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Kinetik of the IgG concentration in the blood of neonatal foals – comparison of foals with focal infectious diseases with healthy foals

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Summary: The aim of the study was to determine the kinetic of serum IgG levels during local infectious foal diseases in the neonatal period. The levels were compared to those of age-matched healthy foals. Time-dependent changes of IgG concentrations were compared between healthy and sick foals as well as between foals with different infectious diseases. The study was designed as a prospective study with a control group. A total of 133 foals with IgG levels of 600 mg/dL or total globulin levels of 21 g/L or more were included into the study. Neonatal foals which developed an infection within the first two weeks of life were assigned to group 1 (n = 69). Typical diseases encountered were omphalitis, diarrhea, pneumonia and septic arthritis. Sick foals were assigned to a clinically healthy foal of the same age as a matching foal. Foals remaining healthy in the first two weeks of life (n = 64) were assigned to group 2. Sick foals were sampled once daily during the first six days of disease, then sampled every second day until recovery. Healthy foals were sampled twice a week during the first two weeks of life. After the second week, all healthy foals were sampled once a week over the complete duration of the disease of the matching group 1 foals. Serum IgG values were determined via capillary zone electrophoresis. Foals with local infectious diseases had similar IgG levels as healthy foals on the first day of the disease as well as during the entire subsequent sampling period. Time-dependent decreases of serum IgG levels during the first weeks of life were moderate and similar between healthy and sick foals. The nature of the local infectious disease and disease severities had no impact on the time-dependent decrease of serum IgG. Both healthy and sick foals with an adequate transfer of passive immunity showed a moderate decrease of IgG levels during the first weeks of life. The serum IgG concentrations did not differ between healthy neonatal foals and foals with local infectious diseases in during the first weeks of life. In foals with an adequate transfer of passive immunity local infectious diseases do not seem to affect the decrease of serum IgG levels significantly.

Keywords: foal, neonatal phase, infectious disease, IgG, gamma globulins, course

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Introduction

Neonatal foals rely on the uptake of antigen-specific maternal colostrum antibodies to be protected against infections in a period where the immature neonatal immune system must still develop (*Jeffcott* 1974b, *Holznagel* et al. 2003, *Perkins* and *Wagner* 2015). To reduce the risk of infection during the first few weeks of life serum IgG concentrations above 800 mg/dl at around 24 hours post natum are considered as an adequate supply of antibodies. Lower serum IgG concentrations (400–800 mg/dl) are defined as a partial (PFPTI) and values below 400 mg/dl IgG as a total failure of passive transfer of immunity (TFPTI) (*Crawford* et al. 1977, *Koterba* et al. 1985). In neonatal foals, serum concentrations of passively absorbed colostral antibodies peak 12 to 18 hours after birth (*Rouse* 1971, *Jeffcott* 1974b, *Tscheschlok* et al. 2016a). During the first few weeks of life these serum antibodies are metabolised and their concentrations also decrease by increasing plasma volumes of growing foals (*Jeffcott* 1974a). Consequently, serum IgG levels decline about 64 % from 18 hours post natum until the seventh to ninth week of life. At the age of three to four months autogenously produced antibodies assume immunological protection of the foals (*Rouse* 1971, *Jeffcott* 1974a, *Sheoran* et al. 2000, *Demmers* et al. 2001). The half-life of the passively transferred antibodies is approximately 20–30 days, depending on the isotype of the immunoglobulins. 12 to 14 weeks post-natum, maternal antibodies are no longer detectable (*Baird* et al. 1987, *Perkins* and *Wagner* 2015). In foals, there is no precisely determined onset of autogenous antibody production. This appears to be individually different and depending mainly on the number of maternal antibodies (*Jeffcott* et al. 1974). Maternal antibodies may reduce the antigenic stimulus needed for the induction of an adaptive humoral immune response in the foal (*Jeffcott* 1974a, *Perkins*

and *Wagner* 2015, *Sievert* et al. 2019). The start of an adaptive humoral immune response also depends on antibody isotypes: IgM and IgG1 are already produced in utero, whereas IgA, IgG3 and IgG5 are produced shortly after birth. Higher concentrations of endogenously produced IgG1, IgG3 and IgG5 are detectable at five to eight weeks of life, with IgG1 showing a very steep rise within three months to concentrations well above those of adult horses. For IgG4 and IgG7, the onset of endogenous formation is reported between 16–20 weeks of life even though the earliest onset of endogenous production is thought to begin as early as around the fifth week of life, but with a very slow rise (*Rouse* 1971, *Perkins* and *Wagner* 2015).

Several studies showed that hypogammaglobulinemia may lead to higher risk of developing infectious diseases in foals compared to those with an adequate supply of maternal antibodies (*Jeffcott* 1972, *McGuire* et al. 1975, *Bublitz* et al. 1991). Other studies question a direct correlation between IgG levels and susceptibility for infections in neonatal foals and emphasize the disease-promoting effect of environmental factors (e.g., hospitalized foals vs. foals in well-managed farm conditions) in addition to low IgG levels (*McGuire* et al. 1975, *Koterba* et al. 1984, *Unterstab* 2016).

Numerous studies addressed initial foal blood IgG values 12 to 24 hours post natum and in foals with an infectious disease. However, to the best of our knowledge, there is no study on the kinetic of serum IgG levels during an infection of neonatal foals.

The aim of the current study was to verify the hypothesis that foals with ongoing infectious diseases metabolize IgG differently resulting in lower and/or faster decreasing serum IgG levels. For this, serum IgG concentrations of neonatal foals with an infectious disease were determined and time-dependant kinetic of serum IgG was compared between sick and healthy foals of the same age.

Materials and methods

Study population

The study was performed as a prospective study with a control group. All foals were born on the same stud farm ensuring that environmental conditions and medical management of neonatal foals were identical. Foaling took place in individual boxes of the foaling stable under supervision of experienced farm staff from February to July of the foaling season 2020. Each foal was closely monitored and it was ensured that foals found the udder of the mare within the first two hours post natum. If this did not happen, foals were given 250 ml colostrum of the mare by a feeding bottle and were further supported to drink from the mare's udder. Twelve hours post natum each foal was clinically examined by veterinarians and humoral immune transfer was evaluated as follows: Serum total globulin (TG) level was defined as the difference of total protein (TP) minus albumin (Alb) or serum IgG concentration was measured by capillary zone electrophoresis (CZE) as validated by *Tscheschlok* et al. (2016b). The cut-off value for insufficient IgG supply of each foal was set at ≥ 21 g/l TG and ≥ 600 mg/dl IgG. Foals that did not reach the cut off values received plasma transfusions until IgG levels raised above the IgG cut-off.

Foals born with an uneventful perinatal period that developed a local infectious disease during the first two weeks of life entered the study. Infectious diseases included typical illnesses of neonatal foals such as omphalitis, diarrhea, pneumonia or septic arthritis but did not include more severe conditions such as neonatal sepsis. Affected foals were closely monitored, treated symptomatically and received antibiotics until recovery. At the time of the diagnosis, a clinically healthy foal of the same age and gender was randomly assigned as a match to the affected foal. Matching foals that got sick during the subsequent sampling period were excluded from the study.

Study design

In total 133 warmblood foals were included in the study. Group 1 contained 69 foals with infectious diseases (44 foals with omphalitis, 21 foals with diarrhea, two foals with bronchopneumonia, one foal with septic arthritis and one foal with both arthritis and pneumonia). In Group 2 (healthy foals) 64 foals remained after five of the 69 initially healthy foals developed an infection themselves during the sampling period. Foals suffering from omphalitis were further classified into three subgroups according to the severity of the infection graded by the following parameters: number of affected structures in the umbilicus determined at sonography (umbilical vein, urachus, umbilical arteries, external umbilical stump), duration of antibiotic treatment, changes of antibiotic agent, and additional clinical findings such as fever and/or abnormal white blood cell counts. This resulted in 14 foals with mild, 23 foals with moderate and seven foals with severe omphalitis.

Blood sampling

Sampling started immediately after diagnosis of the disease and ended with recovery. At each sampling blood (9 ml) was collected in lithium heparin tubes after puncture of one jugular vein. Group 1 foals (sick foals) were sampled once daily during the first six days of disease, then every second day until recovery. Group 2 foals (healthy foals) were sampled twice a week during the first two weeks of life and then once weekly until the fourth week of life for the duration of the disease of the matching foal. Blood was centrifuged for ten minutes at 2000 g. Serum was harvested and stored aliquoted (1.5 ml) at –18 °C until analysis. Serum IgG concentrations were collectively determined by an external laboratory[a] within five months after sampling by electrophoresis.

Statistical analysis

Statistical analyses were performed using analytics software[b] (SAS® enterprise guide 7.1). Pearson correlation was used to analyze correlations between serum total globulin (TG) and IgG concentration twelve hours post-natum in 23 of the foals of the study to validate the use of TG for this purpose.

For normalization, logarithmized IgG values were used. Mean values of serum IgG concentrations on the first day of sampling were compared between sick and healthy foals. Further, serum IgG concentrations were compared between diseases using two-sample t-test. The mean IgG values of sampling days 1 to 6 were used to compare the IgG course, followed by the mean IgG values of every second sampling day (d8, d10, d12, d14). IgG level differences between sick and healthy foals and between various diseases during disease were compared with ANOVA for mixed models using Tukey-Kramer correction. Significance was set at $p < 0.05$ throughout the study.

Results

A total of 133 foals were part of the study. One healthy foal (group 2) was removed from the statistical analysis because its serum IgG (2475 ± 15 mg/dl) deviated significantly from all other foals. The baseline serum IgG values of the examined groups are shown in Table 1.

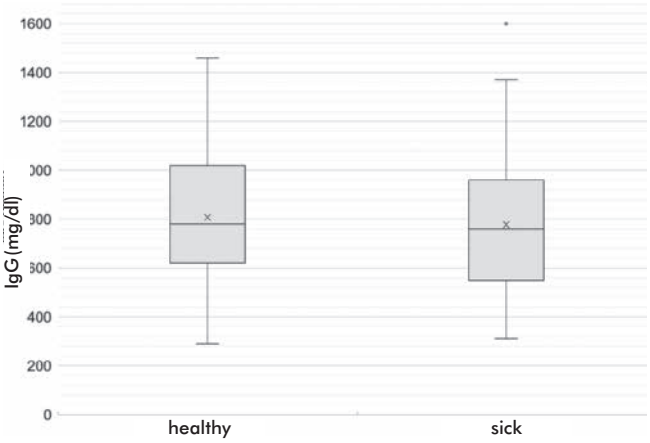

Fig. 1 IgG levels on the first day of sampling of healthy and sick foals, healthy: n = 64, sick: n = 69. | *IgG Konzentrationen am ersten Tag der Beprobung bei gesunden und kranken Fohlen, gesund: n = 64, krank: n = 69.*

The serum IgG concentration on the first day of life was determined in 17 sick and 16 healthy foals. For the other 100 foals included in the study (52 sick foals, 48 healthy foals) serum TG concentrations were determined twelve hours post natum. Total globulin concentrations were positively correlated with IgG values ($r = 0.77$; $p < 0.0001$, $n = 23$).

Mean serum IgG concentration (by electrophoresis) in sick foals was 1041 ± 397 mg/dl (min: 600 – max: 2010 mg/dl) and 1318 ± 331 mg/dl (min: 770 – max: 1870 mg/dl) in healthy foals. The mean serum IgG concentration twelve hours post natum differed significantly between sick and healthy foals ($p = 0.03$). Mean concentration of TG was 29.0 ± 4.5 g/l (min: 21.0 – max: 42.0 g/l) in sick foals and 28.2 ± 4.7 g/l (min: 22.0 – max: 43.0 g/l) in healthy foals. The mean concentration of TG twelve hours post natum did not differ significantly between sick and healthy foals

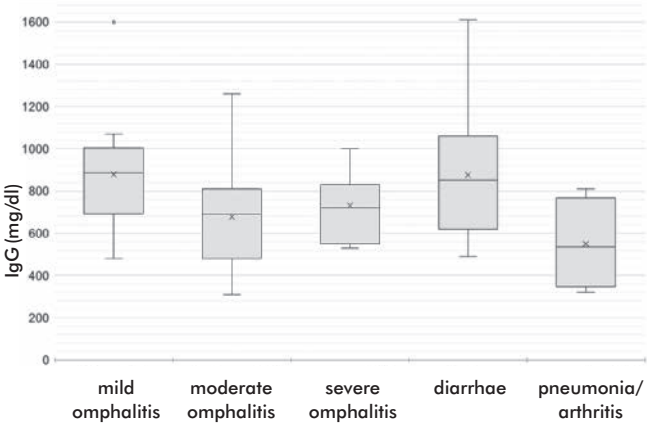

Fig. 2 IgG levels on the first day of sampling in different natures and severities of disease of foals, mild omphalitis: n = 14, moderate omphalitis: n = 23, severe omphalitis: n = 7, diarrhea: n = 21, pneumonia/arthritis: n = 4. | *IgG Konzentrationen am ersten Tag der Beprobung bei verschiedenen Erkrankungsarten und Schweregraden der Erkrankung bei Fohlen, leichte Omphalitis: n = 14, mittelschwere Omphalitis: n = 23, schwere Omphalitis: n = 7, Diarrhoe: n = 21, Pneumonie/Arthritis: n = 4*

Table 1 Comparison of baseline values between foal groups | *Vergleich der Ausgangswerte zwischen den Fohlengruppen*

	Group 1 (healthy)	Group 2 (sick)					
		all	mild omphalitis	moderate omphalitis	severe omphalitis	diarrhea	pneumonia/ arthritis
foals (n)	64	69	14	23	7	21	4
age at sampling start[1]	6.7 ± 3.0 (3–14)	6.4 ± 2.9 (3–14)	7.4 ± 2.9 (3–12)	8.1 ± 2.8 (3–14)	6.9 ± 1.1 (5–8)	3.7 ± 1.2 (3–7)	6.3 ± 2.1 (4–9)
duration of sampling[2]	11.2 ± 8.6 (4–58)	10.0 ± 8.3 (4–55)	6.4 ± 0.9 (5–8)	10.4 ± 2.2 (6–14)	15.1 ± 2.4 (11–18)	5.5 ± 1.0 (4–8)	35.5 ± 19.3 (9–55)
gender	29 M. 35 F	48 M. 21 F	12 M. 2 F	16 M. 7 F	6 M. 1 F	12 M. 9 F	2 M. 2 F
plasma IgG 12 h post natum[3]	1318 ± 331 (770–1870) n = 16	1041 ± 397 (600–2010) n = 17	983 ± 401 (610–1540) n = 4	1043 ± 459 (630–1550) n = 4	913 ± 294 (600–1310) n = 4	1373 ± 588 (850–2010) n = 3	915 ± 134 (820–1010) n = 2
plasma TG 12 h post natum [4]	28.5 ± 4.83 (22–43) n = 48	29.0 ± 4.50 (21–42) n = 52	30.7 ± 3.7 (25–36) n = 10	29.3 ± 5.2 (22–42) n = 19	29.0 ± 3.50 (25–31) n = 3	28.0 ± 4.4 (21–36) n = 18	26.0 ± 28.3 (24–28) n = 2

1) days, mean ± SD (range); 2) days, mean ± SD (range); 3) mg/dl, mean ± SD (range); 4) g/l; mean ± SD (range). F: female, g/l: grams per liter, h: hours, IgG: Immunoglobulin G, M: male, mg/dl: milligrams per deciliter, SD: standard deviation, TG: Total Globulin

($p > 0.05$). The detailed values of serum IgG and TG of the foals with different infectious diseases are listed in Table 1. Foals in group 1 sickened at days 6.4 ± 2.9 (min: 3.0 – max: 14.0 d).

The mean serum IgG concentration at the first sampling of corresponding healthy foals was 808 ± 282 mg/dl (min: 290 – max: 1460 mg/dl) (Figure 1 and Figure 2) compared to 777 ± 281 mg/dl (min: 310 – max: 1610 mg/dl) in sick foals ($p = 0.6$). Detailed serum IgG values determined at the onset of the different infectious diseases are shown in Table 3. The mean serum IgG concentrations determined at the first sampling did not differ significantly between the diseases examined ($p > 0.05$). The assignment of the foals to the three groups according to standard cut-off values of < 400 mg/dl IgG, 400–800 mg/dl IgG and > 800 mg/dl IgG on the first day of sampling are shown in Table 2.

The sampling of healthy foals lasted 11.2 ± 8.6 days (min: 4.0 – max: 58.0 d) with sample collection twice a week, foals with infectious diseases were sampled for 10.0 ± 8.3 days (min: 4.0 – max: 55.0 d) with daily sample collection until day six of disease, then every second day until recovery.

Compared with healthy foals or foals with omphalitis or diarrhea, foals with pneumonia or septic arthritis (four individuals, one with arthritis, two with pneumonia and one with arthritis and pneumonia) showed a lower mean serum IgG concentration (550 ± 218 mg/dl, min: 320 – max: 810 mg/dl) on the first day of sampling. IgG levels of three of the four foals were notably low during the whole time of sampling. Due to the low subject numbers this difference did not reach significance.

Serum IgG values during the entire sampling period are shown in Table 3, Figure 3 and Figure 4. The serum IgG concentrations of healthy and sick foals did not differ significantly during disease. The courses of serum IgG concentrations did not differ significantly between the various diseases (Tab. 4).

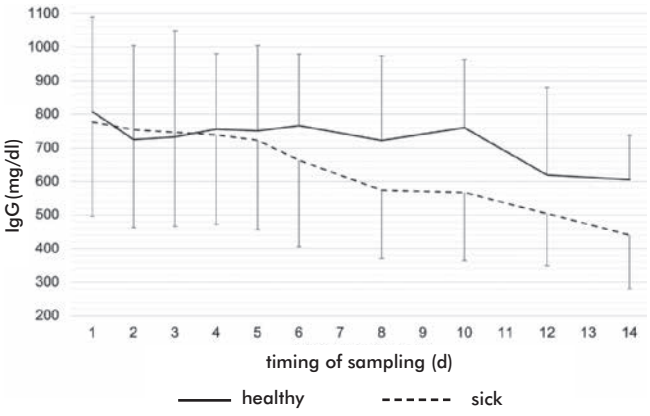

Fig. 3 Course of IgG in the blood of neonatal foals with infectious diseases and healthy foals. | *Verlauf von IgG im Blut von neonatalen Fohlen mit Infektionserkrankungen und gesunden Fohlen.*

Discussion

Only foals with a sufficient IgG concentration at twelve hours post natum were included into the study to set an appropriate transfer of passive immunity at start of life. The cut-off value for an adequate transfer of immunoglobulins to healthy foals on this farm was set at ≥ 600 mg/dl serum IgG or ≥ 21 g/l total globulin (TG). As shown in former studies, serum TG represents a practical and economic quantitative field test for FPTI achieving high sensitivities when analyzer-specific cut-offs are set after validation (*Tscheschlok* et al. 2016b). Levels beneath the usual cut-off value of 800 mg/dl IgG or more are justified for vigorous foals raised under well managed farm conditions (*McGuire* et al. 1975) as they were established on the farm where the current study was performed. Several studies showed that hypogammaglobulinemic foals

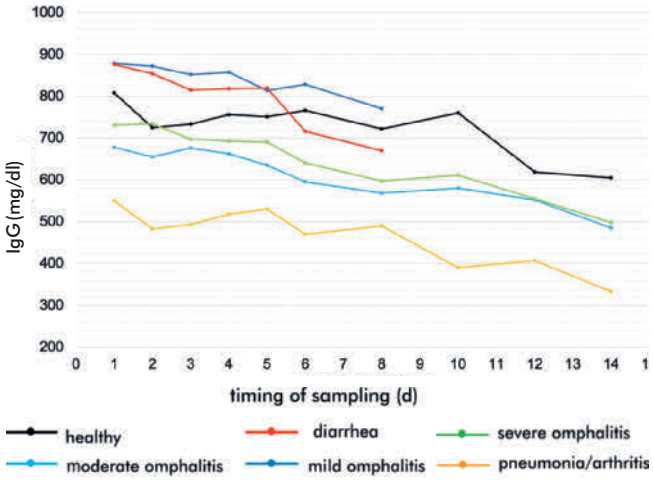

Fig. 4 Course of IgG in the blood of neonatal foals with different natures and severities of disease. | *Verlauf von IgG im Blut von neonatalen Fohlen mit verschiedenen Erkrankungsarten und Schweregraden der Erkrankung.*

Table 2 Plasma IgG values of healthy and sick foals on day one of sampling | *Plasma-IgG-Werte gesunder und kranker Fohlen am ersten Tag der Probenahme*

IgG (mg/dl)	Group 1 (healthy)	Group 2 (sick)			
		all	omphalitis	diarrhea	pneumonia/arthritis
Number of foals (% of group)	64 (100%)	69 (100%)	44 (64%)	21 (30%)	4 (6%)
< 400	5 (8%)	4 (6%)	3 (7%)	0 (0%)	1 (25%)
400–800	30 (47%)	36 (52%)	25 (57%)	9 (43%)	2 (50%)
> 800 mg/dl	28 (44%)	29 (42%)	16 (36%)	12 (57%)	1 (25%)

IgG: Immunoglobulin G, mg/dl: milligrams per deciliter

Table 3 Plasma IgG concentrations[1] during the observation period in healthy foals and foals with an infectious disease. | *Plasma-IgG-Konzentrationen1 während des Beobachtungszeitraums bei gesunden Fohlen und Fohlen mit einer Infektionskrankheit.*

Group	Day of sampling								
	1	2	3	4	5	6	8	10	12	14
healthy (n = 64)	808 ± 282 (290–1460)	724 ± 281 (350–1230)	733 ± 316 (200–1400)	756 ± 225 (390–1200)	751 ± 255 (290–1210)	766 ± 214 (440–1200)	722 ± 252 (290–1210)	760 ± 203 (470–1130)	619 ± 261 (240–1120)	605 ± 133 (480–790)
sick (n = 69)	777 ± 281 (310–1610)	754 ± 292 (260–1580)	746 ± 280 (300–1580)	739 ± 267 (290–1620)	723 ± 267 (310–1580)	663 ± 258 (240–1550)	574 ± 203 (240–1130)	567 ± 203 (200–1020)	504 ± 154 (280–760)	440 ± 160 (240–660)
omphalitis, mild (n = 14)	879 ± 281 (480–1600)	872 ± 302 (390–1570)	852 ± 296 (450–1580)	857 ± 280 (510–1620)	814 ± 272 (420–1580)	828 ± 247 (410–1440)	770 ± 0 (770–770)			
omphalitis, moderate (n = 23)	678 ± 265 (310–1260)	655 ± 265 (300–1200)	676 ± 269 (300–1220)	662 ± 224 (290–1070)	635 ± 240 (310–1140)	595 ± 214 (240–1020)	568 ± 235 (240–1130)	580 ± 230 (200–1020)	501 ± 191 (280–760)	485 ± 191 (350–620)
omphalitis, severe (n = 7)	731 ± 162 (530–1000)	734 ± 231 (470–1070)	697 ± 201 (410–890)	692 ± 156 (500–920)	690 ± 133 (470–880)	640 ± 176 (380–860)	597 ± 138 (390–790)	611 ± 134 (420–780)	555 ± 100 (450–710)	498 ± 184 (310–660)
diarrhea (n = 21)	876 ± 290 (490–1610)	854 ± 290 (420–1580)	815 ± 284 (350–1530)	818 ± 306 (340–1570)	819 ± 300 (420–1500)	716 ± 367 (360–1550)	670 ± 0 (670–670)			
pneumonia/arthritis (n = 4)	550 ± 218 (320–810)	483 ± 208 (260–710)	493 ± 180 (310–680)	518 ± 217 (360–830)	530 ± 199 (370–800)	470 ± 135 (360–660)	490 ± 163 (340–710)	390 ± 78 (300–440)	407 ± 117 (320–540)	333 ± 86 (240–410)

1) mg/dl, mean ± SD (range). IgG: Immunoglobulin G, mg/dl: milligrams per deciliter, n: number, SD: standard deviation

(< 400 mg/dl IgG) are more likely to develop infectious diseases during the first weeks of life than foals with normogammaglobulinemia (≥ 400 mg/dl IgG) especially in hospitalized surroundings (*Crawford* et al. 1977, *Bublitz* et al. 1991, *Chavatte Palmer* et al. 2001). However, it also has been shown that hypo- and normogammaglobulinemic foals did not differ significantly regarding the disease prevalence, the severity of diseases nor in their survival rate (*Baldwin* et al. 1991). In this study, the mean IgG concentration twelve hours post natum differed significantly between foals that later developed a disease and the foals remaining healthy ($n = 34$, $p = 0.03$), though it should be noticed that both groups had mean IgG concentrations well above 800 mg/dl (sick: 1041 ± 397 mg/dl, healthy: 1318 ± 331 mg/dl) and therefore usually would be classified as foals with an adequate transfer of passive immunity. Main TG concentrations twelve hours post natum showed no significant difference between the two study groups.

The aim of the current study was therefore to look at later time points after colostrum intake to evaluate whether infectious diseases subsequently cause an additional decrease of serum IgG levels. Hypothetically, sickness may lead to an enhanced metabolism of circulating proteins including immunoglobulins, thus stronger decrease of the serum IgG concentration in sick versus healthy foals. In this first study addressing the kinetic of serum IgG in neonatal foals, infectious diseases were not related to lower serum IgG concentrations. Neither after colostrum intake (twelve hours post natum) nor at the beginning of the disease serum IgG concentrations appeared to be different between healthy and sick foals. The same was true when looking at the entire period of the various observed diseases. In sum local infectious diseases per se do not affect total serum IgG levels and that healthy foals starting with low IgG levels during the first four weeks of life must not necessarily suffer from infectious diseases.

In an earlier study with healthy neonate foals, initial peak IgG values on the first day of life continuously declined to values well below 400 mg/dl measured by quantitative Oudin method within a two-month period (*Rouse* 1971). These findings are replicated in the presented study although the age of the foals differed in both studies. It should be noted that the decrease of IgG concentrations in our foals was less steep and mean IgG levels of 808 ± 282 mg/dl at days of age 6.7 ± 3.0 of the healthy foals in this study were significantly lower than those described for one week old foals by *Rouse* (1971). In sum, the assumption that foals with local infectious diseases catabolize IgG differently than healthy foals was not confirmed based on serum IgG levels. Levels of specific antibodies may however show changes that are not recognized in the serum IgG concentration. This was shown in neonatal calves, where total IgG concentrations in diarrheic calves were lower than in healthy calves, while E. coli-specific antibody titers were significantly higher in diarrheic calves (*Al-Alo* et al. 2018).

A large proportion of the diseased foals (64 %, 44/69) suffered from omphalitis. This disease was diagnosed and treated at a very early point in the course of the infection and healed uneventfully. As omphalitis is mainly a focal infection, the systemic effect on total blood IgG levels may be neglect-

able. To our best knowledge there is no report on IgG values of omphalitis patients, neither in equines nor other animal species.

In case of the foals suffering from diarrhea (30%, 21/69), it should be taken into account that they may secrete proteins through the gut even though there are no study-based hints that foals with diarrhea show lower serum-protein or gamma-globulin levels due to protein loss through the intestine (*Kuhl* et al. 2011). Studies in other species like cattle suggest, that dehydration and diarrhea or protein-losing enteropathy are related to serum albumin and alpha globulin concentrations as well as an increased rate of gamma globulin catabolism (*Marsh* et al. 1969, *Thornton* and *Willoughby* 1972).

Only few foals (4/69, 6%) in the current study suffered from early onset pneumonia and/or arthritis. On average, these foals showed rather low serum IgG values both at diagnosis and during the disease but the decline of serum IgG concentrations apparently displayed the same time course and shape as seen in the other sick and healthy foals.

Future studies with a larger set of septic foals as patients should be included to evaluate their kinetic of serum IgG levels.

Mean levels of IgG on the first day of sampling in healthy foals, foals with mild forms of omphalitis and foals with diarrhea were above 800 mg/dl. Foals with moderate to severe forms of omphalitis and pneumonia and/or septic arthritis as well as the group of sick foals in general had mean levels below 800 mg/dl but no significant difference could be shown neither between healthy and sick foals in general nor between different types of diseases. The similarity of the distribution of IgG values in the different study groups becomes obvious as individual IgG values of healthy, mildly sick and severely affected foals are found to range from below 400 mg/dl up to 800 mg/dl and well above regardless of the foal's health status (Table 2).

In conclusion, our hypothesis that foals with ongoing local infectious diseases metabolize IgG differently resulting in generally lower and/or faster decreasing serum IgG levels could not be confirmed. Not all infectious diseases have a marked influence on the total amount or on the decrease of serum IgG value in neonatal foals. Beside total serum IgG, other factors of the immune system of the neonate foal may have a more significant impact on the foal's early immune defense such as pathogen-specific antibodies or other immunologic active substances transferred through colostrum (e.g., cytokines, chemokines, complement factors, phagocytic cells, growth factors). The concerted action of these factors in early life not only ensure a proper early innate response towards infectious threads but also regulates the development of protective cellular and humoral adaptive responses of the foal.

Manufacturer's addresses

[a] Laboklin GmbH & Co.KG, Bad Kissingen, Germany
[b] SAS Institute Inc., SAS enterprise guide, Version 7.1, North Carolina, USA

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Table 4 Results of ANOVA for mixed models – comparison of IgG-courses between different diseases | *Ergebnisse von ANOVA für gemischte Modelle – Vergleich von IgG-Verläufen zwischen verschiedenen Erkrankungen*

type of disease	type of disease	Adj P	Pr > |t|	correction
0	1	0.88	0.271	Tukey-Kramer
0	2	0.20	0.023	Tukey-Kramer
0	3	0.99	0.527	Tukey-Kramer
0	4	0.91	0.309	Tukey-Kramer
0	5	0.14	0.015	Tukey-Kramer
1	2	0.11	0.011	Tukey-Kramer
1	3	0.80	0.207	Tukey-Kramer
1	4	1.00	0.847	Tukey-Kramer
1	5	0.06	0.005	Tukey-Kramer
2	3	0.98	0.458	Tukey-Kramer
2	4	0.09	0.009	Tukey-Kramer
2	5	0.79	0.196	Tukey-Kramer
3	4	0.84	0.238	Tukey-Kramer
3	5	0.57	0.102	Tukey-Kramer

Adj P = adjusted p-value, P = significance value, t = difference relative to scatter in sample data, 0 = healthy foals, 1 = foals with mild omphalitis, 2 = foals with moderate omphalitis, 3 = foals with severe omphalitis, 4 = foals with diarrhea, 5 = foals with pneumonia and/or arthritis

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