



RHODOCOCCUS EQUI

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Definition *Rhodococcus equi* is a Gram-positive facultative intracellular pathogen that is a common cause of bronchopneumonia in foals between 3 weeks and 5 months of age. *R. equi* can also cause various extrapulmonary infections (see below). Although *R. equi* can be cultured from the environment of virtually all horse farms, the clinical disease in foals is endemic at some farms and only sporadic at others. Infections are extremely rare in adult horses.

Biology

R. equi is ubiquitous in soil. Unlike most environmental *R. equi*, isolates from pneumonic foals contain an 80–90 kb plasmid encoding, a surface expressed protein designated virulence-associated protein A (VapA). *R. equi* isolates are often classified as virulent, intermediately virulent or avirulent or based on their ability to replicate in macrophages or to induce disease or death in mice. Virulent *R. equi* isolates contain the large plasmid described above and express VapA. Intermediately virulent *R. equi* isolates contain plasmids encoding VapB or VapN that are related to, but distinct from, VapA. In contrast, avirulent *R. equi* do not express Vap antigens. Intermediately virulent and avirulent isolates are not known to cause naturally occurring disease in horses.

Clinical Signs The most common clinical manifestation of *R. equi* infections in foals is bronchopneumonia. Early clinical signs may only include a slight increase in respiratory rate and a mild fever. These subtle clinical signs are often either missed or ignored, allowing the condition to progress. As the disease progresses, clinical signs might include:

- Decreased appetite
- Lethargy
- Fever
- Tachypnea
- Increased effort of breathing characterized by nostril flaring and increased abdominal effort

Cough and bilateral nasal discharge are inconsistent findings.

Because ultrasonographic screening for early detection has become routine practice at some farms endemic for pneumonia caused by *R. equi* (see below), the most frequently recognized form of *R. equi* infection at those farms is a subclinical



form in which foals develop sonographic evidence of peripheral pulmonary consolidation or abscessation without necessarily manifesting clinical signs.

Extrapulmonary manifestations of rhodococcal infections are common. Extrapulmonary disorders might occur concurrent with or independent of pneumonia. Abdominal lesions (see necropsy below) are present in approximately 50% of foals that die from infections caused by *R. equi*. However, the majority of foals with abdominal lesions do not show clinical signs of abdominal disease. Polysynovitis is present in approximately 25–30% of cases with clinical *R. equi* infections. In some foals, lameness might be the result of septic arthritis or, more commonly, osteomyelitis caused by *R. equi*. Uveitis is not uncommon and might result in blepharospasm, ocular discharge, and blindness in severely affected foals. Occasionally, *R. equi* can cause infections of a variety of other extrapulmonary tissues or organs. Although rare, clinical signs resulting from abdominal infection with *R. equi* might include fever, diarrhea, weight loss or failure to thrive, and colic.

Incubation Period	The incubation period following experimental intrabronchial challenge varies from approximately 9 days after administration of a heavy inoculum to approximately 2–4 weeks when a lower inoculum is administered. However, the incubation period under field conditions is unknown and likely varies depending on several factors including the number of virulent bacteria in air samples in the environment, the age of the foal, and host defense mechanisms.
Transmission	Inhalation of virulent <i>R. equi</i> is the major route of pulmonary infection in foals. Ingestion of the organism is an important route of exposure, and likely of immunization, but rarely leads to hematogenously acquired pneumonia unless a foal has multiple exposures to extremely large numbers of bacteria.
Diagnostic Sampling, Testing and Handling	The distinction between lower respiratory tract infections caused by <i>R. equi</i> and those caused by other pathogens is difficult. Detection of abscesses by thoracic ultrasonography or radiography raise the degree of suspicion that pneumonia in a given foal might be caused by <i>R. equi</i> rather than by another microorganism. However, the definitive diagnosis of bronchopneumonia caused by <i>R. equi</i> should be based on bacteriologic culture or amplification of the <i>vapA</i> gene by polymerase chain reaction (PCR) from a tracheobronchial aspirate obtained from a foal with 1) clinical signs of lower respiratory tract disease, 2) cytological evidence of septic airway inflammation, and/or 3) radiographic or ultrasonographic evidence of bronchopneumonia. Amplification of <i>vapA</i> by PCR may be done in conjunction with, but should not replace, bacterial culture because PCR does not permit identification of other bacterial pathogens and <i>in vitro</i> antimicrobial susceptibility testing of <i>R. equi</i> isolates. The definitive diagnosis of extrapulmonary infections (e.g. abdominal abscess, osteomyelitis) caused by <i>R. equi</i> must rely on bacteriologic culture or PCR amplification of <i>vapA</i> from samples from the site of infection. The diagnosis of extrapulmonary disorders from sites at which <i>R. equi</i> cannot be detected (e.g. uveitis or polysynovitis) should be based on isolation of <i>R. equi</i> from a tracheobronchial aspirate or other primary sites of infection. The diagnosis of enterocolitis caused

by *R. equi* is problematic because isolation of *R. equi* from feces cannot be taken as evidence of enterocolitis caused by *R. equi*.

Post-mortem

The most common lesion is pyogranulomatous bronchopneumonia with abscessation. Abdominal lesions such as ulcerative enterocolitis or typhlitis, suppurative inflammation of the mesenteric and/or colonic lymph nodes, or abdominal abscesses are not uncommon. Polysynovitis and/or osteomyelitis might be present. Other very rare extrapulmonary manifestations of *R. equi* infections in foals include guttural pouch empyema, sinusitis, pericarditis, nephritis, as well as hepatic, renal, and intracranial abscessation.

Environmental Persistence

R. equi is ubiquitous in soil.

Specific Control Measures

In the absence of an effective vaccine, control and prevention of the disease at farms endemic for infections caused by *R. equi* have relied on passive immunization and screening to promote earlier recognition of the disease.

Administration of hyperimmune plasma (HIP)

Intravenous administration of commercially available and licensed plasma containing antibody against *R. equi* is recommended as an aid for preventing pneumonia caused by *R. equi* at endemic farms. Although the data are conflicting, and not all controlled clinical trials have shown a statistically significant reduction in the cumulative incidence of *R. equi* pneumonia, most studies have demonstrated reduction of relative risk, suggesting some benefit of HIP. The optimal amount of plasma to be transfused and the optimal age at which transfusion should occur remain to be determined. There is experimental evidence that administration of HIP before infection is important. Therefore, it is commonly recommended that foals receive transfusion of at least 1 L of HIP no later than the 2nd day of life. Because early administration may result in the decline of passively transferred antibody to a non-protective level at a time when foals are still susceptible to *R. equi* and when environmental challenge is high, it is a common practice to administer a 2nd dose of HIP at 2–4 weeks of age. Currently, there is insufficient information to recommend one brand of licensed antibody product over another. Transfusion of HIP is not completely effective and therefore does not eliminate the need for careful monitoring of foals at risk.

Screening

R. equi pneumonia is often not recognized until it is well advanced and, therefore, difficult to treat. The rationale for screening is the assumption that detecting foals in the early stages of disease along with appropriate treatment of affected foals will improve outcome. It is important to emphasize that screening methods are not diagnostic tests. A useful screening test is one in which the probability of disease is high with a positive test result (high positive predictive value) and very low with a negative test result (high negative predictive value). A variety of screening techniques have been described including visual inspection of foals for clinical signs of pneumonia, monitoring rectal temperatures, measurement of



hematological variables or acute phase proteins, serology, and thoracic imaging using ultrasonography. Systematic comparisons of these tests have not been performed but studies indicate that serology to detect antibodies against *R. equi* and measurement of fibrinogen or serum amyloid A concentrations are not useful screening tests.

Over the past 10–15 years, control of *R. equi* infections at many farms where the disease is endemic has relied on early detection of subclinical pulmonary disease using thoracic ultrasonography and initiation of treatment with antimicrobial agents prior to development of clinical signs.

Ultrasonography of the chest offers several advantages over other screening tests:

1. Results are specific for the presence of pulmonary pathology
2. Results are available immediately
3. The procedure allows for assessment of lesion severity and response to therapy

Although controlled studies are lacking periodic ultrasonography of the chest appears to have decreased mortality due to *R. equi* pneumonia at some farms relative to historical data. However, recent double blinded randomized placebo controlled studies at an endemic farm documented that the majority of foals with small pulmonary lesions (sum of lesion diameters [or abscess score] of 1-10 cm) recover without antimicrobial therapy. In addition, antimicrobial treatment of foals with small ultrasonographic lesions did not significantly hasten lesion resolution compared to administration of a placebo. In contrast, studies performed at the same farm showed that treatment of foals with lesion scores > 10 cm provided a significant benefit over administration of a placebo. The extent to which these results might be extrapolated to other farms is unknown.

Because it is impossible to know which specific foals might recover spontaneously from subclinical disease, and because *R. equi* infections can cause severe disease, many breeding farms elect to treat all foals with ultrasonographic lesions. This approach has resulted in an increased number of foals treated for presumptive *R. equi* pneumonia. The temporal association between this widespread use of macrolides and rifampin because of ultrasonographic screening and emergence of macrolide and rifampin resistance has been documented at some farms. Additional studies are needed to determine the risks and benefits of treating subclinically affected foals.

**Release of
Animals from
Isolation**

There are no isolation requirements for foals with this disease.

**Biosecurity
Issues for
Receiving
Animals**

Foals with pneumonia caused by *R. equi* shed higher numbers of *R. equi* in their feces than healthy foals or foals with subclinical lesions. Therefore, pneumonic foals might be an important source of contamination of the environment with virulent *R. equi* but there is no evidence that *R. equi* infection is contagious



among foals and exposure to virulent *R. equi* is widespread in the environment of foals. Thus, currently no environmental management practice or biosecurity measure has sufficient evidence on which to base recommendations for controlling and preventing *R. equi* pneumonia.

**Zoonotic
Potential**

R. equi can occasionally cause severe pulmonary or systemic infections in immunosuppressed people. Infections with *R. equi* are extremely rare and typically less severe in immunocompetent individuals.

Useful Links

<http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2011.00835.x/abstract>