

A practical look at the treatment of different mycoplasma species

Mycoplasma species still play a crucial role in modern pig production. Mycoplasma hyopneumoniae is the most important contributor to respiratory infections in pigs. Other mycoplasma species like M. hyorhinis, M. suis and M. hyosynoviae also frequently occur and provoke totally different clinical symptoms, but are often underdiagnosed.

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The overall prevalence and the economic impact of these small bacteria is much higher than generally assumed, justifying well considered control and treatment protocols.

Mycoplasma hyopneumoniae

This pathogen is ubiquitous within swine herds throughout the world and is the causative agent of enzootic pneumonia, characterised by non-productive coughing.

- The catarrhal pneumonia leads to consolidation of the lung and is mainly observed in the cranio-ventral lobes. Any infection automatically results in a decrease of the average daily weight gain and an increase of the number of days to market. Pigs showing the highest pneumonia score need one additional week to slaughter.
- Transmission from sows (mainly low parity sows) to suckling piglets, as well as spreading among pigs is important.

- The attachment to the cilia of the respiratory tract by different adhesins and lipoproteins results in a diminished function of the mucociliary apparatus. The subsequent damage of the cilia and epithelium together with a down-modulation of the immune response at later stages enhances secondary invasion by other bacterial and viral infections. Therefore, this pathogen is considered to be the key trigger in the development of Porcine Respiratory Disease Complex.

- The slow replication leads to a long incubation period of more than two weeks. Furthermore, the infection shows persistence for several months, indicating a certain degree of immune evasion of the microbe.

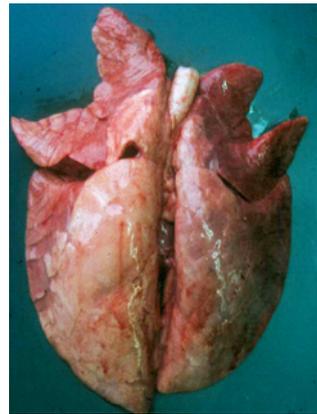
- Pig dense areas are at higher risk due to airborne transmission. This means a continuous challenge for the biosecurity of surrounding farms.

Culture of all mycoplasma species and their isolation is extremely slow (4-8 weeks) and specific media are needed.

On the other hand, genetic material detection (Polymerase Chain Reaction- PCR) gives quick results with high accuracy. For M. hyopneumoniae diagnosis, a PCR test can be performed preferably from lung tissue, laryngeal swabs and tracheobronchial swabs or lavage.

Histopathological examination of the lungs reveals typical peribronchial cuffing. Furthermore, antibodies which can be detected 4-6 weeks after first infection can also be used as a diagnostic tool (Table 1).

Vaccination against M. hyopneumoniae improves performance parameters in fattening pigs. Although a considerable



Left, M. hyopneumoniae, right, M. hyorhinis.

number of piglets are vaccinated nowadays, typical mycoplasma lung lesions are still frequently detected at slaughter. We should bear in mind that the vaccination of piglets:

- Does not stop further colonisation and horizontal spreading among pigs.
- Reduces clinical symptoms only to a certain extent.
- May be countered by maternal antibodies.
- Can fail if the vaccine strain does not cross-protect against the field strain(s). Different M. hyopneumoniae strains can even be present in the same herd.
- Is less effective in the case of simultaneous PRRS or PCV2 virus circulation.

Mycoplasma hyorhinis and Mycoplasma hyosynoviae

- M. hyorhinis is present in most of the pig farms even without clinical disease and is commonly detected in tonsils, nasal cavities and lungs. M. hyorhinis induced rhinitis results in sneezing and can evolve into conjunctivitis and pneumonia. The trigger for systemic spreading is stress due to transfer, overcrowding, non-adjusted ventilation or concurrent infections like PRRS. The level of colonisation of the piglets is low during lactation, but the bacteria spreads rapidly in recently weaned piglets. Normally, M. hyorhinis is not considered to cause

clinical infections during the fattening period. The incubation period is 3-10 days, therefore disease is observed at 3-10 weeks of age.

When performing necropsy, polyarthritis and polyserositis (pleurisy, pericarditis and peritonitis) are frequently observed. Swollen joints cause lameness and reluctance to move.

- Many farms are also subclinically infected with M. hyosynoviae in tonsils and nasal cavities. The rate of transmission from sows to piglets is low. Colonisation takes place at the end of the nursery period in apparently healthy pigs. Factors that predispose to, or determine systemic spreading are not yet fully known. Clinical symptoms are observed in pigs of 10-25 weeks of age.

M. hyosynoviae is often isolated in the infected joints of gilts, just after transfer to the breeding herd. The swollen joints are soft and fluctuating, containing a serofibrinous synovial fluid.

Logically, these two infections can be confused with Streptococcus suis or Haemophilus parasuis (Glässer's disease) infections, which also frequently occur at the same age.

Arthritis may also be caused by Erysipelothrix rhusiopathiae infections. The antimicrobials generally applied for the latter infections (amoxicillin, sulphonamides) are not successful for the treatment of mycoplasma infections, indicating that a differential

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Table 1. Differences between mycoplasma species.

	M. hyopneumoniae	M. hyorhinis M. hyosynoviae	M. suis
Diagnosis	Serology	yes	no
	PCR	yes	yes
	Culture	yes (difficult)	yes (difficult)
Commercial vaccines	yes	no	no
Eradication	yes	?	?



Fig. 1. Haemoglobin content and technical parameters of pigs suffering from *M. suis* before and after tiamulin treatment (Vetmulin, Huvepharma).

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diagnosis is indispensable for good veterinary practice. Antibody detection is not commercially available. Commercial vaccines are not marketed for *M. hyorhinis* and *M. hyosynoviae*.

Mycoplasma suis

M. suis attaches and penetrates the erythrocytes and therefore leads to haemolytic anaemia. The organism has an enormous impact on readability due to impaired oxygen transport capacity in pigs. This worldwide distributed mycoplasma species can be transmitted iatrogenically, via blood (directly or via blood suckling arthropods), urine, saliva, nasal and vaginal exudates. Intra-uterine infection of piglets may also be possible.

A study in Germany revealed that piglets were infected in 40.3% of 196 tested farms. *M. suis* can be diagnosed by PCR tests or staining of the blood in combination with low haemoglobin values. Diagnosis based upon culture is not possible.

Pale suckling and weaned piglets suffering from this haemotrophic disease show significantly lower technical performance and, in addition, more secondary infections like diarrhoea and *Streptococcus suis* infections. Impaired fertility and hypogalactia is often noted in infected sows. However, this infection is often not included in the differential diagnosis and its impact is underestimated.

The suppression of mycoplasma infections in pigs is an important step to improve the health status and welfare significantly and can be performed in three different ways:

- **Eradication of *M. hyopneumoniae*:** Possible by depopulation and repopulation or partial depopulation with strategic medication.
- **Control:** Vaccination, quarantine measures and farm management (housing, ventilation).
- **Treatment:** Once a herd is infected, or vaccines are unable to control these infections sufficiently, the use of antimicrobials is still required.

Mycoplasma treatment

The clinical outcome of an antimicrobial treatment depends upon three crucial steps in the veterinarian's decision making process:

- Selecting the correct antimicrobial, taking into consideration:
 - Known or expected antimicrobial susceptibility of the pathogen.
 - Ability of the antimicrobial to reach sufficiently the infection site.
- Product choice: a highly bio-available/potent active compound and an appropriate formulation.
- Correct dosing and administration.

Selecting the correct antimicrobial

Mycoplasma species have no cell wall and lack certain metabolic pathways, both important targets for most antimicrobials. Antimicrobial susceptibility testing is rather complicated and time consuming and, therefore, is only performed in select laboratories.

The antimicrobial susceptibility surveys, farm history and clinical experience of the veterinarian are important pillars to select the most convenient antimicrobial.

M. hyopneumoniae shows an excellent in vitro susceptibility to tiamulin, as the Minimal Inhibitory Concentration to inhibit growth of 90% of different strains tested (MIC₉₀) is not higher than 0.12µg/ml. In addition to the susceptibility outcome, the active substance needs to reach sufficient concentrations in the target tissues.

Pharmacokinetic data of tiamulin clearly show that the concentrations in the lungs and the joints are several times higher than the MIC₉₀ values for the present mycoplasma species.

Furthermore, this molecule is classified by the World Health Organisation in the lowest level of importance for resistance development in humans.

A recent field trial (Fig. 1) in a herd suffering from *M. suis* in sows and piglets demonstrated an excellent clinical recovery and consequently, improved performance parameters

after an oral administration of 10mg tiamulin/kg bodyweight/day for 14 consecutive days to all sows and piglets.

Product choice

The formulation of a veterinary antimicrobial product influences the clinical outcome of the treatment to a large extent.

The stability, solubility and bio-availability of the active ingredient are determined by the product choice (brand).

Often, veterinary products containing the same amount of active substance are considered as equivalent. However, the behaviour of a pharmaceutical product depends upon several product features, such as:

- Quality of the active: crystal form and size, presence of undesired substances such as heavy metals or impurities.
 - Choice and quality of the salt.
 - Formulation: used excipients and type of formulation.
- Huvepharma has more than 60 years expertise in formulation, guaranteeing optimal efficacy in the field. Vetmulin, the Huvepharma brand of tiamulin, is presented in several formulations meeting the requirements of each specific field case of mycoplasma treatment.
- The water soluble granules and oral solution show a perfect solubility and 24 hour stability in water of different hardness.
 - Vetmulin premix and oral granules are produced by a unique microgranulation technology, ensuring tiamulin is captured in microgranules which are in turn fully embedded in a starch matrix.

Compared to simple powder mixtures, this technology offers four benefits:

- Perfect homogeneity in the final feed = efficacy.
- Less risk of carry-over and subsequent cross-contamination = safety.
- Better flowability = easy administration.
- Protection against heat and moisture = stability.
- The injectable formulation offers

a perfect way to start a treatment which can be followed by oral medication, if required.

Correct dosing and administration

● Dosing should be based upon bodyweight, regardless of the application form. Incorrect dosing is avoided by taking into account the changing ratio of bodyweight versus water or feed intake. Correct dosing can easily be achieved with the Huvepharma dose calculator, an App available for mobile devices, which is free of charge.

- The dosage regimen also needs our attention. A daily dose can be administered in different ways, either continuously or as a pulse. Tiamulin is a time dependent antimicrobial. The efficacy is determined by the period during which the bacteria are exposed to the antimicrobial at the infection site. A concentration just above the MIC is sufficient for optimal clinical results. For this reason, the highest efficacy of tiamulin can be expected if administered over a period of 12-24 hours per day.
- Vetmulin orally administered at a daily dose of 10mg tiamulin hydrogen fumarate per kg bodyweight, for a minimum of five days, quickly controls infections caused by different mycoplasma species. Antimicrobial treatment should be initiated as soon as the first symptoms occur; for example four weeks before the first detection of antibodies against *M. hyopneumoniae*.

All the above mentioned mycoplasma species (*M. hyopneumoniae*, *M. hyorhinis*, *M. hyosynoviae* and *M. suis*) have an enormous impact on the general health status. Apart from the involvement of the respiratory system, some species also enter the bloodstream and cause different clinical signs, such as arthritis, polyserositis and anaemia.

In the case of detrimental mycoplasma infections, Vetmulin (tiamulin) offers the best and fastest solution to significantly improve the health status of pigs. ■

References are available from the author on request