**Introduction**

Respiratory disease is an economically devastating syndrome affecting swine production worldwide. Mycoplasma hyopneumoniae (M. hyo) is a key pathogen involved with enzootic pneumonia (EP) and the Porcine Respiratory Disease Complex (PRDC). Enzootic pneumonia is composed of M. hyo and secondary bacteria such as Pasteurella multocida, Streptococcus suis, Haemophilus parasuis, and Actinobacillus pleuropneumoniae. Recently, the term PRDC has been adopted to describe the severe respiratory disease that develops as a result of the combination of viral and bacterial pathogens. The most common components of PRDC include M. hyo, swine influenza virus (SIV), and porcine reproductive and respiratory syndrome virus (PRRSV) and the subsequent secondary bacteria.

Exposure to M. hyo is prevalent worldwide with an incidence approaching 100% of herds in some surveys.\(^1,2\) As many as 80% of the pigs surveyed at slaughter or diagnostic labs have evidence (lesions or CF antibodies) of prior exposure to M. hyo.\(^1,3,4\) Infection results in decreased growth rates and poor feed conversions. Additional studies have found reductions in growth rates (between 8 and 85 kg body weight) of up to 15.9% in pigs infected during lactation and 12.7% reduction between 50 and 85 kg body weight. They also observed a concurrent 13.8% decline in feed efficiency.\(^5\)

**Clinical signs**

Mycoplasma hyopneumoniae infection alone results in a chronic, non-productive cough. It is a disease with high morbidity, low mortality, and minimal effect on growth performance. Enzootic pneumonia and PRDC, however, are much more clinically severe diseases resulting in decreased daily gains and feed efficiencies, anorexia, unthriftiness, fever, cough, and dyspnea in 18 - 20 week old pigs. It has been estimated that PRDC affects 10 million pigs annually in the US costing producers millions of dollars in treatment and lost performance.\(^6\)
Pathogenesis

M. hyo attaches to the mucosal surface of the cilia lining the respiratory tract, resulting in the destruction of these cilia and the loss of the mucociliary defense system. The function of these cilia is to expel particles from the respiratory tract and serves as an initial physical defensive barrier. Loss of the mucociliary apparatus allows for increased colonization by secondary bacteria such as Pasteurella multocida. The mycoplasma organism also interacts with the immune cells of the respiratory tract resulting in the release of proinflammatory cytokines, such as tumor necrosis factor (TNF) and interleukins, and activation of lymphocytes. This interaction actually minimizes the immune system’s ability to effectively respond to the infection.

Direct contact with respiratory tract secretions appears to be the most common mode of transmission. Airborne transmission has also been proposed. The disease becomes established in a herd and is maintained via sow to pig or pig to pig transmission. M. hyopneumoniae has a relatively long incubation period (10 - 16 days or longer) and is exacerbated by stressors such as increased stocking density, inadequate ventilation, and exposure to other pathogens. These factors contribute to the emergence of clinical signs in the grow-finish period although actual infection frequently occurs in suckling pigs or the late nursery.

DIAGNOSIS

Gross lesions observed in the lungs of infected pigs consist of purple to gray areas of consolidation located in the ventral portions of the cranial and middle lobes, the accessory lobes, and the cranial portion of the caudal lobes of the lungs. Microscopic lesions include the accumulation of neutrophils around the airways and alveoli. As the disease progresses, the perivascular cuffing becomes more pronounced. Secondary bacterial infections and management factors such as overcrowding and poor ventilation influence the severity of these lesions.

The most common serologic tests used to diagnose MPS include indirect hemagglutination (IHA), complement fixation (CF), and ELISA. An indirect ELISA, called Tween 20, and a blocking ELISA have been developed. It has been shown that the Tween 20 detects infection earlier, but the blocking ELISA has less cross-reactivity with other mycoplasmas. Tween 20 OD readings peak approximately 5 - 7 weeks post-infection and can last for at least 52 weeks. M. hyopneumoniae is very difficult to isolate and identify rendering diagnosis by culture not feasible.

Attempts are often made to diagnose M. hyo infection using data collected at slaughter. However, studies have shown little or no correlation between slaughter lesions and the severity of mycoplasma pneumonia or effect on average daily gain. In many cases, mycoplasma lesions resulting from early infection have resolved and are not obvious at slaughter. Therefore, the impact of M. hyo infection may be underestimated if relying solely on slaughter analysis. However, Amilton et al., in a study to be presented at IPVS in Ames, Iowa, have shown that evaluating lung lesions can be a valuable tool to monitor the incidence of pneumonia at slaughter.
Treatment

Various antibiotics have been evaluated for their effectiveness in treatment and/or control of mycoplasmal infections. Tetracyclines have been shown to have variable impact on M. hyopneumoniae infections. Although, tetracyclines do not prevent infection and lesions tend to develop following cessation of therapy, one study indicates that repeated administration of oxytetracyclines during lactation and early nursery phases may reduce M. hyo-induced pneumonia in older pigs. Also, all isolates examined in a recent study demonstrated MICs ≤ 0.5 µg/ml for tetracyclines. A recent study in Japan, however, showed increasing resistance to chlortetracyclines.

Tylosin was reported to reduce the severity of the disease when injected at a dose of 10 mg/kg daily starting the day before exposure and continuing for 3 days post-infection. However, other studies (Ross, unpublished - 1981; and Ross and Skelly, unpublished - 1982) have failed to show significant impact on the incidence or severity of the disease and elevated MICs. Tilmicosin, a semisynthetic macrolide, has been shown to have MICs ≤ 8 µg/ml.

Results have been variable following administration of lincomycin. There is evidence that 200 g/ton fed for 3 weeks reduces the incidence and severity of disease and results in improved performance. Feeding continuously at 500 g/ton, however, did not prevent transmission to susceptible in-contact pigs in an unpublished study conducted by Dr. Richard Ross at Iowa State University.

Tiamulin, although not approved for the treatment or control of M. hyopneumoniae in the US, has been shown to have some effect on the disease when administered in feed (200 ppm for 10 days or 30 ppm continuously), water (0.006%), and parenterally (15 mg/kg for 3 days). A subsequent study, however, was unable to detect a beneficial effect when administered in the drinking water at 60, 120, or 180 ppm for 10 days. In vitro resistance to tiamulin, SDZ PMD 296, tylosin and oxytetracycline has also been reported.

Susceptibility to the aminoglycosides (gentamycin, apramycin and spectinomycin) varied but most isolates demonstrated MICs ≤ 4 µg/ml in a recent study. Multiple quinolones have also been reported to be effective against M. hyopneumoniae in vitro. They are not approved for use in swine in the US and thus I have no experience with their use. Obviously, due to their lack of a cell wall, all mycoplasma isolates are resistant to the β-lactams ampicillin, penicillin and ceftiofur that function by inhibition of bacterial cell wall synthesis.

CONTROL

Due to the relative refractoriness of mycoplasma to many of the commonly used antibiotics and the severity of secondary bacterial complexes, it is usually more effective to attempt to control the disease rather than treat it. Effective control measures are multifactorial involving management factors to minimize exposure and predisposing stressors and maximizing immunity. Numerous management factors have been suggested, such as proper stocking density, adequate ventilation, decreased age spread, and all-in, all-out production flow, to minimize the effects of exposure.
Vaccines have also been developed to minimize the clinical effects of exposure to mycoplasma and provide some protection against development of lung lesions. It has been shown that M. hyo vaccines stimulate the production of M. hyo-specific IgG and IgA antibodies following challenge and decrease production of proinflammatory cytokines, in particular, TNF. Therefore, even though vaccination does not prevent colonization or infection, it appears to minimize the inflammatory effects following infection.\textsuperscript{33} This reduction in cytokine production may also contribute to the finding that vaccination against M. hyo reduced the potentiation of PRRSV-induced pneumonia by M. hyo.\textsuperscript{34}

Two factors appear to be critical when determining the proper timing of M. hyo vaccination, maternal antibody and PRRS status. Maternal antibodies appear to be somewhat protective for the young pig, but also appear to inhibit the formation of an active immune response.\textsuperscript{35} It is important to determine the maternal antibody levels present prior to vaccination. Also, the timing of exposure to PRRS virus appears to impact the effectiveness of M. hyo vaccination. It has been shown that exposure to PRRS virus during or following M. hyo vaccination decreases the efficacy of the M. hyo vaccine.\textsuperscript{34} Therefore, if PRRS virus is present in a herd, M. hyo vaccination should be completed prior to PRRS virus exposure.

It is also important to realize that serum antibodies produced by M. hyo vaccination are slow to develop. Titers may not be measurable for at least 2 weeks following the second vaccination. Unchallenged pigs may become seronegative within 4 - 6 weeks after vaccination. Studies have shown, however, that there is no correlation between the level of serum antibodies and protection. Vaccinated pigs that are subsequently challenged develop a strong anamnestic response resulting in significantly higher titers than vaccination alone.\textsuperscript{36}

There have been a number of studies recently evaluating the efficacy of one-dose vaccination protocols compared to two doses. It has been shown that, in well-controlled laboratory or production systems, one dose can be as effective as two doses. The choice of one dose vs. two must be made based on a number of factors. One dose may work well 1)where the incidence of mycoplasma is low, 2)in all-in all-out by site production systems, 3) in the absence of other PRDC pathogens (particularly PRRS or SIV), 4)where there is a narrow age spread on the farm, and 5)in the presence of low maternal antibodies. However, many systems will experience better efficacy using a two-dose regimen. Two-dose protocols 1) allow for better timing relative to variable maternal antibodies, 2) give each animal a second chance to mount an immune response, 3) provide better protection in continuous and commingled flows as well as all-in all-out buildings on continuous flow sites, and 4) tend to be more effective in the face of increased disease pressure from secondary pathogens, PRRS, or SIV. Consultation with a veterinarian familiar with the production system and local disease challenges should be performed prior to selecting a one or two dose protocol.

CONCLUSION

In conclusion, respiratory disease is a costly health concern in most swine producing areas worldwide. Mycoplasma hyopneumoniae is a major contributor and predisposing factor in many of these cases. Exposure results in establishing
secondary bacterial infections important in PRDC and Enzootic pneumonia and has been associated with the potentiation of PRRS-induced pneumonia. The clinical signs, lesions, and production losses associated with M. hyo infection are further exacerbated by inadequate management practices. Although, treatment with some antibiotics appears to be beneficial, it is expensive and often ineffective. Modern commercial vaccines offer a reliable level of control and are more economical than antibiotic treatment. Vaccination against M. hyo has been shown to decrease the incidence of lung lesions, improve production performance, and may decrease the effects of PRRS infection.

1 REFERENCES


