

# Study of the development of ultrasonographic findings in the lung of foals with pneumonia

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**Summary:** Pneumonia in foals is one of the major diseases in a horse breeding farm. As prevention is difficult, early diagnosis, well monitored treatment and reliable prognosis are important to minimise losses. The localization of pulmonary lesions of foals with different severity of abscessing bronchopneumonia and their development during treatment were observed to find a parameter that signals the worsening of pneumonia early. The prospective clinical study was performed with four groups of foals with pulmonary lesions of different severity that were followed up during treatment. The severity of pulmonary lesions in 453 foals with subclinical and clinical pneumonia on a horse breeding farm was determined by ultrasonography of the thorax. After pneumonia had been diagnosed, the clinical examination was done weekly, the white blood cells (WBC) were counted and ultrasonography of the thorax, including measurement of the abscess score, was performed twice weekly until recovery. One hundred and thirty-five foals had a small pneumonia (abscess score: 5–9.5 cm) and received no antibiotic treatment; 219 foals had a mild (abscess score: 10–15 cm), 91 foals had a moderate (abscess score: 15–20 cm) and 66 foals a severe pneumonia (abscess score: > 20 cm). All foals fully recovered in a max. of 9.5 weeks of treatment. Most lesions were localized in the cranio-ventral area of the lung and more severe in the right lung than on the left side. In severely affected foals, those who needed a change of treatment had 74% lesions of the size of 2 cm or larger, while foals with success of the first treatment had only 48% of the same size. The number of ultrasonographic findings decreased mostly within the first two weeks after diagnosis, independently of the severity of the lesions. The clinical score on the day of diagnosis was higher in foals who later needed a change of treatment, while the WBC count is neither reliable for early diagnosis nor a hint for a prognosis of treatment success. In conclusion the size of consolidations seems to be of prognostic value in severely affected foals. The important period in monitoring foals with pneumonia during treatment is the first two weeks after diagnosis is done because the decrease of ultrasonographic findings and the need for a change of treatment is obvious in that period of time.

**Keywords:** foals, pneumonia, ultrasonographic examination, localization of lesions, development of lesions

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## Introduction

Pneumonia is an important disease in foals and causes severe disorders during the first six months of life. *Streptococcus equi* ssp. *zooepidemicus* (*Strep. zoo.*) and *Rhodococcus equi* (*R. equi*) are the most frequent agents in abscessing pneumonia in foals (Lavoie et al. 1994). *R. equi* is a facultative intracellular bacterium which can survive and replicate in macrophages. It is widespread around the world and frequently detected in the soil of horse farms (Takai 1985). The infection can be endemic or sporadic on a farm. *Strep. zoo.* is a normal inhabitant of the upper respiratory tract and also a common pathogen of pulmonary abscesses in horses (Hoffman 1993).

Pneumonia is responsible for high costs to the breeder, due to veterinary care, medication and losses of foals if the diagnosis is made later in the course of the disease (Cohen et al. 2000). The treatment success is higher when pulmonary lesions are less severe (Cohen et al. 2002). Therefore, a reliable method of early diagnosis is necessary, especially on farms with endemic infections due to *R. equi* and *Strep. zoo.* Early diagnosis programmes

include clinical examination, haematological parameters and ultrasonographic examination of the thorax (Giguere et al. 2011). In the case of *R. equi* infection, the respiratory symptoms point to a pneumonia only at a late stage of the disease and sometimes the foals show little to no clinical signs even shortly before death (Giguere and Prescott 1997). Furthermore, regular measuring of the rectal temperature and the respiratory rate has been recommended for screening programs (Cohen et al. 2002). The evaluation of blood samples for the white blood cell (WBC) count (Falcon 1985), fibrinogen (Giguere et al. 2003, Giguere and Prescott 1997) and Serum amyloid A concentration (Cohen 2005, Giguere et al. 2016, Thomé et al. 2018) have been previously reviewed for early detection, showing some reliable results for the diagnosis of *R. equi* pneumonia.

Diagnostic imaging of the lung, either radiography or ultrasonographic examination, is very sensitive and specific in the diagnosis of pneumonia in foals. Radiographic imaging of pulmonary lesions has been described as strongly suggestive of *R. equi* (Cohen et al. 2002), even though the sensitivity is not as high as ultrasonography (Venner et al. 2014). The latter is

frequently used for screening in farms with endemic pneumonia as it is not invasive to the foals, takes little time, and the results are immediate and highly sensitive to pulmonary abscesses. The limitation of this technique is that only peripheral lesions can be revealed, thus, central-seated lesions remain undetected.

The current standard treatment of the *R. equi* pneumonia is rifampin in combination with a macrolide, most frequently azithromycin.

In this study we describe the distribution of pulmonary lesions and the development after diagnosis in foals with pneumonia. A further aim was to find a parameter that signals the worsening of pneumonia early during observation time.

## Method and Materials

### Study Population

The study was conducted on a stud farm of warmblood horses in the breeding season of 2018. Earlier studies on this farm revealed endemic incidence of *R. equi*, detected from tracheobronchial aspirates (Hennig 2020 submitted, Heyers 2007, Kilian 2008, Lämmer 2010) and post-mortem examination (Weimar 2006).

All the foals of the farm were monitored from birth until the age of 5.5 months. Each foal was examined clinically weekly, an Ethylenediaminetetraacetic acid (EDTA) blood sample for determining the WBC count was taken and ultrasonographic examination of the chest was performed.

**Table 1** Clinical score (according to Ohnesorge et al. 1998, modified) | Klinischer Score (modifiziert nach Ohnesorge et al. 1998)

Clinical Score	Aberrances	Score
Nasal discharge	Normal	0
	Serous	1
	Mucous, purulent	2
Lymph nodes	Normal	0
	Enlarged	1
Auscultation Lung	Normal	0
	Mild (raw sounds)	1
	Severe (rattle, rhonchus)	2
Auscultation Trachea	Normal	0
	Mild (raw sounds)	1
	Severe (rattle, rhonchus)	2
Rectal temperature	Normal (< 39.0 °C)	0
	Mildly elevated (39.0–39.4 °C)	1
	Highly elevated (> 39.5 °C)	2
Dyspnoea	No	0
	yes	3
Respiratory frequency	Below 80/min	0
	Above 80/min	1

The clinical parameters included rectal temperature, nasal discharge, lymph nodes, auscultation of the lung and trachea, dyspnoea and the respiratory frequency, combined in a clinical score (Table 1). If the clinical score was below or equal to 2, the foal was considered as clinically healthy. The WBC count cut-off value was above 13,000 G/L.

### Ultrasonographic method

A portable unit (Esaote Tringa Linear, Milano, Italy) with a 7.5 MHz linear transducer was used for the ultrasonographic examination. Both sides of the thorax were drenched with 99 % alcohol and intercostal spaces 3 to 14 were examined from dorsal to ventral. The consolidations were recorded on a form with the precise localization (right and left lung, number of the intercostal space, the dorsal part, middle part or the ventral part of the lung) and the diameter in cm. Consolidations with an irregular form were evaluated by measuring the smallest and the widest diameter and taking the average of the two values. The diameter of all consolidations was added to an “abscess score” at the end of each ultrasonographic examination. The abscess score was a marker for the severity of the pulmonary disorder.

### Study design

All foals were examined every week; those with an abscess score above 5 cm were included in the study. They were divided in four groups, each with a different severity of pneumonia, i.e. different abscess score range and different treatment. The day of diagnosis of pneumonia, i.e. the day of admission into the study, was defined as the examination day (ED) 1, while the interval between two EDs was 3–4 days. The WBC counts and findings from ultrasonography were recorded on every ED and the clinical score was available for every other ED.

A total of 453 foals were included in this study. A foal could appear in more than one group if it needed a change of treatment. This was the case for 94 foals.

The abscess score of foals with the smallest pneumonia (group 1) was from 5 to 9.5 cm. These foals did not receive any treatment. If the abscess score of foals in group 1 increased above 10 cm, they received treatment and reappeared in groups 2 to 4.

The foals with a mild pneumonia (group 2) had an abscess score between 10 and 14.5 cm. Those were treated with trimethoprim-sulfadiazine (TMS; 30 mg/kg p.o., every 12 h).

The foals with a moderate pneumonia (group 3) had an abscess score between 15 and 19.5 cm. Those were treated with rifampin (10 mg/kg p.o., every 24 h) and tulathromycin (2.5 mg/kg i.m., once a week).

The foals with severe pneumonia (group 4) had an abscess score above 20 cm and were treated with rifampin (10 mg/kg p.o., every 24 h) and azithromycin (10 mg/kg p.o., every 24 h).

Foals were monitored in this study until the ultrasonographic examination of the lung revealed a maximum of two consoli-

dations with a diameter of 0.5 cm for at least two consecutive examinations. Thus, the score had to be 1 cm or smaller for termination of the treatment. At that point, it was considered that foals had recovered from pneumonia.

#### Data and analysis

The Statistical Analysis System for Windows SAS was used to analyse the data collected. An error probability of  $p < 0.05$  was considered significant for the complete analysis. The normality of the abscess score, the clinical score and the WBC count was tested with the Shapiro-Wilk test. The data were almost normally distributed, therefore, the median with the 1<sup>st</sup> and 3<sup>rd</sup> quartile was determined. Development of the abscess score, the clinical score and the WBC count was evaluated with the Friedman Permutation test;  $p < 0.05$  was adjusted after Sidák (Sidák, 1967). The difference among the abscess score, clinical score, WBC count and variation of lesion size between foals with and without treatment change was tested with the Signed Rank Test. The correlation between the abscess score, the clinical score and the WBC count was analysed with the correlation analysis by Spearman. In order to analyse the distribution of the abscess score to the right and left side of the lung, the normality was tested with the Kolmogorov-Smirnov test and the distribution analysis with the Signed Rank Test. The probability of a localization of the abscesses in each side of the lung was tested with the Signed Rank Test.

## Results

### Clinical and sonographic findings at diagnosis

The median of the abscess score, the clinical score and the WBC count was recorded on the day of diagnosis for all groups (Table 2).

The average abscess score on the day of diagnosis represents the severity of pneumonia of each group. According to the group definition, the abscess score was the smallest (median: 6.5 cm; 1<sup>st</sup> quartile: 6 cm; 3<sup>rd</sup> quartile: 8 cm) in group 1 and the highest (median: 22.3 cm; 1<sup>st</sup> quartile: 21 cm; 3<sup>rd</sup> quartile: 26 cm) in the foals with severe pneumonia (group 4).

The foals with severe pneumonia, i.e. a high abscess score, had a higher clinical score (median: 4.0) than the foals with mild pneumonia (median: 3.0). There was a similar mean WBC count in all four groups.

The mean abscess score, clinical score and WBC count were compared among the foals with and without a change of treatment (Table 2, second column "subgroup"). Only a few foals needed a change of treatment in group 3 (moderate pneumonia) and 4 (severe pneumonia). The foals with small pulmonary lesions that needed treatment later on had a significantly ( $p < 0.032$ ) higher clinical score than the foals that healed without treatment.

Of the foals with small pulmonary lesions (group 1), 64% healed without treatment; 84% of foals with mild pneumonia, 97% of the foals with moderate pneumonia and 91% of the foals with severe pneumonia recovered with the first treatment protocol.

### Localization of pulmonary lesions in foals with pneumonia

The addition of all diameters of consolidations visualised at sonography was compared in all foals with pneumonia on the day of diagnosis. When all groups were analysed, the percentage of the abscess score on the right side was 56.8% and, therefore, pulmonary lesions were significantly more severe on the right side ( $p < 0.001$ ) than the left side (43.2%).

The addition of the diameter of all abscesses was higher on the right side of the lung than on the left side in each group (Table 3).

**Table 2** Findings on the day of diagnosis "pneumonia". First column: median (25%; 75%) of the whole group (total). Second column differentiates the group in TS = treatment success and CT = change of treatment (subgroup); \* = significant difference; Group 1 = abscess score 5–9.5 cm; Group 2 = abscess score 10–14.5 cm; Group 3: abscess score 15–19.5 cm; Group 4 = abscess score > 20 cm | Befunde am Tag der Diagnose "Pneumonie". Erste Spalte: Median (25%; 75%) der gesamten Gruppe. Die zweite Spalte unterteilt die Gruppe in TS = Therapieerfolg und CT = Therapieumstellung (Untergruppe); \* = signifikanter Unterschied; Gruppe 1 = Abszess Score 5–9,5 cm; Gruppe 2 = Abszess Score 10–14,5 cm; Gruppe 3 = Abszess Score 15–19,5 cm; Gruppe 4 = Abszess Score über 20 cm

	Parameter	Abscess score (cm)				White blood count (G/L)		
		subgroup	total median	subgroup	total median	subgroup	total median	subgroup
Group 1 (n = 135)	TS (n = 86)		6.5 (6; 8)	6.8 (5.6; 7.9)	3 (2; 4)	2* (2; 3)	14.650 (12.675; 17.400)	15.000 (12.950; 17.325)
	CT (n = 49)			6.5 (6; 8)		3* (2; 4)		13.800 (12.075; 18.125)
Group 2 (n = 219)	TS (n = 183)		11 (10; 12)	11 (10; 12)	3 (2; 4)	3 (2; 4)	15.400 (11.950; 17.850)	15.400 (12.000; 17.800)
	CT (n = 36)			11 (10; 11)		4 (2; 5)		15.600 (11.475; 18.325)
Group 3 (n = 91)	TS (n = 88)		16 (15.5; 17)	16 (15.5; 17)	3 (2; 4.5)	3 (2; 5)	14.300 (11.950; 17.350)	14.050 (12.100; 17.275)
	CT (n = 3)			18 (17.5; 18.5)		3 (2.5; 3.5)		10.100 (8.000; 14.250)
Group 4 (n = 66)	TS (n = 60)		22.3 (21; 26)	22 (21; 25.3)	4 (3; 5)	4 (3; 6)	14.250 (11.975; 16.800)	14.600 (11.725; 17.000)
	CT (n = 6)			25.3 (21.3; 29.3)		5 (4.3; 5)		14.100 (13.825; 14.375)

The percentage of abscess score on the right side of the lung was significantly higher than on the left side of the lung in foals with small to moderate pneumonia (groups 1 to 3). In foals with severe pneumonia (group 4), the percentage of abscess score on the right and the left side of the lung did not differ significantly.

#### Comparison of localization of pulmonary lesions between cranial-ventral and caudo-dorsal regions of the lung

The localization of the abscess scores in % are shown in Figures 1a to 1d separately for the left and the right side of the lung and for each group on the day of diagnosis. Most pulmonary lesions were localized in the cranio-ventral segment of the lung, i.e. in the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> intercostal spaces and specifically in the middle and ventral areas (3B, 4B, 4C and 5C). The lung was divided into two areas for further analysis of the localization of the lesions: an area of "high incidence" containing the four areas specified previously with the highest probability of abscess appearance and an area of "low incidence" consisting of the rest of the lung.

The area of "high incidence" in foals with small pulmonary lesions (group 1) showed significantly more lesions than the area of "low incidence" in the first 10 examinations ( $p < 0.0001$ ). Pulmonary lesions in foals with mild (group 2) and moderate pneumonia (group 3) appeared significantly more frequently in the area of "high incidence" than in the area of "low incidence" ( $p < 0.0001 - p < 0.0352$ ) in the first 14 examinations.

Significantly more lesions were recorded in the area of "high incidence" than in the area of "low incidence" in foals with severe pneumonia (group 4) as well but not at every examination. Significantly more lesions appeared in the area of "high incidence" at EDs 3 to 8 ( $p < 0.0001 - p < 0.0271$ ) on the right side of the lung, and significantly more lesions appeared in the area of "high incidence" at EDs 6 to 9 ( $p < 0.0001 - p < 0.01$ ) on the left side of the lung.

**Table 3** Abscess score (in %) in foals with pneumonia on the right and the left side of the lung on the day of diagnosis; \* = significant difference between left and right; Group 1 = abscess score 5–9.5 cm; Group 2 = abscess score 10–14.5 cm; Group 3: abscess score 15–19.5 cm; Group 4 = abscess score > 20 cm | Abszess Scores (in %) von Fohlen mit Pneumonie auf der rechten und der linken Seite der Lunge am Tag der Diagnose; \* = signifikanter Unterschied zwischen links und rechts; Gr. 1 = Absz. Score 5–9,5 cm; Gr. 2 = Absz. Score 10–14,5 cm; Gr. 3 = Absz. Score 15–19,5 cm; Gr. 4 = Absz. Score über 20 cm

	Right (%)	Left (%)	p =
Group 1 (n = 135)	61.3	38.7	0.001*
Group 2 (n = 219)	55.4	44.6	0.0025*
Group 3 (n = 91)	58.0	42.0	0.0014*
Group 4 (n = 66)	53.1	46.9	0.097

#### Correlation of the diameter of consolidations in foals with pneumonia on the day of diagnosis with the prognosis of the first treatment

Regarding foals with small pulmonary lesions or mild pneumonia (group 1 and 2), the size of consolidations at diagnosis was similar in foals that recovered and those that needed treatment (group 1) or change of treatment (group 2). When the size of the lesions was compared in foals with moderate or severe pneumonia (group 3 and 4), the foals that recovered had more lesions of smaller size (below or equal to 1 cm) on the day of diagnosis, while the foals with a change of treatment had more lesions of 2 cm and above. In foals with severe pneumonia, those with a change of treatment had significantly more lesions larger than 2 cm diameter (Figure 2a and b) than foals with treatment success.

#### Duration of treatment to complete recovery from pneumonia

The foals with small pulmonary lesions (group 1) recovered within 3 weeks, while the foals with mild to severe pneumonia (groups 2 to 4) needed 4 weeks to heal (Table 4). Many foals had an abscess score lower than 1 cm earlier than 4 weeks after diagnosis; however, some foals showed an increase of the abscess score at later examinations.

#### Development of the abscess score

The development of the abscess score in all four groups is shown in Figures 3a to 3d for the first 5 weeks divided in 10 EDs. The abscess score mostly decreases over the first two weeks of treatment. The reduction of the abscess score in foals with mild pulmonary lesions (group 1) was highly significant ( $p < 0.001$ ) between the first two EDs and all following EDs.

The decrease of the abscess score in foals with mild to severe pneumonia (groups 2 to 4) was noticed within the first two weeks after diagnosis. The decrease of the abscess score was

**Table 4** Time (in weeks) needed for healing or until change of treatment pneumonia in foals; Group 1 = abscess score 5–9.5 cm; Group 2 = abscess score 10–14.5 cm; Group 3: abscess score 15–19.5 cm; Group 4 = abscess score > 20 cm | Zeitspanne (in Wochen), die für Ausheilung oder bis zur Behandlungs-umstellung von Fohlen mit Pneumonie; Gr. 1 = Absz. Score 5–9,5 cm; Gr. 2 = Absz. Score 10–14,5 cm; Gr. 3 = Absz. Score 15–19,5 cm; Gr. 4 = Absz. Score > 20 cm

	Healed (weeks) (number of foals)	Change of treatment (weeks) (number of foals)
Group 1 (n = 135)	3.2 (± 1.8) (n = 86)	1.5 (± 1.2) (n = 49)
Group 2 (n = 221)	3.9 (± 1.7) (n = 183)	2.3 (± 2.1) (n = 36)
Group 3 (n = 91)	4 (± 2.2) (n = 88)	1.7 (± 2) (n = 3)
Group 4 (n = 66)	4 (± 1.6) (n = 66)	1.8 (± 1.3) (n = 6)

highly significant ( $p < 0.0001$ ) from ED 1, ED 2 and ED 3 to all following EDs. Later EDs showed no significant decrease.

*Development of the clinical score*

The major decrease of the clinical score, to a range of 2 to 2.5, was noted within the first 2.5 weeks after diagnosis in all four groups. The decrease of the clinical score in foals with mild pulmonary lesions (group 1) was not significant. The average clinical score at diagnosis in foals with mild to severe

pneumonia (groups 2 to 4) was significantly higher compared to the further examinations.

*Development of the WBC count*

The development of the WBC count in foals with small pulmonary lesions (group 1) showed no significant change during the first 5 weeks after diagnosis. The median WBC count of the foals with mild pneumonia (group 2) was 16,600 G/L and 16,600 G/L of the foals with moderate pneumonia (group 3) as well, both reached at ED 3. The median WBC count of the foals with severe pneumonia was reached at ED 4 with 17,700 G/L. The WBC count for foals with mild to severe pneumonia (groups 2 to 4) showed a slight but significant

C	B	A	left	right	A	B	C
♥	6,4	0,7	3	3	1,5	17	♥
8,3	6,6	0,3	4	4	0,4	7,2	16,8
5,8	3,2	0,2	5	5	0,6	2,4	7,3
3,2	0,9	0,2	6	6	0	1,7	3
1,3	0,4	0	7	7	0	0,5	0,7
0,4	0,7	0	8	8	0	0,6	0,2
0	0,3	0	9	9	0	0	0,4
0,2	0	0	10	10	0	0	0,2
0	0	0	11	11	0	0	0,2
0	0	0	12	12	0	0	0
0	0	0	13	13	0	0	0
0	0	0	14	14	0	0	0

**Fig. 1a** Localization of abscess scores (in %) in foals (n = 135) with small pulmonary lesions on the day of diagnosis; intercostal space 3 to 14 and level A = dorsal to C = ventral; colour code: strong gray = high number of lesions, white = no lesions; ♥ = localization of the heart | *Lokalisation der Abszesse (in %) in Fohlen (n = 135) mit kleinen pulmonalen Läsionen am Tag der Diagnose; Interkostalraum 3 bis 14 und Level A = dorsal bis C = ventral; Farbkodierung: dunkelgrau = hohe Anzahl an Läsionen, weiß = keine Läsionen; ♥ = Lokalisation des Herzens*

C	B	A	left	right	A	B	C
♥	6,4	0,7	3	3	2,1	10,6	♥
7,2	4,4	1,2	4	4	1,2	6,9	11,2
7,1	2,6	0,6	5	5	0,3	3,1	7,7
3,1	1,6	0,2	6	6	0,2	1,4	3,7
2	1,1	0,1	7	7	0	0,8	2,2
1,5	0,5	0,2	8	8	0	1,1	1,4
0,8	0,2	0,1	9	9	0,1	0,8	1,1
0,4	0,3	0	10	10	0	0,1	0,8
0,3	0	0	11	11	0	0,3	0,2
0,1	0	0	12	12	0	0	0,2
0	0	0	13	13	0	0	0
0	0	0	14	14	0	0	0

**Fig. 1c** Localization of abscess scores (in %) in foals (n = 91) with moderate pneumonia on the day of diagnosis; intercostal space 3 to 14 and level A = dorsal to C = ventral; colour code: strong gray = high number of lesions, white = no lesions; ♥ = localization of the heart | *Lokalisation der Abszesse (in %) in Fohlen (n = 91) mit mittelgradiger Pneumonie am Tag der Diagnose; Interkostalraum 3 bis 14 und Level A = dorsal bis C = ventral; Farbkodierung: dunkelgrau = hohe Anzahl an Läsionen, weiß = keine Läsionen; ♥ = Lokalisation des Herzens*

C	B	A	left	right	A	B	C
♥	7,2	0,6	3	3	1,5	13,6	♥
8,4	5,1	0,3	4	4	0,7	6,3	11,1
6,8	3,2	0,3	5	5	0,4	3,1	8,2
4,2	1,8	0,2	6	6	0,1	1,2	5
2	0,9	0,1	7	7	0,1	0,6	2,3
0,6	0,9	0,04	8	8	0	0,4	1
0,3	0,2	0,04	9	9	0	0,1	0,6
0,2	0	0	10	10	0	0	0,1
0,04	0	0	11	11	0	0,04	0,04
0	0	0	12	12	0	0,1	0
0	0	0	13	13	0	0	0
0	0	0	14	14	0	0	0

**Fig. 1b** Localization of abscess scores (in %) in foals (n = 219) with mild pneumonia on the day of diagnosis; intercostal space 3 to 14 and level A = dorsal to C = ventral; colour code: strong gray = high number of lesions, white = no lesions; ♥ = localization of the heart | *Lokalisation der Abszesse (in %) in Fohlen (n = 219) mit geringgradiger Pneumonie am Tag der Diagnose; Interkostalraum 3 bis 14 und Level A = dorsal bis C = ventral; Farbkodierung: dunkelgrau = hohe Anzahl an Läsionen, weiß = keine Läsionen; ♥ = Lokalisation des Herzens*

C	B	A	left	right	A	B	C
♥	5	0,9	3	3	1,4	7,8	♥
7,2	4,8	1	4	4	0,8	4,5	8,4
5,9	3,2	0,7	5	5	0,5	3,5	6,2
4,1	1,3	0,3	6	6	0,3	1,9	3,7
2,5	1,7	0,3	7	7	0,3	1,5	3
2,2	0,5	0,1	8	8	0,3	0,8	2,2
2	0,7	0,1	9	9	0	0,7	1,6
1,2	0,5	0	10	10	0	0,3	0,9
0,7	0	0	11	11	0,1	0,1	0,9
0,3	0,03	0	12	12	0,2	0,1	0,5
0	0	0	13	13	0	0,1	0,1
0	0	0	14	14	0	0,03	0

**Fig. 1d** Localization of abscess scores (in %) in foals (n = 66) with severe pneumonia on the day of diagnosis; intercostal space 3 to 14 and level A = dorsal to C = ventral; colour code: strong gray = high number of lesions, white = no lesions; ♥ = localization of the heart | *Lokalisation der Abszesse (in %) in Fohlen (n = 66) mit hochgradiger Pneumonie am Tag der Diagnose; Interkostalraum 3 bis 14 und Level A = dorsal bis C = ventral; Farbkodierung: dunkelgrau = hohe Anzahl an Läsionen, weiß = keine Läsionen; ♥ = Lokalisation des Herzens*

( $p < 0.001$ ) increase until ED 3. After that, the WBC count decreased, also significantly, until ED 5 ( $p < 0.001$ ).

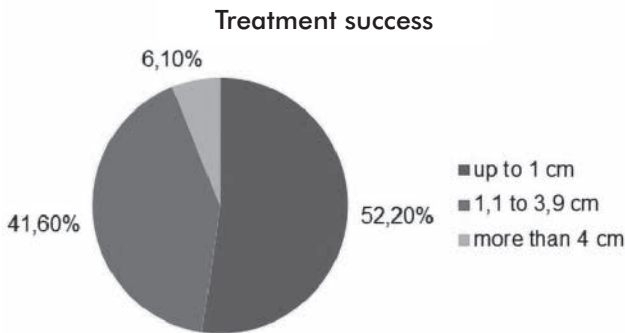
**Discussion**

The localization and development of pulmonary findings of foals with different severities of abscessing bronchopneumonia were described in the current study. The purpose was to show where in the lung the abscesses mostly appear and to find a parameter that might show the worsening of pneumonia early.

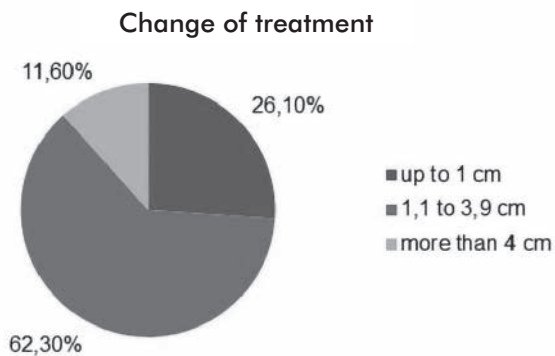
The endemic incidence of *R. equi* on the stud farm was confirmed in several studies (Hagist 2016, Heyers 2007), therefore, the monitoring and treatment were designed for the early diagnosis and effective recovery of pneumonia due to *R. equi*. Based on a recent study, 27.5% of the foals with an abscess score from 10–15 cm healed without treatment (Rutenberg et al. 2017), therefore, pulmonary lesions of a max. of 10 cm were defined as the cut-off for the foals with the smallest pulmonary lesions in group 1. Of the 135 foals in group 1 with an abscess score between 5 cm and 10 cm, 63.7% healed without treatment. This percentage is consistent with results of earlier studies (Venner et al. 2013, Venner and Credner

2014, Venner et al. 2012), where 44, 67 and 88% (respectively) of foals with abscess scores below 10 cm healed without treatment even though the numbers of patients in these studies were (with 25 to 32 foals) lower than in the current study. These taken together confirm that resolution of pneumonia in foals is possible without treatment in mild cases; however, close monitoring is advised in order to identify foals with a worsening of the disease.

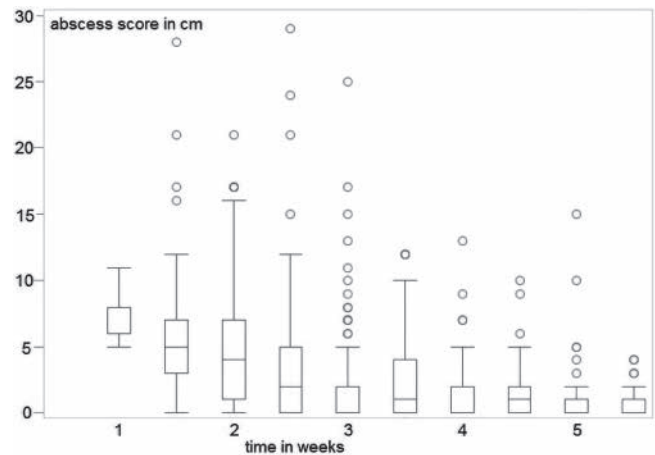
The treatment of the foals with mild pneumonia with TMS has been mentioned in earlier literature (Prescott and Sweeney 1985, Sweeney et al. 1987, Wilson 1992). In the current study, 85.6% of 219 foals with an abscess score from 10 cm to 15 cm recovered during treatment with TMS. Only 27.5% of the foals recovered without treatment in an earlier study at this severity of pneumonia (Rutenberg et al. 2017). The advantage of TMS is the much lower costs for the owner. The TMS as a treatment was successful, but as it is not effective against *R. equi*, other pathogens, for example, *Strep. equi zooepidemicus*, must have been causing the pneumonia in those foals.



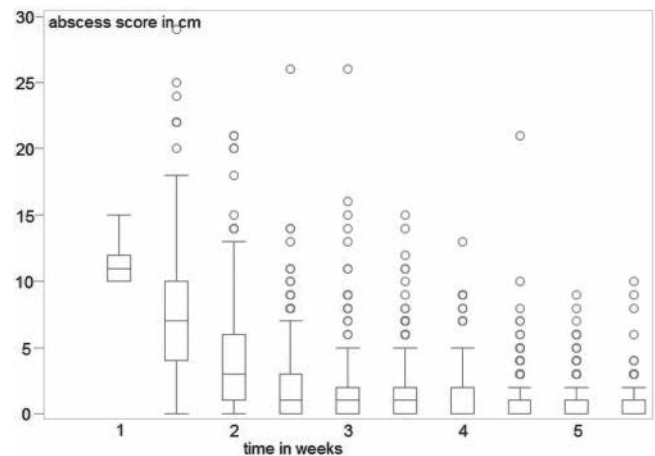
**Fig. 2a** Number of different abscess sizes on the day of diagnosis in foals with severe pneumonia (group 4;  $n = 66$ ) with treatment success (TS;  $n = 60$ ) | Anzahl verschiedener Abszessgrößen am Tag der Diagnose bei Fohlen mit hochgradiger Pneumonie (Gruppe 4;  $n = 66$ ) mit Therapieerfolg (TS;  $n = 60$ )



**Fig. 2b** Number of different abscess sizes on the day of diagnosis in foals with severe pneumonia (group 4;  $n = 66$ ) with change of treatment (CT;  $n = 6$ ) | Anzahl verschiedener Abszessgrößen am Tag der Diagnose bei Fohlen mit hochgradiger Pneumonie (Gruppe 4;  $n = 66$ ) mit Therapieumstellung (CT;  $n = 6$ )



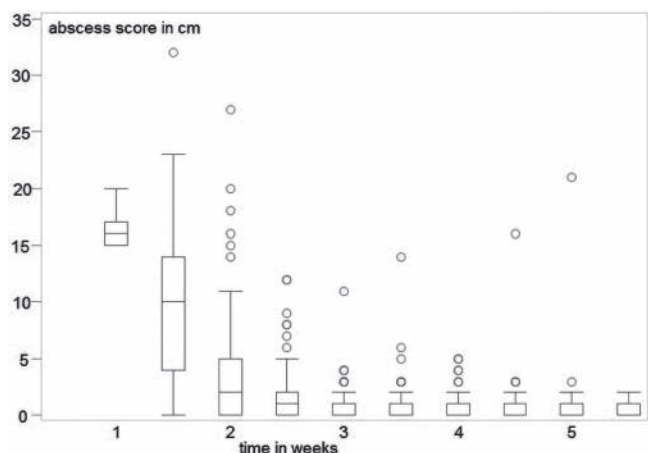
**Fig. 3a** Abscess score of foals with small pulmonary lesions ( $n = 135$ ) during the first five weeks (two examinations per week) after diagnosis of pneumonia | Abszess Score von Fohlen mit kleinen pulmonalen Läsionen ( $n = 135$ ) während der ersten fünf Wochen (2 Untersuchungen pro Woche) nach der Diagnose der Pneumonie



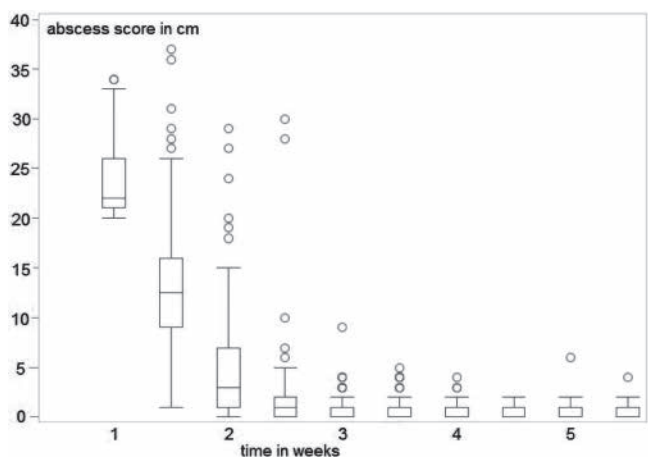
**Fig. 3b** Abscess score of foals with mild pneumonia ( $n = 219$ ) during the first five weeks (two examinations per week) after diagnosis of pneumonia | Abszess Score von Fohlen mit geringgradiger Pneumonie ( $n = 219$ ) während der ersten fünf Wochen (2 Untersuchungen pro Woche) nach der Diagnose der Pneumonie

The treatment of the foals with moderate pneumonia (abscess score of 15–20 cm) with rifampin and tulathromycin was successful in 96.7% of 91 foals in our study. The effectiveness of tulathromycin as a monotherapy has been evaluated earlier and was reported to be good in 90% of the foals with an abscess score of 10 to 15 cm (Rutenberg et al. 2017). The initial abscess score in the current study was higher with 15 to 20 cm and still the treatment was successful in all except three foals. Therefore, the combined treatment of rifampin and tulathromycin is effective in foals with moderate pneumonia, while the success in foals with severe pneumonia needs to be further evaluated.

The foals with severe pneumonia (abscess score above 20 cm) and treatment with rifampin and azithromycin were successfully treated in 90.9% of the 66 cases. Previous studies on the efficiency of the combination of rifampin and azithromycin sustained similar success rates: 93% in foals with an abscess score of 8 to 15 cm (Venner and Credner 2014) and 95% in foals with an abscess score of 10 to 15 cm (Rutenberg et



**Fig. 3c** Abscess score of foals with moderate pneumonia ( $n = 91$ ) during the first five weeks (two examinations per week) after diagnosis of pneumonia | Abszess Score von Fohlen mit mittelgradiger Pneumonie ( $n = 91$ ) während der ersten fünf Wochen (2 Untersuchungen pro Woche) nach der Diagnose der Pneumonie



**Fig. 3d** Abscess score of foals with severe pneumonia ( $n = 66$ ) during the first five weeks (two examinations per week) after diagnosis of pneumonia | Abszess Score von Fohlen mit hochgradiger Pneumonie ( $n = 66$ ) während der ersten fünf Wochen (2 Untersuchungen pro Woche) nach der Diagnose der Pneumonie

al. 2017). In contrast to the latter, the current study included foals with dyspnoea and an abscess score above 20 cm. Because of the success of rifampin and tulathromycin in foals with moderate pneumonia, it would be interesting to compare the efficiency of rifampin and tulathromycin with rifampin and azithromycin in the treatment of foals with severe pneumonia.

The localization of the abscesses in the lung of foals with *R. equi* pneumonia has been described previously. One author stated that more abscesses are found on the right side of the lung than on the left side without providing any number (Hillidge 1986). This was confirmed in a study on 12 foals with severe pneumonia (Özsoy and Hazirolu 2009). Another study of 149 foals with mild pneumonia concluded that the number of pulmonary abscesses was similar on the left and right side (Althaus 2004). The difference between these statements could originate from different severities of pneumonia at diagnosis.

In the current study, pulmonary lesions were significantly more severe on the right side (56%) than on the left (43%) side of the thorax for the foals with small pulmonary lesions and mild to moderate pneumonia. This might be due to the anatomical course of the trachea that makes a curve around the Arcus aortae on the right side, therefore, the airstream has a shorter distance and straight course to the right lung (Waibl 2004). More pulmonary lesions were detected on the right side (53.1%) than on the left side (46.9%) in foals with severe pneumonia, but the difference was not significant.

The localization of pulmonary lesions has been described to be mainly cranial and ventral in the lung and more severe in this area (Reef et al. 2004). This was confirmed in the current study as pulmonary lesions concentrated mostly cranio-ventrally, around the heart area. Consolidations in all foals with small pulmonary lesions and mild to severe pneumonia were visualized in the segments of the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> intercostal space, especially in the middle and the ventral area. A possible explanation for cranio-ventral bronchopneumonia is the settling of pathogens in the entry zone of the lung or following gravitation. Additionally, a reduced vascular perfusion, insufficient defence mechanism and regional differences in ventilation are discussed (López 2007). A higher infective dose in the severely diseased foals could be a reason that leads to the wider spread in the lung.

The whole lung should be scanned for the diagnosis of pneumonia, even if most lesions seem to be localized cranio-ventrally, because single lesions can also be found in the other areas. The cranio-ventral area of the lung is covered by the heart shadow at radiology and lesions can be missed. This is why ultrasonography is regarded as more sensitive (Venner et al. 2014). Radiographic imaging can be used additionally, especially in a foal where there is a suspicion of pneumonia but with no findings at ultrasonographic examination.

The size of consolidations at diagnosis can be a sign that a change of treatment might be necessary later but only for foals with severe pulmonary lesions. Foals with severe pneumonia but small lesions responded more frequently to the first

treatment than foals with severe pneumonia and larger lesions. The contact surface for antibiotic treatment is smaller in consolidations with a larger diameter, which could be a reason why the treatment protocol needs to be changed in foals with large lesions. The diameter of lesions in foals with mild to moderate pneumonia is not helpful for prognosis.

The mean value of the abscess score decreased impressively in the first two weeks of treatment in all four groups. The period of time necessary for the lung to be completely healed, which was shown at ultrasonographic examination, was 3.2 weeks for foals with small pulmonary lesions and around 4 weeks for those with mild to severe pneumonia. There is a wide range of recommended durations of treatment of *R. equi* pneumonia in foals. Some authors suggest the period till the radiographic findings and WBC are normal (Hillidge 1987), while others advise a duration of 4 to 9 weeks and until the plasma fibrinogen is normal (Giguere and Prescott 1997) to 3 to 12 weeks depending on the severity of the initial pneumonia (Giguere 2017). To use only the clinical appearance is insufficient, because foals often seem to be clinically better long before the consolidations are resolved (Solvis et al. 2005). Ultrasound is a good method to make the decision for discontinuing the treatment. Monitoring those foals further in order to diagnose recurrence is recommended due to the fact that ultrasound only shows the periphery of the lung and it is not ruled out that superficial aeration could be the reason that lesions are no longer viewable (McCracken and Solvis 2009).

If a change of treatment was necessary in the patients of our study, it became apparent within the first two weeks after diagnosis. Therefore, an ultrasonographic examination, twice a week after starting treatment, can help to conclude if the pulmonary lesions are responding to treatment or if the treatment needs to be adjusted.

## Conclusion

Ultrasonography is a useful technique in the screening and monitoring of foals with pneumonia during treatment. The uneven distribution of pulmonary lesions in the lung at diagnosis, with more findings on the right side and cranio-ventral, supports the usefulness of ultrasound compared to radiology, especially as these areas are covered by the heart shadow on chest radiographs. However, it is important for a precise evaluation and prognosis to examine the entire lung to avoid overlooking any lesions in the other areas.

The size of consolidations at diagnosis in foals with severe pneumonia can be a sign that a change of treatment might be necessary later. The foals with small lesions responded better to the first treatment than foals with larger lesions. The first 2 weeks of treatment are the most important for prognosis while monitoring.

Most pulmonary lesions resolved within the first 2 weeks after diagnosis and the need for a change of treatment also became obvious mostly in this period. Therefore, ultrasonographic examination helps to determine the prognosis and to decide when to discontinue treatment.

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Erweiterte Zusammenfassung

### Studie zur Entwicklung ultrasonographischer Befunde der Lunge von Fohlen mit Pneumonie

Die Pneumonie des Fohlens ist eine der bedeutendsten Krankheiten während der Aufzucht. Da die Prophylaxe sich schwierig darstellt, sind eine frühe Diagnose, eine gut überwachte Behandlung und eine zuverlässige Prognose wichtig, um die Verluste bei den Fohlen zu minimieren. Ziel der Studie war es, einen Parameter zu finden, der früh auf eine mögliche Verschlechterung der Pneumonie hinweist. Zu diesem Zweck wurde die Verteilung der Konsolidierungen in der Lunge von Fohlen mit abszedierender Pneumonie unterschiedlichen Schweregrades beschrieben und deren Entwicklung während der Behandlung überwacht.

Es handelt sich um eine prospektive klinische Studie mit 4 Gruppen von Fohlen mit Bronchopneumonie mit unterschiedlichem Schweregrad, die während der Behandlungszeit fortlaufend untersucht worden sind. Bei 453 Fohlen eines Gestütes mit subklinischer und klinischer Pneumonie ist mithilfe der ultrasonographischen Untersuchung der Schweregrad der Konsolidierungen in der Lunge festgestellt worden. Die Durchmesser aller im Ultraschall festgestellten Läsionen wurden zu einem Abszess-Score in cm addiert. Bei Läsionen in der Lunge mit einer unregelmäßigen Form wurde der Durchschnitt des kleinsten und des größten Durchmessers verwendet. Nachdem die Pneumonie diagnostiziert war, ist bis zur Ausheilung wöchentlich eine klinische Untersuchung der Fohlen durchgeführt und zweimal in der Woche die Leukozytenzahl im Blut bestimmt, sowie die ultrasonographische Untersuchung der Lunge durchgeführt. Die klinische Untersuchung hat sich aus der Messung der Körpertemperatur, der Beurteilung von Nasenausfluss und der Mandibularlymphknoten und ggf. einer Dyspnoe, dem Zählen der Atemfrequenz und der Auskultation von Trachea und Lunge zusammengesetzt. Diese Parameter sind in einem klinischen Score von 0 bis 13 zusammengefasst worden, wobei ein Score bis 2 als physiologisch betrachtet worden ist. Der Grenzwert der Leukozytenzahl im Blut liegt bei einem Wert über 13.000 G/L. In Gruppe 1 sind die Fohlen, die an einer milden Bronchopneumonie erkrankt waren aufgenommen worden.

Bei der sonographischen Lungenuntersuchung wurden wenige Konsolidierungen, also ein Abszess-Score zwischen 5 und 9,5 cm, festgestellt. Diese Fohlen sind ohne Behandlung weiter überwacht worden. Trat bei den Fohlen dieser Gruppe ein Anstieg des Abszess-Scores auf über 10 cm auf, so wurden diese in eine der folgenden Gruppen aufgenommen und entsprechend behandelt: Gruppe 2 hat sich aus den Fohlen mit geringgradiger Pneumonie zusammengesetzt. Bei diesen Fohlen ist ein Abszess-Score zwischen 10 und 14,5 cm gemessen und die Fohlen sind mit Trimethoprim-Sulfadiazin (30 mg/kg p.o., alle 12 h) behandelt worden. Die mittelgradig erkrankten Fohlen mit einem Abszess-Score zwischen 15 und 19,5 cm sind in Gruppe 3 aufgenommen worden und haben Rifampicin (10 mg/kg p.o., einmal täglich) und Tulathromycin (2,5 mg/kg i.m., einmal wöchentlich) als antibiotische Behandlung erhalten. In Gruppe 4 sind die hochgradig erkrankten Fohlen mit einem Abszess-Score von über 20 cm zusammengefasst, welche mit Rifampicin (10 mg/kg p.o., einmal täglich) und Azithromycin (10 mg/kg p.o., einmal täglich) behandelt worden sind. Ist bei den Fohlen der Gruppen 2 bis 4 eine Verschlechterung aufgetreten oder eine Besserung ausgeblieben, ist die Therapie umgestellt und die Fohlen weiter kontrolliert worden. Die Behandlung ist als abgeschlossen bezeichnet worden, wenn die Fohlen klinisch unauffällig gewesen sind und bei der ultrasonographischen Untersuchung der Lunge maximal zwei Konsolidierungen mit einem Durchmesser von höchstens 0,5 cm in zwei aufeinander folgenden Untersuchungen festgestellt worden sind. Die Daten sind mithilfe des Statistical Analysis System (SAS) für Windows ausgewertet worden. 135 Fohlen zeigten wenige Lungenabszesse (Gruppe 1) und erhielten keine antibiotische Behandlung. Von diesen 135 Fohlen benötigten 49 Fohlen später doch eine antibiotische Behandlung. 219 Fohlen sind mit einer geringgradigen Pneumonie (Gruppe 2) aufgefallen und haben Trimethoprim-Sulfadiazin als Behandlung erhalten. Von diesen Fohlen sind 36 (16,4%) Fohlen auf eine andere antibiotische Behandlung umgestellt worden, da es entweder zu einer Verschlechterung der Ultraschallbefunde der Lungen gekommen oder eine Besserung unter der Therapie ausgeblieben ist. 91 Fohlen sind mit einer mittelgradigen Pneumonie (Gruppe 3) aufgefallen und mit Rifampicin und Tulathromycin behandelt worden. Bei nur drei (3,3%) Fohlen

der Gruppe 3 musste die Behandlung umgestellt werden. 66 Fohlen sind mit einer schweren Pneumonie (Gruppe 4) aufgefallen, die mit Rifampicin und Azithromycin behandelt worden ist. Von diesen Fohlen sind sechs (9,1 %) während der Therapie auf eine Behandlung mit einem anderen Antibiotikum umgestellt worden. Alle Fohlen, die keine Therapieumstellung benötigt haben, sind vollständig mit einer maximalen Behandlungszeit von 9,5 Wochen ausgeheilt. Die durchschnittliche Behandlungszeit hat drei (Gruppe 1) beziehungsweise vier Wochen (Gruppe 2 bis 4) betragen. Bei der Diagnose der Fohlen mit wenigen Abszessen (Gruppe 1) ist ein medianer Abszess-Score von 6,5 cm festgestellt worden. Fohlen mit geringgradiger Pneumonie (Gruppe 2) haben am Tag der Diagnose einen Abszess-Score von 11,0 cm gehabt. Bei Fohlen mit mittelgradiger Pneumonie (Gruppe 3) hat der Median des Abszess-Scores 16,0 cm und bei Fohlen mit hochgradiger Pneumonie (Gruppe 4) 22,3 cm betragen. Je schwerer die Fohlen erkrankt gewesen sind, desto höher ist der klinische Score (Gruppe 1: Median 3,0 bis Gruppe 4: Median 4,0) gewesen. Der klinische Score am Tag der Diagnose ist bei den Fohlen mit einer kleinen Anzahl an Abszessen (Gruppe 1), die später doch eine antibiotische Therapie benötigt haben, mit einem Median von 3,0 höher gewesen als bei den Fohlen, die ohne Behandlung ausgeheilt sind (klinischer Score: Median 2,0). Die mediane Leukozytenzahl im Blut aller Gruppen hat trotz unterschiedlichen Schweregrades der Pneumonien am Tag der Diagnose keinen signifikanten Unterschied gezeigt (von 14.250 G/L in Gruppe 4 bis 15.400 G/L in Gruppe 2). Bezüglich der Lokalisation der Lungenbefunde konnte beobachtet werden, dass der größte Anteil der Konsolidierungen bei allen Fohlen, unabhängig vom Schweregrad der Krankheit, im kranialen und ventralen Bereich der Lunge darzustellen war. Zudem zeigten sich die Lungenbefunde der ultrasonographischen Untersuchung schwerwiegender in der rechten Lungenhälfte (mit 56,8%) als in der linken Lungenhälfte (mit 43,2%). Zwischen den geringgradig und hochgradig erkrankten Fohlen hat sich am Tag der Diagnose kein Unterschied in der Größe der Abszesse gezeigt. Nur bei den schwerer kranken Fohlen, bei denen im Laufe der Behandlung eine Therapieumstellung auf ein anderes Antibiotikum notwendig geworden ist, haben 73,9% der Läsionen einen Durchmesser von 2 cm oder größer gehabt. Bei Fohlen mit erfolgreicher erster Therapie der Gruppe 4 sind nur 47,7% der Abszesse größer oder gleich 2 cm groß gewesen. Der Verlauf der ultrasonographischen Lungenbefunde hat sich durch einen deutlichen Rückgang innerhalb der ersten beiden Wochen nach der Diagnose ausgezeichnet, unabhängig vom Schweregrad der Krankheit. Der klinische Score ging bei allen Fohlen ebenfalls innerhalb der ersten zwei Wochen nach der Diagnose in den als normal definierten Bereich zurück. Die Leukozytenzahl im Blut der Fohlen mit einer geringen Anzahl an Lungenabszessen zeigte im Verlauf keine Veränderungen. Im Verlauf der Krankheit ist bei den geringgradig bis hochgradig kranken Fohlen (Gruppe 2 bis 4) zunächst ein Anstieg der durchschnittlichen Blutleukozytenzahl bis zu 1,5 Wochen nach der Diagnose festgestellt worden. Bei den darauffolgenden Untersuchungen ist die Blutleukozytenzahl langsam wieder bis in den Normalbereich gesunken.

Pulmonale Läsionen bei Fohlen mit Pneumonie treten vor allem im kranio-ventralen Bereich der Lunge auf. Bei Fohlen mit wenigen ultrasonographischen Befunden der Lunge können klinische Befunde einer respiratorischen Krankheit prognostische Hinweise geben, dass im Verlaufe des Monitorings eine antibiotische Therapie notwendig wird. Schwer kranke Fohlen mit kleinen Läsionen heilen besser als Fohlen mit größeren Läsionen, somit ist die Größe der Abszesse prognostisch hilfreich. Darüber hinaus sind die ersten beiden Wochen nach der Diagnose für die Überwachung der Fohlen mit Pneumonie während der Behandlung am wichtigsten, weil sich im Fall eines Therapieerfolgs die ultrasonographischen Befunde in diesem Zeitraum meist zurückbilden. Demzufolge wird auch die Notwendigkeit einer Umstellung der Therapie während dieser ersten zwei Wochen offensichtlich. Schließlich ist die Leukozytenzahl im Blut weder zuverlässig für eine frühe Diagnose, noch gibt sie einen Hinweis für die Prognose des Behandlungserfolgs.

**Schlüsselwörter:** Fohlen, Pneumonie, Ultraschalluntersuchung, Lokalisation der Läsionen, Entwicklung der Läsionen

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