it can be expensive when many foals are being screened every 1 to 2 weeks beginning at around 3 weeks of life. Second, TU lacks adequate specificity to be used for a screen-and-treat (positives) program: such programs result in many foals being unnecessarily treated because the proportion of foals with lesions that remain subclinical is generally quite high.7,8,11,46 This over-treatment increases veterinary medical costs, the number of foals (and occasionally mares) experiencing adverse reactions, and pressure for development of resistance to antimicrobials used to treat *R. equi*.12

**IV. SUMMARY**

Efforts continue to develop an effective vaccine for *R. equi*. While this seems a feasible goal, highly effective prevention is lacking. Transfusion of hyperimmune plasma remains the most effective prevention available, but should not be expected to be uniformly effective. Until a vaccine is available, screening remains a valuable approach. A solution that leverages the sensitivity of TU with greater specificity is being sought by investigators.

**REFERENCES AND FOOTNOTES**


\[\text{b} \text{ Zylexis®, Zoetis, Florham Park, NJ 07932.}