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**Retrospektive Auswertung der Diagnostik porziner Mykoplasmen im
Tierspital-Informationssystem der Vetmeduni Wien**

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Wien, den 09.09.2025


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ABSTRACT

Infections with *Mycoplasma* (*M.*) *hyopneumoniae*, *M. hyorhinis* and *M. hyosynoviae* in pigs can lead to problems in different age groups. The clinical pictures caused by these pathogens can be highly variable both in terms of the organ systems affected and the severity of the disease.

The overall aim of this work was to comprehensively investigate the relationship between the detection of *M. hyopneumoniae*, *M. hyorhinis* and *M. hyosynoviae* and the occurrence of macroscopic and histological lesions in pigs. In particular, the relationship between pathogen detection and the observed pathomorphological changes was analyzed. Another focus was the evaluation of possible correlations between the occurrence of co-infections with regard to *M. hyopneumonia* and *M. hyorhinis* and the frequency of lesions.

For this study, a retrospective analysis of the animal hospital information system (TIS) of the University of Veterinary Medicine, Vienna regarding *Mycoplasma* spp. diagnostics from pig samples from 2019 to 2022 was carried out. In addition to positive test results, such as detection by PCR or cultivation, macroscopic and histological lesions were also systematically recorded and evaluated. Particular attention was paid to the investigation of possible correlations between the diagnostic findings and the pathological changes.

The analysis of the data showed a connection between the presence of co-infection and the occurrence of lung lesions in samples in which *M. hyopneumoniae* and *M. hyorhinis* were detected. Another important finding is that *M. hyorhinis* alone can also lead to Mycoplasma-typical lung lesions. This study also showed that successful pathogen detection was accompanied by the detection of lesions in most cases. *M. hyorhinis* and *M. hyosynoviae* in joints were an exception here, as the number of cases evaluated in this area was too small to be able to make a representative statement.

SUMMARY

Infektionen bei Schweinen mit *Mycoplasma (M.) hyopneumoniae*, *M. hyorhinis* und *M. hyosynoviae* können in verschiedenen Altersgruppen zu Problemen führen. Die durch diese Erreger verursachten Krankheitsbilder können sowohl hinsichtlich der betroffenen Organsysteme als auch des Schweregrades der Erkrankung sehr unterschiedlich sein.

Das übergeordnete Ziel dieser Arbeit war es, den Zusammenhang zwischen dem Nachweis von *M. hyopneumoniae*, *M. hyorhinis* und *M. hyosynoviae* und dem Auftreten makroskopischer und histologischer Läsionen bei Schweinen umfassend zu untersuchen. Insbesondere wurde die Beziehung zwischen dem Erregernachweis und den beobachteten pathomorphologischen Veränderungen analysiert. Ein weiterer Schwerpunkt war die Bewertung möglicher Zusammenhänge zwischen dem Auftreten von Co-Infektionen mit *M. hyopneumonia* und *M. hyorhinis* und der Häufigkeit von Läsionen.

Im Rahmen dieser Arbeit wurde eine retrospektive Analyse des Tierspitalinformationssystems (TIS) der Veterinärmedizinischen Universität Wien zur Mykoplasmandiagnostik aus Schweineproben der Jahre 2019 bis 2022 durchgeführt. Neben positiven Testergebnissen, wie dem Nachweis durch PCR oder Kultivierung, wurden auch makroskopische und histologische Läsionen systematisch erfasst und ausgewertet. Besonderes Augenmerk wurde auf die Untersuchung möglicher Korrelationen zwischen den diagnostischen Befunden und den pathologischen Veränderungen gelegt.

Die Analyse der Daten zeigte einen Zusammenhang zwischen dem Vorhandensein einer Koinfektion und dem Auftreten von Lungenläsionen in Proben, in denen *M. hyopneumoniae* und *M. hyorhinis* nachgewiesen wurden. Eine weitere wichtige Erkenntnis ist, dass auch *M. hyorhinis* allein zu Mykoplasmen-typischen Lungenläsionen führen kann. Diese Studie zeigte auch, dass ein erfolgreicher Erregernachweis in den meisten Fällen mit dem Nachweis von Läsionen einherging. *M. hyorhinis* und *M. hyosynoviae* in Gelenken bildeten hier eine Ausnahme, da die Zahl der ausgewerteten Fälle in diesem Bereich zu gering war, um eine repräsentative Aussage treffen zu können.

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1. List of abbreviations

TIS = Tierspitalinformationssystem / veterinary information system

SLP= Schwein lebender Patient (living animal or complete carcass)

SEP= Schwein Eingangsprobe (singular samples)

BB= Betriebsbesuch (farm visits)

SVT= Proben von Versuchstieren (samples from animal trials)

M. hyopneumoniae = *Mycoplasma hyopneumoniae*

M. hyorhinis = *Mycoplasma hyorhinis*

M. hyosynoviae = *Mycoplasma hyosynoviae*

M. suis = *Mycoplasma suis*

CNS = central nervous system

BALF = bronchoalveolar lavage fluid

S. suis = *Streptococcus suis*

IAP = infectious anemia in pigs

G. parasuis = *Glaesserella parasuis*

PRRSV = *porcine reproductive and respiratory syndrome virus*

swIAV = *swine influenza A virus*

i.e. = id est

2. Introduction

This thesis analyses the diagnostics of mycoplasma infections in pigs. This work also aims to clarify the role of *Mycoplasma (M.). hyorhinis* in lung lesions normally associated with *M. hyopneumoniae*. In addition, the extent to which co-infections with *M. hyopneumoniae* and *M. hyorhinis* are important for the disease progress was investigated. Attention was also focused on *M. hyorhinis* in order to examine whether this pathogen has a potential role in the pathogenesis of serositis, arthritis and CNS-associated pathologies. In addition, the potential impact of *M. hyosynoviae* was also considered, particularly with regard to its involvement in the development of arthritis. Therefore, the detection of mycoplasma from different organs was analyzed and a comparison between the detection and the corresponding lesions was made.

2.1. Mycoplasma in pigs

With regard to the cell wall structure, three large groups of bacteria are distinguished: those that are gram positive, gram negative and cell wall-less. Mycoplasma belong to the cell wall-less bacteria and require special culture media to be cultivated and additional inhibitors against other bacteria are necessary due to the slow growth of mycoplasma. Since mycoplasma lack a rigid cell wall, different forms of the bacteria occur. These vary from spherical or pear-shaped cells to branched or helical filaments (1).

There are 5 types of mycoplasma species that regularly occur in pigs. These are *M. hyopneumoniae*, *M. hyorhinis*, *M. flocculare*, *M. hyosynoviae* and *M. suis*. This thesis, however, focuses on *M. hyopneumoniae*, *M. hyorhinis*, *M. hyosynoviae*, as these species do have notable pathogenic potential and are frequently detected (2).

2.1.1. *Mycoplasma hyopneumoniae*

M. hyopneumoniae is the primary cause of enzootic pneumonia (EP), which is a respiratory disease characterized by coughing and retarded growth. If the pig is only affected by *M. hyopneumoniae*, it is referred to as porcine mycoplasmosis, but if other bacterial pathogens are also present, it is called EP (2). The most frequently found secondary pathogens include *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Glaesserella (G.) parasuis*, *M. hyorhinis* and *Streptococcus (S.) suis* (3,4). In addition, viral pathogens such as porcine reproductive and respiratory syndrome virus (PRRSV) or swine influenza A virus (swIAV) may

also be present (5,6). EP is characterized by high morbidity and low mortality. The pathological lesions on the lungs are mainly seen in the cranioventral areas presenting as catarrhal pneumonia, whereby enlargement of the bronchial and mediastinal lymph nodes is also possible; histologically, peribronchial round cell infiltrates and hyperplasia of the bronchus-associated lymphatic tissue (BALT) are seen (2,7).

2.1.1.1. Symptoms

The symptoms depend on the pathogenicity of the above-mentioned secondary pathogens. Porcine mycoplasmosis is a disease with a non-productive cough and minimal influence on the growth of the pigs. In the case of EP, the non-productive cough is accompanied by a stronger influence on growth and mild fever (2). The cough can last from weeks to months (8). When pigs become infected with *M. hyopneumoniae* that have not previously been exposed to the pathogen, pigs of all ages can be affected and morbidity can be as high as 100% (2). The interaction of PRRSV and an infection with *M. hyopneumoniae* can also lead to a worsening of the symptoms that occur and the infection can last longer (6).

2.1.1.2. Diagnostics

The cultivation of *M. hyopneumoniae* is difficult because it takes a lot of time and the requirements for the culture medium are very high. For this reason, a negative culture is not considered proof that the sample material does not contain *M. hyopneumoniae*. If the sample material contains other pathogens such as *M. hyorhinis*, *M. hyorhinis* can easily overgrow *M. hyopneumoniae*, as this pathogen grows much faster and would therefore falsify the result of the culture (9). For these reasons, the PCR method is the gold standard for the detection of *M. hyopneumoniae* (2).

2.1.2. *Mycoplasma hyosynoviae*

M. hyosynoviae causes non-purulent arthritis, mostly in fattening pigs and gilts (2). The pathogen has a particularly high affinity for joints and also has a high morbidity in herds, which in turn can lead to a high economic loss for the owner (7).

2.1.2.1. Symptoms

An infection with *M. hyosynoviae* is manifested by lameness and increased joint filling in the hind extremities. Affected animals often put less weight on the limb with the infected joint and

show pain when walking (2). Affected joints show some macroscopic changes such as increased filling with yellowish-brownish serofibrinous to serosanguinous fluid. In chronically infected joints, the joint capsule may have already expanded due to the increased filling (7).

2.1.2.2. Diagnostics

Synovia taken under sterile conditions from a living or already euthanized pig is best suited for diagnostics. If it is not possible to obtain synovia, swabs can alternatively be taken from the joint surfaces. However, the cultural detection of *M. hyosynoviae* from infected joints is difficult because the pathogen concentration is often below the detection level. A good alternative is detection using the PCR method (2).

2.1.3. *Mycoplasma hyorhinis*

M. hyorhinis is a pathogen that affects the upper respiratory tract in pigs, but it can also cause polyserositis, arthritis, otitis, meningitis and conjunctivitis. It can be detected directly from the respective organs as well from nasal swabs or bronchoalveolar lavage (2,10,11).

2.1.3.1. Symptoms

M. hyorhinis can lead to various diseases such as polyserositis, arthritis, otitis, but an infection can also remain asymptomatic (2). Polyserositis and arthritis often occur in pigs between three and ten weeks of age, occasionally also in young adult pigs, often after increased exposure to stress. However, the symptoms of an infection can vary and range from swollen joints and lameness to inappetence and increased body temperature (7). *M. hyorhinis* can also cause conjunctivitis, but this disease is not considered to be a major economic loss, although sporadic occurrence in pig herds of this disease is possible. As the disease does not have a major economic impact, it is not tested often enough to accurately assess the role of *M. hyorhinis* as a trigger in this event (12).

2.1.3.2. Diagnostics

From a diagnostic point of view, it should be noted that the macroscopically visible lesions are very similar to changes caused by an infection with *G. parasuis* or *S. suis*.

In serofibrinous or fibrinopurulent polyserositis, the typical lesions include fibrin clasp in the abdominal cavity, which extend for example from the abdominal wall to the organs (7). If joints

are affected, the changes would be represented by fibrin deposits in the joint, swelling and hyperemia of the synovial membrane (2,13). Samples are taken from joints or body cavities involved in the infection for diagnostic purposes. However, it is important to avoid a chronically ill animal during sampling, as co-infections with other pathogens can also occur in these animals, which can make the detection of *M. hyorhinis* more difficult (2). If a synovial sample is taken for detection, it is recommended that it is taken under aseptic conditions before the affected joint is opened. This applies to samples taken intra vitam as well as post-mortem. If no synovial fluid can be taken from the post-mortem samples, a bacteriological swab can also be taken from the joint. In the case of polyserositis, it is recommended to take a swab sample from the serosa of the altered areas in the abdominal cavity or thoracic cavity (2). To detect *M. hyorhinis* in a pig with conjunctivitis, it is recommended to take a conjunctival swab, as with all other samples, it is possible to carry out a culture or PCR afterwards (12). However, culture is only possible on special culture media and with samples from acute or subacute lesions, as the risk of overgrowth from co-infection would be too great in chronic diseases (2).

3. Material and methods

3.1. Material

The TIS is the digital program in which all patient data is stored at the Vetmeduni Vienna. Each patient has their own TIS-ID and therefore their own personal file. The file contains information about the patient's owner, findings of all kinds, surgical protocols, results of clinical examinations and treatment plans. With regard to this thesis, the findings in the "Mycology and microbiology" category were relevant, as the test results for mycoplasma can be found there.

In TIS there are different types of samples from swine: SLP (living animal or complete carcass), SEP (singular samples), BB (farm visits), SVT (animals/ samples from animal trials). Histological examinations are typically also carried out on the SLP samples, because they involve sending in an entire body of a swine. On the other hand, with the SEP samples, there are often no histological examinations because only organ or swab samples were submitted.

3.2. Methods

In this thesis, the data from the TIS of the University of Veterinary Medicine of Vienna were retrospectively analyzed from January 2019 to December 2022. This data comes from samples from all over Austria, which were sent to the University Clinic for Swine for further diagnostics regarding mycoplasma infection.

The following sample materials were examined for the above-mentioned pathogens: Lung, serosal swabs, synovia, CNS material, oral fluids and bronchoalveolar lavage fluid (BALF).

Table 1 different sample materials

<i>Mycoplasma hyopneumoniae</i>	<i>Mycoplasma hyorhinis</i>	<i>Mycoplasma hyosynoviae</i>
lung	serosasal swabs	serosa
oral fluids	CNS material	synovia
BALF	lung	
	synovia	

BALF = bronchoalveolar lavage fluid; CNS material = central nervous system material

In addition to the bacteriological findings, the pathological findings were examined regarding to macroscopic and histological lesions and included in the evaluation. These included macroscopic findings such as fibrino-purulent inflammation in the joint as well as swelling,

pneumonia of the cranial lobes, serositis with adhesions due to fibrin or fibrinous adhesions between organs and the chest/abdominal wall. Histological changes would for example be manifested by peribronchial round cell infiltrates in the lungs or infiltration of the leptomeninges with neutrophil granulocytes in cases of meningitis.

Table 2 pathological findings histological

	typical lesions	
	macroscopic	histological
lungs	pneumonia of the cranial lobes	peribronchial round cell infiltrates
joints	fibrin deposits, swelling	infiltration with neutrophilic granulocytes, inflammatory round cells
CNS	fibrin deposititis, hyperaemic meninges	infiltration of the leptomeninges with neutrophilic granulocytes
serosa	fibrin deposits	infiltration with neutrophilic granulocytes

CNS = central nervous system

The data was then entered into an Excel file. Culture was classified as: sporadically/after enrichment (1), low grade (2), moderate grade (3), high grade (4) or negative (0) if the culture was unsuccessful. For PCR findings, a decision was only made between positive (1) and negative (0).

Table 3 cultivation / PCR results

	cultivation	PCR
0	negative	negative
1	sporadically/after enrichment	positive
2	low grade	
3	moderate grade	
4	high grade	

3.3. Analyses

All the data mentioned above were entered into an Excel file. Once all the necessary data had been collected, the statistical analysis was performed using SPSS (IBM SPSS Statistics, IBM, Armonk, NY, USA). For the analysis of the collected data, descriptive statistics in the form of cross tables were performed. Firstly, the proportion of submitted samples sent in that were positive was analyzed and then attention was paid to whether there was a connection between the positive detection of the pathogens and the existence of lesions. In addition, the lung samples were analyzed for co-infections of *M. hyopneumonia* and *M. hyorhinis*. A list of comparisons can be found in tables 4 -17.

4. Results

A total of 730 samples from the years 2019 to 2022 were evaluated. Attention was paid to which mycoplasma was predominantly detectable in which sample material.

4.1. Pathogen detection in the context of histologic lesions

4.1.1. Detection of *M. hyorhina* in the presence and absence of histological lesions

4.1.1.1. Detection in lung tissue

Table 4 detection of *M. hyorhina* in lung tissue

<i>M. hyorhina</i> lungs		
	occurrence	percentage
not detected	96	49,5
successfully detected	98	50,5
total	194	100

A total of 194 samples of lung tissue were analyzed for *M. hyorhina*, using culture or PCR as detection methods. Detection was successful in 98 samples, i.e. 50,5%, while *M. hyorhina* could not be detected in 96 samples, i.e. 49,5%.

Table 5 detection of *M. hyorhina* in the presence and absence of histological lesions in the lungs

<i>Mycoplasma hyorhina</i> (lung)	no typical lesions	typical lesions	total
not detected	33 (19,9%)	47 (28,3%)	80 (48,2%)
successfully detected	53 (31,9%)	33 (19,9%)	86 (51,8%)
total	86 (51,8%)	80 (48.2%)	168

Table 5 shows the detection of *M. hyorhina* in the presence or absence of typical histologic lesions in the lungs. Only cases in which *M. hyorhina* was investigated in the lungs and a histological examination of lung tissue was performed were included in this comparison (n = 186). *M. hyorhina* was successfully detected in 86 samples. In 33 samples, *M. hyorhina* was successfully detected in combination with the typical histological lesions.

4.1.1.2. Detection in serosal swabs

Table 6 detection of *M. hyorhinis* in serosal swabs

<i>M. hyorhinis</i> serosa		
	occurrence	percentage
not detected	191	80,3
sucessfully detected	47	19,7
total	238	100

A total of 238 samples of serosal swabs were analyzed for *M. hyorhinis*, using culture or PCR as detection methods. Detection was successful in 47 samples, i.e. 19,7%, while *M. hyorhinis* could not be detected in 191 samples, i.e. 80,3%.

Table 7 detection of *M. hyorhinis* in the presence and absence of histological lesions of the serosa

<i>Mycoplasma hyorhinis</i> (serosa)	no typical lesions	typical lesions	total
not detected	48 (23.3%)	119 (57,8%)	167 (81,1%)
sucessfully detected	4 (1,9%)	35 (17,0%)	39 (18,9%)
total	52 (25,2%)	154 (74,8%)	206

Table 7 shows a comparison between the detection of *M. hyorhinis* and the occurrence of typical lesions on the serosa. Only cases in which *M. hyorhinis* was investigated in serosal swabs and a histological examination of serosal structures was performed were included in this comparison (n = 206). *M. hyorhinis* was successfully detected in 39 samples. In 35 samples, *M. hyorhinis* was successfully detected in combination with the typical histological lesions.

4.1.1.3. Detection in joints

Table 8 detection of *M. hyorhinis* in joints

<i>M. hyorhinis</i> joints		
	occurrence	percentage
not detected	65	90,3
sucessfully detected	7	9,7
total	72	100

A total of 72 samples from joints were analyzed for *M. hyorhinis*, using culture or PCR as detection methods. Detection was successful in 7 samples, i.e. 9,7%, while *M. hyorhinis* could not be detected in 65 samples, i.e. 90,3%.

Table 9 detection of *M. hyorhinis* in the presence and absence of histological lesions in the joints

<i>Mycoplasma hyorhinis</i> (joints)	no typical lesions	typical lesions	total
not detected	16 (32,7%)	30 (61,2%)	46 (93,3%)
successfully detected	1 (2,0%)	2 (4,1%)	3 (6,1%)
total	17 (34,7%)	32 (65,3%)	49

Table 9 shows a comparison between the detection of *M. hyorhinis* and the occurrence of typical lesions in the joints. Only cases in which *M. hyorhinis* was investigated in the joints and a histological examination of joint-associated tissue was performed were included in this comparison (n = 49). *M. hyorhinis* was successfully detected in 3 samples. In 2 samples, *M. hyorhinis* was successfully detected in combination with the typical histological lesions.

4.1.1.4. Detection in the CNS

Table 10 detection of *M. hyorhinis* in the CNS

<i>M. hyorhinis</i> CNS		
	occurrence	percentage
not detected	60	80
successfully detected	15	20
total	75	100

CNS = central nervous system

A total of 75 samples of the CNS were analyzed for *M. hyorhinis*, using culture or PCR as detection methods. Detection was successful in 15 samples, i.e. 20%, while *M. hyorhinis* could not be detected in 60 samples, i.e. 80%.

Table 11 detection of *M. hyorhinis* in presence and absence of histological lesions of CNS material

<i>Mycoplasma hyorhinis</i> (CNS)	no typical lesions	typical lesions	total
not detected	17 (25%)	37 (54,4%)	54 (79,4%)
successfully detected	5 (7,4%)	9 (13,2%)	14 (20,4%)
total	22 (32,4%)	46 (67,6%)	68

CNS = central nervous system

Table 11 shows a comparison between the detection of *M. hyorhinis* and the occurrence of typical lesions in the CNS. Only cases in which *M. hyorhinis* was investigated in the CNS and a histological examination of the meninges was performed were included in this comparison (n = 68). *M. hyorhinis* was successfully detected in 14 samples. In 9 samples, *M. hyorhinis* was successfully detected in combination with the typical histological lesions.

4.1.2. Detection of *M. hyopneumoniae* in the presence and absence of histological lesions

Table 12 detection of *M. hyopneumoniae* in lung tissue

<i>M. hyopneumoniae</i> lungs		
	occurrence	percentage
not detected	216	64,7
sucessfully detected	118	35,3
total	334	100

A total of 334 samples of lung tissue were analyzed for *M. hyopneumoniae*, using culture or PCR as detection methods. Detection was successful in 118 samples, i.e. 35,3%, while *M. hyopneumoniae* could not be detected in 216 samples, i.e. 64,7%.

Table 13 detection of *M. hyopneumoniae* in presence and absence of histological lesions in the lungs

<i>Mycoplasma hyopneumoniae</i> (lungs)	no typical lesions	typical lesions	total
not detected	66 (28,6%)	73 (31,6%)	139 (60,2%)
sucessfully detected	23 (10%)	69 (29,8%)	93 (39,8%)
total	89 (38,6%)	142 (61,4%)	231

Table 13 shows a comparison between the detection of *M. hyopneumoniae* and the occurrence of typical lesions in the lungs. Only cases in which *M. hyopneumoniae* was investigated in the lungs and a histological examination of lung tissue was performed were included in this comparison (n = 231). *M. hyopneumoniae* was successfully detected in 93 samples. In 69 samples, *M. hyopneumoniae* was successfully detected in combination with the typical histological lesions.

4.1.3. Detection of *M. hyosynoviae* in the presence and absence of histological lesions

Table 14 detection of *M. hyosynoviae* in joints

<i>M. hyosynoviae</i> joints		
	occurrence	percentage
not detected	66	97,1
sucessfully detected	2	2,9
total	68	100

A total of 68 samples from joints were analyzed for *M. hyosynoviae*, using culture or PCR as detection methods. Detection was successful in 2 samples, i.e. 2,9%, while *M. hyosynoviae* could not be detected in 66 samples, i.e. 97,1%.

Table 15 detection of *M. hyosynoviae* in the presence and absence of histological lesions in the joints

<i>Mycoplasma hyosynoviae</i> (joints)	no typical lesions	typical lesions	total
not detected	17 (34%)	31 (62%)	48 (96%)
successfully detected	1 (50%)	1 (50%)	2 (4%)
total	18	32	50

Table 15 shows a comparison between the detection of *M. hyosynoviae* and the occurrence of typical lesions in the joints. Only cases in which *M. hyosynoviae* was investigated in the lungs and a histological examination of joint associated tissue was performed were included in this comparison (n = 50). *M. hyosynoviae* was successfully detected in 2 samples. In 1 sample, *M. hyosynoviae* was successfully detected in combination with the typical histological lesions.

4.2. Mycoplasma co-infection in the lung tissue

Table 16 detection of *M. hyorhinis* and *M. hyopneumoniae* with regard to a co-infection

	<i>Mycoplasma hyopneumoniae</i> (lung)		
<i>Mycoplasma hyorhinis</i> (lung)	not detected	successfully detected	total
not detected	12	21	33
successfully detected	20	15	35
total	32	36	68

Table 16 shows a comparison between the detection of *M. hyorhinis* and *M. hyopneumoniae* in the lungs. This table only includes samples that were tested for both *M. hyorhinis* and *M. hyopneumoniae* in lung tissue. A total of 68 samples from the lung were examined for the presence of *M. hyorhinis* and *M. hyopneumoniae*. In 15 samples *M. hyopneumoniae* and *M. hyorhinis* were successfully detected.

4.3. Comparison between *M. hyorhinis* detection by culture and PCR

Table 17 comparison of the cultural detection of *M. hyorhinis* and the PCR detection of *M. hyorhinis* in the lungs

		<i>Mycoplasma hyorhinis</i> (PCR)			
		not investigated	negative	positive	total
<i>Mycoplasma hyorhinis</i> (cultivation)	not investigated	0	24	14	38
	not detected	61	11	0	72
	after enrichment	9	4	0	13
	low grade	11	0	1	12
	moderate grade	24	0	5	29
	high grade	27	0	3	30
	total	132	39	23	194

In table 17, the cultural detection of *M. hyorhinis* and the PCR detection of *M. hyorhinis* in the lungs were compared. A total of 388 samples from the lungs were examined for the presence of *M. hyorhinis* either by PCR or using cultivation. The PCR was negative in 4 samples, but *M. hyorhinis* was detected in the culture after enrichment. This indicates a higher sensitivity of the culture.

5. Discussion

An important aim in the evaluation of the data in this study was to investigate the interaction between the detection of *M. hyopneumoniae* in the lungs and the presence of macroscopic and histological lesions. In this study, a total of 334 samples were analyzed regarding the presence of *M. hyopneumoniae* (table 12), 35,3% of which were positive for *M. hyopneumoniae*. In 231 of these 334 cases an accompanying histopathologic investigation was also performed (table 13). Overall, 58.5 % of samples resulted in the expected correlation of the detection of both, the pathogen and the corresponding lesions (29.9 %) or detection of neither pathogen nor lesions (28.6 %). Histopathologic lesions, like peribronchial infiltration with round cells and migration of neutrophil granulocytes, suggestive of infection with *M. hyopneumoniae* were identified in 142 samples. These lesions after *M. hyopneumoniae* infection were, among others, described in a study by Woolley et al. (14), which investigated the development of macroscopic lung lesions in pigs infected with two different strains of *M. hyopneumoniae* (Hillcrest and Beaufort strain). On day 21 after infection, the lesions occurred predominantly in the left apical, cardiac and accessory lobes of the lung, whereas on day 28 they were only detectable in the ventral lobe after infection with the Hillcrest strain. Therefore, in this work macroscopic lesions which were predominantly localized in the apex/cranioventral lobes, were considered as Mycoplasma-typical. In the study by Woolley et al. (14), the primary histologic changes in *M. hyopneumoniae* infection were described as peribronchial and perivascular lymphocytic hyperplasia accompanied by alveolar exudate containing macrophages, monocytes, and polymorphonuclear leukocytes. The samples in this study were taken at times after the onset of clinical signs, with the exact time of infection remaining unknown. Since the changes observed in the study by Woolley et al. (14) and the changes in the samples analyzed in this study are similar, it is not possible to conclude if the time of sampling affects the detection of lesions. Contrasting this, Almeida et al. (15) also analyzed lung tissue for macroscopic and microscopic lesions after an experimental infection with *M. hyopneumoniae*. The microscopic lesions were graded, which also included peribronchiolar and perivascular lymphoplasmacytic hyperplasia. These microscopic changes were described in the study as characteristic of swine mycoplasmal pneumonia. It was described in the study that the microscopic lesions tend to occur later in the infection with *M. hyopneumoniae*, whereas the macroscopic lesions decrease towards the end

of the infection, leaving behind scar tissue, which was described as grey fish flesh in the study by Almeida et al. (15). Unfortunately, we have no information about how long the infection with *M. hyopneumoniae* persisted in the samples of this study, and for this reason no statement can be made about the correlation between the duration of infection and the occurrence of microscopic lesions. For future studies it would be important to include the chronicity of the infections in the analysis in order to be able to better describe the correlation between the development of lesions and the duration of the infection. Another very interesting point for a future study would be to include the clinical symptoms of the pigs in the evaluation in order to be able to assess a possible connection between the occurrence of symptoms and the presence and severity of the lesions.

When analyzing the data in this study, attention was also paid to the correlation between the detection of *M. hyopneumoniae* and *M. hyorhinis* in lung tissue (table 16), as the role of *M. hyorhinis* as a pulmonary pathogen is still controversial. At least one of these pathogens was successfully detected in 56 samples. In 20 cases only *M. hyorhinis* could be detected, in 15 cases even both pathogens. In 21 cases, only *M. hyopneumoniae* was detected. It should be noted that the effect of the co-infection of *M. hyopneumoniae* and *M. hyorhinis* is controversially discussed in various studies. In the paper by Ferreira et al. (16), the occurrence of co-infections of *M. hyopneumoniae*, *M. hyorhinis* and *M. flocculare* was investigated, also focusing on a correlation of these co-infections with macroscopic and microscopic lesions. The study discusses that *M. hyopneumoniae* is the primary pathogen and causes the primary lung changes and that *M. hyorhinis* and *M. flocculare* can only aggravate these changes and are more likely to be referred to as secondary pathogens. In contrast to the significant positive correlation between the detection of *M. hyopneumoniae* and the occurrence of lung lesions, no significant correlation could be shown between the detection of *M. hyorhinis* and lesions. Similarly, no positive correlation was found between the detection of *M. hyopneumoniae* and *M. hyorhinis*. The study by Renzhammer et al. (3) showed a negative correlation between the occurrence of *M. hyopneumoniae* and *M. hyorhinis*. In contrast to these results, the paper by Tonni et al. (17) found that a co-infection of *M. hyopneumoniae* and *M. hyorhinis* correlated positively. Although *M. hyorhinis* was detected in the respiratory tract of pigs in this study, it is assumed that it is a colonizer of the respiratory tract of pigs. Despite proven co-infections between *M. hyopneumoniae* and *M. hyorhinis*, this does not mean that there is necessarily an interaction

between these two pathogens. In order to gain a more comprehensive understanding of the clinical relevance of co-infections with *M. hyorhinis* and *M. hyopneumoniae*, it would be of scientific interest to conduct further studies on this topic. More in-depth investigations could provide more precise insights into the extent to which such co-infections influence the course of the disease and what significance they have. Another scientifically relevant aspect is to systematically investigate the influence of the pathogens on the severity of the lesions. Unfortunately, nothing was mentioned by Lee et al. (19) regarding the influence of these pathogens on the severity of the lesions in order to be able to compare the results of the study with those of the study by Thacker et al. (6). With regard to the lesions, it should be noted that there was no association between the detection of *M. hyorhinis* and a worsening of the lung lesions (17). This result is consistent with the results of the study by Ferreira et al. (16). In the study by Li et al. (20), the lung microbiome of healthy and diseased pigs was analyzed. Among other things, attention was paid to the interaction between *M. hyopneumoniae* and *M. hyorhinis*. *M. hyopneumoniae* is considered the main pathogen responsible for enzootic pneumonia, while *M. hyorhinis* is regarded as negligible. However, *M. hyopneumoniae* as well as *M. hyorhinis* can lead to the development of lung lesions, but an interaction of the two pathogens leads to more severe lung lesions, as the relative frequency of the pathogens was significantly higher in lungs with severe lesions (21). The results of this study also provided evidence that *M. hyorhinis* is potentially responsible for the development of lung lesions. This finding is consistent with the results of the study by Li et al. (20). The discussion about the role of *M. hyorhinis* in the pathogenesis of respiratory diseases remains complex and multifaceted. While there is still discussion regarding the correlation of co-infections with lung lesions, the data collected in this work provide additional evidence for the role of *M. hyorhinis* as a lung pathogen independent from *M. hyopneumoniae*.

According to the data analysis of this study, *M. hyorhinis* was successfully detected in 86 lung samples (table 5). Typical lung lesions were only detected in 33 of these 86 samples, showing that the presence of *M. hyorhinis* does not necessary lead to lung infection and corresponding lesions (16,22). However, there were also 47 samples in which *M. hyorhinis* was not detected, but which also showed the typical lesions. However, it should be noted that in this specific data comparison no consideration was given to *M. hyopneumoniae*, which in turn could explain the occurrence of lesions without *M. hyorhinis* pathogen detection. The study by Luehrs et al. (22)

investigated whether *M. hyorhinis* can cause the same lung lesions as *M. hyopneumoniae*. *M. hyorhinis* was increasingly detected in lungs that had lesions, but there was hardly any successful detection of *M. hyorhinis* in the lungs with the most severe lesions. It was also found by Luehrs et al. (22) that there was no correlation between the occurrence of co-infections of *M. hyorhinis* and *M. hyopneumoniae* and an increase in pneumonia. This finding was also obtained in a study by Falk et al. (23). In comparison to the studies by Ferreira et al. (16) and Tonni et al. (17), the result is controversial, as these two studies concluded that there is a correlation between the detection of a co-infection with *M. hyorhinis* and *M. hyopneumoniae* and the worsening of the lesions. The study by Adrian Luehrs et al. (22) however concluded that *M. hyorhinis* does not play a significant role as a pathogen of enzootic pneumonia but acts as a secondary pathogen and no evidence was found that *M. hyorhinis* alone can lead to the same lesions as *M. hyopneumoniae*. These results contradict the findings of this work, as *M. hyorhinis* was successfully detected in 20 lung samples alongside the Mycoplasma typical macroscopic and histologic lesions, but *M. hyopneumoniae* could not be successfully detected in these samples (table 16). The results of the study by Palzer et al. (24) underline these results, as they were also able to prove that *M. hyorhinis* can cause pneumonia with the typical lesions and clinical symptoms, as *M. hyorhinis* was detected significantly more frequently in the BALF samples from clinically abnormal animals than in the samples from healthy animals.

In this study, in addition to considering the effects of *M. hyorhinis* on the lungs, a special focus was placed on its potential role as a pathogen of the central nervous system (CNS). The aim was to analyze the occurrence of *M. hyorhinis* as a CNS pathogen and to investigate the correlation between the detection of this pathogen and the occurrence of histological lesions. The extent to which the detection of the pathogen correlates with specific pathomorphological changes in the tissue was examined. In the data set of this study, a total of 68 samples from the CNS were tested for *M. hyorhinis* and histologically examined (table 11). *M. hyorhinis* was detected in 14 of these samples, and histological lesions such as infiltration with neutrophil granulocytes, histiocytes or signs of purulent meningoencephalitis were also detected in 9 of these samples. However, there were also 37 samples in which *M. hyorhinis* could not be detected, although histological changes were present. This could indicate an infection with another pathogen such as *S. suis* or *G. parasuis*. No data on the clinical symptoms of the pigs were collected in this study, but this would be a good approach for possible future studies. In a

case series of Bünger et al. (11), it was possible to detect *M. hyorhinis* in the brain or cerebrospinal fluid of 8 pigs. In these pigs, either neurological symptoms or histological lesions could be detected, sometimes even both. The authors came to the conclusion that *M. hyorhinis* could be the cause of fibropurulent meningoencephalitis, but that further investigation and proof is necessary. In a retrospective study by Ko et al. (10), the exact relationship between the detection of *M. hyorhinis*, the occurrence of histological lesions and the occurrence of clinical symptoms was investigated. The histological changes in the CNS manifested themselves as meningitis or lymphocytic meningoencephalitis. It is of great significance that *M. hyorhinis* could be detected directly in the existing lesions in the brain by means of *in situ* hybridization. Both studies agree that the exact pathomechanism of *M. hyorhinis* in connection with the CNS lesions have not yet been clarified, but the authors assume that *M. hyorhinis* manages to overcome the blood-brain barrier and can thus enter the brain to cause the CNS lesions. The authors concluded that there is a connection between the detection of *M. hyorhinis*, the CNS lesions and the occurrence of neurological symptoms. For this reason, the pathogen should be at least considered as a differential diagnosis in the future when neurological symptoms occur. With regard to this study, it should be noted that the detection of other CNS pathogens was not taken into account in the analysis of the data set, which in turn could explain the occurrence of histological lesions without successful detection of *M. hyorhinis*. For further studies, it would be useful to also consider other CNS pathogens and to include the occurrence of neurological or other clinical symptoms in the data analysis in order to better assess the role of *M. hyorhinis* as a CNS pathogen.

In addition to the role of *M. hyorhinis* as a pathogen of the central nervous system, this study also investigates the presence of this pathogen in cases of polyserositis. In the data set of this study, *M. hyorhinis* was detected less frequently in pigs with serositis than expected. A total of 238 serosal swabs were analyzed, and *M. hyorhinis* was successfully detected in only 47, i.e. 19.7% (table 6). In cases where histopathology was also performed, *M. hyorhinis* was successfully detected in a total of 39 samples from the serosa (table 7). Of these 39 samples, 35 showed typical lesions such as fibrin clasp between the organs or between organs and the abdominal wall. Histologically, an immigration of neutrophil granulocytes could be detected. Friis et al. (25) investigated the role of *M. hyorhinis* in the development of serositis in piglets. Samples were taken from the peritoneum, pericardium and pleura. *M. hyorhinis* was isolated in

9 of 26 cases, and non-hemolytic *E. coli* was also detected in 4 of these cases. In the cases in which only *M. hyorhinis* could be detected, concomitant respiratory diseases such as pneumonia were also found. To be able to assess the pathogenicity of *M. hyorhinis* in relation to serositis, an experimental infection of two piglets was also carried out in the study by Friis et al. (25). In these two cases, the typical serofibrinous changes in the abdominal cavity also occurred, indicating that *M. hyorhinis* plays a role in the development of serositis. However, it is important to note that the study describes the association between the occurrence of serositis due to infection with *M. hyorhinis* and a weakened immune system. Friis et al. (25) think that a weakened immune system plays a significant role in the hematogenous spread of *M. hyorhinis* and thus in the development of serositis and the development of lesions. In this study, the interaction between a weakened immune system and the occurrence of serositis as a result of an infection with *M. hyorhinis* was not sufficiently considered. Given the potential relevance of this factor, this aspect should be investigated in more detail in future studies. In the study by Földi et al. (26), 5-week-old piglets were examined for the presence of *M. hyorhinis* and serositis. If signs of serositis were present, a swab sample was taken for culture and detection of *M. hyorhinis* by PCR. Chronic serositis was described in by Földi et al. (26) with characteristics such as thickening of the serosa and adhesions between serosal surfaces in the abdomen and thorax. Unfortunately, the study by Földi et al. (26) did not describe in detail the histological lesions that were looked for in the evaluation of the samples; again, only the thickening of the serosa and adhesions were mentioned, which were also mentioned in the macroscopic lesions. However, the macroscopic lesions mentioned in the study by Földi et al. (26) are consistent with the lesions found in this study. It would have been very interesting to be able to make a comparison with the histological lesions. The study by Friis et al. (25) does not describe the changes resulting from infection with *M. hyorhinis* in sufficient detail to compare them well with the changes found in the data set of this study. Although the study to be compared mentions serofibrinous changes, no histological examination of the samples is mentioned. In summary, however, it can be said that the results of the data set of this study do not contradict the results of the study by Friis et al. (25), as the occurrence of fibrinous changes or the formation of fibrin clasp is mentioned in both evaluations.

In this study, attention was also given to the role of *M. hyorhinis* in the development of arthritis and the pathological changes that may result from an infection. In the data analyzed in this

study, *M. hyorhinis* was detected in the joints a total of three times (table 8). One of the samples examined showed changes such as increased filling with cloudy contents as well as thickening and discoloration of the joint capsule, but the other sample showed no macroscopic or histological abnormalities. It is important to note that 30 samples in which *M. hyorhinis* could not be detected also showed such lesions. This can be explained by the fact that other pathogens might be responsible for these changes, but these were not taken into account for this study (table 6). In the study by Salogni et al. (28), 8 to 12-week-old post-weaning pigs suffering from arthritis and symptoms such as swollen joints and lameness were examined. *M. hyorhinis* was detected in the altered joints of 57 of 178 pigs. Serofibrinous arthritis was detected in 31 of 57 cases, but serous arthritis was detected in 24 of 57 cases, whereas purulent arthritis was detected in only two cases. A co-infection of *M. hyorhinis* and *G. parasuis* was detected in twelve pigs and a co-infection of *M. hyorhinis* and *Streptococcus* spp. in eight pigs. In conclusion, *M. hyorhinis* plays an important role in the development of post-weaning arthritis in pigs, but the severity of the disease also depends on possible co-infections with other pathogens such as *G. parasuis* and *Streptococcus* spp. In addition to these pathogens, *M. hyosynoviae* is also considered an important pathogen regarding the development of arthritis in pigs. However, no consideration was given to the presence of injuries in the joint area, which could play a role in predispositions. In conclusion, the changes described in the study by Salogni et al. (28) are consistent with the macroscopic lesions found in this dataset. Although *M. hyosynoviae* was detected in only a few cases in the study by Salogni et al. (28), previous research has shown that this pathogen plays a significant role in the development of arthritis, particularly in older pigs (13).

In this study, a total of 50 samples from joints were tested for *M. hyosynoviae* (table 9). However, *M. hyosynoviae* could only be detected in two samples, and histological lesions could only be recognized in one sample. It is important to note that only a few samples, 18 to be precise, underwent histologic examination. In these samples, infiltration with neutrophilic granulocytes and inflammatory round cells and necrosis of the synoviocytes were observed. The comparative study by Wegner et al. (29) investigated whether there was a correlation between the occurrence of lameness, *M. hyosynoviae* infection and osteochondrosis. The authors assumed that infection with *M. hyosynoviae* plays a role in the development of osteochondrosis, but only in conjunction with additional factors. Claw lesions and the presence

of osteochondropathy were mentioned as additional factors. It was initially hypothesized that cartilage lesions might favor *M. hyosynoviae* infection; however, this assumption could neither be confirmed nor refuted in the study by Nielsen et al. (30). In contrast, Lawrisuk et al. (31) were able to confirm this hypothesis in their research. Another hypothesis in the study by Wegner et al. (29) was that there is a nutritional component. However, this could only be proven in one pig. In general, macroscopic examination of the joints can reveal increased joint filling with partially cloudy synovia and fibrin effusions in the joint; histologically, the migration of neutrophilic granulocytes and inflammatory round cells as well as the deposition of fibrin were described. However, it is important to note that these changes have also been found in joints in which it was not possible to detect *M. hyosynoviae*. In the 2 samples in which *M. hyosynoviae* was detectable, changes such as heavy filling with cloudy contents as well as thickening and discoloration of the joint capsule were found. In Wegner et al. (29), the macroscopic changes were limited to a slight increase in joint filling and oedematisation of the joint capsule, a lymphoplasma-histiocytic inflammation as well as a fibrino-suppurative synovialitis was described histologically. In comparison, the macroscopic lesions in the joints found in the study by Wegner et al. (29) are largely consistent with those of this study. However, correlations with the presence of cartilage lesions or nutrition-related correlations were not further investigated or considered in this study. In the study by Lauritsen et al. (32), the relationship between the occurrence of arthritis caused by *M. hyosynoviae* and the age of the affected pigs was investigated. A group of 13-week-old pigs was compared with a group of 6-week-old pigs after they had been artificially inoculated with *M. hyosynoviae*. However, it was found that the clinical signs and pathological changes did not vary. In contrast, the study by Lauritsen et al. (33) mentioned that piglets suffer less frequently from arthritis caused by *M. hyosynoviae* when they are protected by maternal antibodies. This would also explain, among other things, why so few positive results were found when analyzing the samples in this study, as only very few samples from fattening pigs or breeding sows were analyzed here, as most of the samples came from rearing or suckling piglets.

When evaluating the data in this study, attention was also paid to the comparison of the cultural detection method and PCR for *M. hyorhinis*. It should be noted that only for lung tissue enough samples were investigated in order to make a comparison between two detection methods. At this point it should be emphasized that the PCR was negative in four samples, while *M.*

hyorhinis grew in culture after enrichment. The number of samples is so small because there were not very many samples in which both cultivation and PCR were performed. However, there were no samples in which the PCR was positive and nothing grew during cultivation, which speaks in favor of a higher sensitivity of cultivation. Unfortunately, there are no comparative studies for *M. hyorhinis*, but Sibila et al. (4) compared the sensitivity of cultivation with that of PCR for *M. hyopneumoniae* detection. It was found that culture has a higher sensitivity than PCR, but culture is more difficult to perform than PCR. The sensitivity of the culture remains higher than that of the PCR in the case of a prolonged infection, as the PCR is often negative at a low concentration of mycoplasma, whereas the mycoplasma are often still detectable in culture. These findings were also confirmed by the study by Sorensen et al. (34). To summarize, it can be said that the data from this study show that cultural detection is more sensitive, but it should be noted that the cultivation of *M. hyorhinis* differs significantly from that of *M. hyopneumoniae*, as it is not as time-consuming.

In conclusion, it should be emphasized that the most important findings of this study are that *M. hyorhinis* is capable of causing pulmonary lesions on its own, without necessarily requiring an infection with *M. hyopneumoniae*. Furthermore, it could be shown that co-infections with *M. hyorhinis* and *M. hyopneumoniae* are possible in principle. However, the exact interaction of both pathogens with regard to the pathogenesis of lung lesions has not yet been sufficiently researched. Against this background, it appears necessary to carry out further studies in order to analyze the mechanisms of co-infections and their influence on the development of the disease in more detail.

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