Pferdeheilkunde – Equine Medicine 40 (2024) 5 (September/October) 449–454 DOI 10.21836/PEM20240503

Kinetic of acute-phase proteins in foals – a review

Dorothea Hildebrandt[1] *and Monica Venner*[2]

[1] Clinic for Horses, University of veterinary Medicine Hanover, Foundation, Hanover, Germany
[2] Equine Clinic, Destedt, Germany

Summary: Acute phase proteins (APPs) are proteins that form part of the non-specific innate immune system and are increasingly being used in veterinary medicine as a non-specific diagnostic tool. This review is intended to help veterinarians obtain an overview of the data published to date on the diagnostic value of the most important APP in foals. In addition to the current analytical laboratory methods, the various inflammations and infections in which the various APPs can be helpful as inflammation parameters will be discussed. Serum amyloid A (SAA) is regarded as the only "major" APP in horses and is also playing an increasingly important role in the diagnosis of inflammation in foals. Studies show that SAA, due to its rapid rise (100–1000-fold) and higher sensitivity, should be preferred as an early indicator of inflammation, especially in comparison to fibrinogen. For example, increased SAA values were described for non-specific bacterial infections as well as for specific diseases such as enteritis (SAA: 178.7 ± 99.1 mg/l) or diarrhoea (SAA: 132 ± 143 mg/l). The average SAA concentration of the healthy foals in this study was 19.37 ± 9.41 mg/l. Fibrinogen is the most frequently measured positive APP in equine medicine, as there are simple and quick methods for its determination. In contrast to SAA, fibrinogen is a „moderate "APP and therefore a fibrinogen concentration of 2–4 g/l is frequent in healthy horses, whereas SAA is extremely low (<0.5–20 mg/l) in healthy horses. Furthermore, fibrinogen concentration only increases two- to four-fold in response to an inflammatory stimulus. Fibrinogen concentrations are significantly higher in foals with bacterial infections (fibrinogen: 6.6 g/l; 0.8–12.2 g/l) than in those with an uncertain or non-bacterial issue (fibrinogen: 3.5 g/l; 1.8–7.5 g/l). C-reactive protein, haptoglobin and ceruloplasmin show small increases after inflammation or infection in the studies available and, based on the current study situation, only appear to be of limited use as inflammation parameter in foals.

Keywords: horse, acute-phase proteins, C-reactive protein, serum amyloid A, fibrinogen, haptoglobin, ceruloplasmin, review, foals

Citation: Hildebrandt D, Venner M (2024) Kinetic of Acute-Phase Proteins in foals – a review. Pferdehelk Equine Med 40, 449–454; DOI 10.21836/PEM20240503

Korrespondenz: PD Dr. Monica Venner, Pferdeklinik Destedt GmbH, Trift 4, 38162 Destedt; mvenner @gmx.de

Submitted: May 20, 2024 | **Accepted:** June 13, 2024

Introduction

Monitoring an inflammatory response in animals can be challenging as classic signs of inflammation are not always clinically manifest. The early detection of an inflammatory event, particularly in foals, can increase the chance of recovery and reduce the duration of treatment and mortality.

Acute phase reaction (APR) is a non-specific and complex response of the organism following infection, inflammation and trauma and is triggered by tissue-damaging processes, such as bacterial and viral infections. The cytokines produced locally in the focus of inflammation initiate the APR cascades by stimulating multiple cells, leading to the production and circulation of the acute-phase proteins (APPs) in the bloodstream [1].

The APPs are a group of blood proteins in all mammals that are part of the non-specific innate immune system. The concentration depends on the severity of the disease and the extent of tissue damage in the animal affected [2].

Depending on the protein and the species, the positive APP (their plasma concentration increases during the APR) are classified as "major", "moderate", and "minor" according to their response to stimulation. Major APPs have very low or undetectable serum concentrations (< 1 µg/L) in healthy individuals and increase dramatically after stimulation (100–1000-fold). Generally, their concentration peaks after 24–48 hours and then declines rapidly during the recovery period. Moderate and minor responders are already present in the plasma of healthy animals and increase only about 1–10-fold during the APR. They peak at two to three days and decline more slowly than major responders. Negative APPs (e.g. albumin, transferrin) decrease in concentration during the inflammatory response [3,4].

There are many studies on APPs as an unspecific diagnostic tool in veterinary medicine and their diagnostic usefulness is well validated for species other than the horse or particularly the foal. To the best of the authors knowledge, there are no reviews on APPs exclusively in foals, and information on APPs other than fibrinogen and serum amyloid A (SAA) in foals is lacking. This review focuses on published information about the most important APPs in foals.

C-reactive Protein (CRP)

C-reactive protein belongs to the positive APPs. It is mainly produced by hepatocytes and regulated by pro-inflammatory cytokines, such as interleukin 6.

The CRP is considered to be a sensitive biomarker of infection and inflammation in many species, where the serum concentration increases dramatically after stimulation. It has been reported that the concentration of CRP varies by approximately 25 % during inflammatory disease [5].

The current laboratory methods for testing CRP in horses are commercially available equine-specific enzyme-linked immunosorbent assays (ELISA) and single radial immunodiffusion [1,6].

It has been suggested that CRP in horses is a minor responder, as studies show that the concentration does not increase as dramatically as is seen in humans, where CRP is considered to be a major APP. However, CRP serum concentrations have been shown to be higher in horses with clinical signs of inflammation, for example, shipping fever (18.3 ± 9.2 mg/l), cellulitis (19.8 ± 11.9 mg/l) and pneumonia (32.6 ± 15.8 mg/l), than in healthy horses (7.4–8.7 mg/l) [7].

There is a lack of information on the change in serum CRP concentration in foals following an inflammatory event. It has been shown that there is an age-dependent change in the concentration in healthy growing foals, as the concentration of serum CRP appears to be very low at birth (≤ 1 mg/l) and increases within three days (6.1 ± 4.4 µg/ml), has the maximum in 12-month-old foals (12.7 ± 2.7 mg/l) and decreases gradually between 18 months (9.4 ± 2.8 mg/l) and 4 years (6 ± 1.2 mg/l) [7]. In addition, it can be assumed that the serum concentration of CRP increases with non-specific inflammation as it is elevated in foals with toxic neutrophils ($n = 35$; $p < 0.0001$), enterocolitis ($n = 14$; $p = 0.003$), colic ($n = 8$; $p = 0.004$), rib fractures ($n = 10$; $p = 0.008$) and septic arthritis ($n = 2$; $p = 0.004$). However, this study on 40 foals with sepsis also shows that CRP does not indicate the presence of sepsis in neonate foals, as the serum concentration of CRP does not differ between septic, sick nonseptic and healthy foals (septic foals (n = 40):15 mg/ml (0–336 mg/ml); sick foals (n = 40): 6 mg/ml (0–260 mg/ml); healthy foals (n = 39): 39 mg/ml (0–240 mg/ml)) [6].

Serum amyloid A

Serum amyloid A (SAA) proteins belong to the apolipoprotein family. They are produced in the liver and adipocytes and play an important role in the organism of animals [8]. The SAA synthesis becomes stimulated by inflammation-related cytokines, such as interleukin 1, interleukin 6 and tumour necrosis factor α [9].

Several methods have been developed for measuring SAA in horses. The immunoturbidimetric assay is currently considered to be the most accurate, but ELISA assays are also used to measure SAA concentrations [1,10,11].

The SAA in horses is considered to be the only major responder and the most sensitive reflector of a horse's inflammatory status. The concentration of this protein is very low in healthy horses (< 0.5–20 mg/l) but increases rapidly (100–1000-fold) within a few hours during an acute phase. When the inflammation has resolved, the SAA values drop again within 12 hours [4]. Exemplarily, in adult horses with experimentally induced non-infectious arthritis (n = 24), SAA increased at 16 hours (46–286 mg/l) and peaked 227-fold higher than the baseline 36–48 hours after intra-articular injection [12,13]. It has been reported that SAA may be a more sensitive marker of inflammatory disease in horses than traditional markers, such as blood leucocytes or serum fibrinogen. [4] It also appears to be a useful aid in the detection of postoperative inflammatory or infectious complications, such as after castration or emergency laparotomy [14–16].

In contrast to the other APPs, there are several studies on the change in SAA concentration in foals during an inflammatory event. It has been reported that SAA levels are higher in foals with verified bacterial infections than in those with non-bacterial or uncertain diagnosis [17]. On the other hand, elevated SAA values have been described in specific inflammatory disorders in foals (≤ 12 months old) showing clinical signs of inflammation due to enteritis (n = 6; SAA: 178.7 ± 99.1 mg/l) or diarrhoea (n = 30; SAA: 132 ± 143 mg/l), in comparison to healthy foals (n = 108; SAA: 19.37 ± 9.41 mg/l) [18].

Serum levels appeared to be higher in septic foals (1079.7 ± 1254.5 mg/l) than in sick non-septic foals (312.1 ± 685.4 mg/l), and also correlate with the sepsis score, in a retrospective study of SAA concentration in septic neonatal foals (n = 590). The diagnostic and prognostic sensitivities of SAA were low, while the specificities were high. Therefore, since high sensitivity of a biomarker is more important for the early detection of sepsis, the authors conclude that SAA was most useful for ruling out sepsis but not for early diagnosis [19].

It is shown in the study by *Passamonti* et al. (2014) on the use of SAA for the early detection of Rhodococcus equi (R.equi) infected foals (n = 15) that the SAA concentration does not change significantly with the development of sonographic evidence of preclinical/subclinical R. equi pneumonia. The authors conclude that measurement of the SAA concentration is not suitable for the early diagnosis or screening of rhodococcosis in foals when testing is conducted at one-week intervals [20]. Similarly, the study by *Thomé* et al. (2018) on thirty-three foals monitored weekly from two weeks to five months of age also showed a significant increase in the SAA concentration in most of the foals with severe pneumonia (SAA: 80.2 mg/l; 0.6–167 mg/l) but not in those with a subclinical pneumonia (SAA: 5.6 mg/l; 0.2–92.2 mg/l). The SAA concentration of the healthy foals in this study ranged from 0.1–161 mg/l (median: 18 mg/l). The authors concluded that the SAA concentration does not seem to be a reliable detector for foals with moderate pulmonary changes due to bronchopneumonia. Nevertheless, it appears to be an appropriate parameter to use in the process of treatment decision [21].

Furthermore, measuring SAA seems to be useful for 'real-time' monitoring of the clinical course of foals with R. equi pneumonia and their response to treatment when clinical manifestations are present [17,20]. This is also shown in the study by *Lankenfeld* et al. (2021), on the SAA concentration in foals with severe or moderate pneumonia (n = 52) at the time point of diagnosis and during the treatment period. The study showed that SAA concentrations were higher in those foals with severe pneumonia and lower in foals in which the bronchopneumo-

nia was no longer in the clinical phase. However, it is also apparent that a rapid decrease in SAA during the treatment does not always appear to coincide with the healing of the lesions in the lung tissue [22].

The SAA levels were measured with a point-of-care assay in another study. Foals with pneumonia caused by R. equi (n = 31; 212 mg/l; 7–781 mg/l) and foals with pneumonia caused by other bacteria (n = 23; 27 mg/l; 0–604 mg/l) had a significantly higher SAA concentration ($p < 0.001$) than clinically healthy foals (n = 44; 0 mg/l; 0–5 mg/l). There was no significant difference in SAA concentrations between foals with pneumonia caused by R. equi and those with pneumonia caused by other bacteria. However, the authors also concluded that a high level of SAA alone is not necessarily an indication for antimicrobial therapy in foals, as a small group of the clinically healthy foals also had high SAA levels (> 200 mg/l) without any apparent signs of disease [23].

Haptoglobin

Haptoglobin (Hp) is a glycoprotein that is mainly produced in the liver and mediated by cytokines such as IL-6. It is a major APP in many species, such as ruminants, where Hp levels can increase up to 100-fold after a stimulation [24]. It is reported to have an intermediate response in horses and increases moderately within four to six days after an inflammatory event. Exemplarily, the Hp increased significantly (12.9 ± 2.6 g/l) in foals with enteritis (n = 6) compared to the healthy foals (5.2 ± 2.4 g/l) [6,25] Serum Hp in horses is reported to be a sensitive and early indicator of haemolysis as it decreases in horses with intravascular and extravascular haemolytic anaemia [1]. Haptoglobin is also considered to be a superior marker of chronic inflammation in horses. The Hp concentrations in sick horses (e.g. with pneumonia, bacterial cholangiohepatitis, gastric ulcers), were significantly ($p < 0.05$) elevated in those with clinical signs lasting more than seven days, compared to patients with clinical signs of four days or less [26]. It was suggested that Hp be considered as a valuable diagnostic tool for monitoring inflammation and treatment efficacy in chronic diseases such as laminitis or placentitis. Four adult horses in the study had clinical signs associated with laminitis, placentitis, pyometra and renal failure for more than five days and showed elevated Hp concentrations (> 0.7 g/l) at normal SAA levels. [27]

Similar to SAA, Hp is thought to be increased in foals with inflammation due to pneumonia caused by Rhodococcus equi, as the sick foal group (n = 19) in one study had a higher Hp level (13.2 ± 2.0 g/l) than the healthy group (6.84 ± 1.5 g/l) (n = 18) [28].

Equine-specific ELISA assays are used to measure Hp [6,28].

Fibrinogen

Fibrinogen is a glycoprotein that is mainly synthesized by hepatocytes and mediated by IL-6 and glucocorticoids [29]. It is considered to be the most commonly measured positive APP in equine practice as there are simple and rapid methods for its determination. The standard measurement used for fibrinogen is considered to be the heat precipitation method. However, it is considered to be insensitive to small changes as this method can only detect changes of more than 1 g/l [30]. The heat precipitation method is increasingly being replaced by the modified Clauss method in veterinary medicine [31].

Fibrinogen as a moderate APP has an intermediate response in horses and is also present in high concentrations in the blood of healthy horses (2–4 g/l). The fibrinogen concentration increases only two to four times in response to an inflammatory stimulus (3–11 g/l), has a response time of approximately 24 to 72 hours and peaks at 72 to 144 hours [4]. This is also shown in the study of *Belgrave* et al. (2013) on 111 clinically normal and 101 clinically sick horses. In contrast to SAA values, which increased up to 20.5-fold in median SAA concentration, fibrinogen levels only increased less than twofold in sick horses (e.g. with pneumonia, enterocolitis, meningitis) compared to healthy horses [32].

Concentrations of 4 g/l are considered to be the upper physiological limit of plasma fibrinogen concentration in adult horses. By contrast, physiological concentrations of plasma fibrinogen in foals seem to vary dramatically in the first weeks of life (2.77–5.04 g/l) [20].

Fibrinogen is not considered a good indicator of sepsis in newborn foals, as described in the study by *Borba* et al. (2020) on 46 foals. Placentitis was experimentally induced in 38 mares to identify early blood markers as indicators of sepsis in the foal. In contrast to SAA levels, which increased significantly in septic foals, fibrinogen levels did not differ between septic, non-septic and control groups at birth. However, septic foals had higher fibrinogen levels (> 7 g/l) at 12 and 24 hours, which could be considered as an inflammatory indicator of intrauterine sepsis in late gestation [33].

In addition, it is reported that high fibrinogen levels (≥ 9 g/l) are considered to be a predictor of physical or epiphyseal osteomyelitis in the neonatal foal (n = 76). The study also showed that plasma fibrinogen concentrations in the range of 5–8 g/l were associated with septic arthritis alone or systemic infection (pneumonia), but should not be used as a definitive diagnostic test because of the low positive predictive value in these groups [34].

Fibrinogen levels in foals appear to change during an inflammatory event, as reported in a study by *Hultén* et al. (2002) on 25 foals with clinical signs of infectious disease. The main presenting signs were neonatal weakness (n = 9), pneumonia (n = 6) and diarrhoea (n = 10). The foals with verified bacterial infections (n = 8) had significantly higher fibrinogen levels (mean concentration: 6.6 g/l; 0.8–12.2 g/l) than those with uncertain or nonbacterial diagnoses (n = 17; mean concentration: 3.5 g/l; 1.8–7.5 g/l). However, the study also showed that SAA responded more rapidly to an equid Herpesvirus 1 infection in one foal than fibrinogen [17].

It is also reported that the fibrinogen concentration may be useful for the early identification of foals infected with R. equi, although this study on 165 foals also shows that the measurement of white blood cell concentrations was significantly more sensitive

and more specific. However, fibrinogen concentrations > 6 g/l were described to have a positive predictive value of 86.1 % on a farm with a prevalence of R. equi disease of 40 % [35].

Ceruloplasmin

Ceruloplasmin (Cp) is a copper-containing glycoprotein synthesized in the liver and is one of the major plasma proteins [36,37]. It is considered to be an APP in horses with a response in the intermediate or late phase of acute inflammation. It seems to peak seven to ten days after an inflammatory stimulus and may remain elevated for several weeks [1,38].

Among other methods, the immunoturbidimetric and enzymatic assays are currently the most commonly methods for the measurement of Cp [39].

As an APP, it increases dramatically in response to inflammatory processes, such as in the study of *Smith* and *Cipriano* (1987) on eleven Shetland ponies. The ponies were treated with turpentine oil intramuscularly in the pectoral region to induce acute local inflammation. Serum Cp increased significantly in the ponies treated (n = 7) in contrast to healthy ponies (n = 4) and remained elevated for one to three weeks after the initial insult [40].

Ceruloplasmin shows significant age-dependent changes in foals. The mean Cp concentration in the serum of healthy newborn foals was 21.41 ± 2.98 µmol/l, increasing to the adult value of 35.44 ± 4.70 µmol/l in 1-year-old horses and peaking at 45.22 ± 5.52 µmol/l in two-year-old horses. Thereafter, it decreases slightly with age [38].

Ceruloplasmin also plays an important role as a ferroxidase in the distribution of iron in the blood. Inflammatory reactions are thought to redistribute the iron available in the serum and the rapidly available iron is stored in ferritin [34]. The enzyme Cp is required for the storage of iron in ferritin. It is thought that the increased storage of iron in ferritin also increases the Cp levels and, thus, also the copper levels in the blood [40,41].

The possibility that the serum iron level in foals changes in response to an acute systemic reaction and, thus, also the Cp level, is shown in a study by *Klöpping* et al. (2023). The study on foals with bronchopneumonia (n = 150) showed that the sick group (n = 84) had significantly lower serum iron concentrations (mean concentration: 9.84 µmol/l; 6.44–13.78 µmol/l) than the healthy group (mean concentration: 28.11 µmol/l; 21.66–32.05 µmol/l). In addition, the sick foals also showed an increase in serum ferritin levels (mean concentration: 10.33 pmol/l; 5.57–14.38 pmol/l) compared to the healthy group (mean concentration: 8.53 pmol/l; 4.49–8.98 pmol/l). This also shows that acute systemic inflammation does not necessarily lead to an absolute iron deficiency but initially only to a redistribution of iron in the body [41].

Conclusion

In conclusion, it can be said that APPs play an important role in foals as a non-specific diagnostic tool for the early detection of inflammation. Although fibrinogen is also a widely used diagnostic tool in horses, SAA particularly appears to be a more sensitive and earlier indicator of inflammation in foals and especially in the monitoring of a treatment. Furthermore, SAA and fibrinogen, as non-specific inflammation parameters, should not be used as the sole indicator of infection and inflammation in the foal, but are very helpful in combination with other diagnostic tools.

References

1 Jacobsen S (2007) Review of Equine Acute-Phase Proteins. American Association of Equine Practitioners (AAEP) 53, 230–235, CABI 20083097770
2 Murata H, Shimada N, Yoshioka M (2004) Current research on acute phase proteins in veterinary diagnosis: an overview. Vet J 168, 28–40, DOI 10.1016/S1090-
3 Eckersall PD, Bell R (2010) Acute phase proteins: Biomarkers of infection and inflammation in veterinary medicine. Vet J 185,23–27, DOI 10.1016/j.tvjl.2010.04.009
4 Jacobsen S, Andersen PH (2007) The acute phase protein serum amyloid A (SAA) as a marker of inflammation in horses. Equine Vet Educ 19, 38–46, DOI 10.2746/095777307X177235
5 Sproston NR, Ashworth JJ (2018) Role of C-Reactive Protein at Sites of Inflammation and Infection. Front Immunol 9, 754, DOI 10.3389/fimmu.2018.00754
6 Zabrecky KA, Slovis NM, Constable PD, Taylor SD (2015) Plasma C-reactive protein and haptoglobin concentrations in critically ill neonatal foals. J Vet Intern Med 29, 673–677, DOI 10.1111/jvim.12568
7 Kazuto Yamashita TF, Masahiro Okumura, Mitsuyoshi Takiguchi, Nobu Tsunoda, Shinya Mizuno (1991) Serum C-Reactive Protein (CRP) in Horses: The Effect of Aging, Sex, Delivery and Inflammations on its concentration. J-Stage 53,1019–24, DOI 10.1292/jvms.53.1019
8 Jain S, Gautam V, Naseem S (2011) Acute-phase proteins: As diagnostic tool. J Pharm Bioallied Sci 3,118–27, DOI 10.4103/0975-7406.76489
9 Yamada T (1999) Serum Amyloid A (SAA): a Concise Review of Biology, Assay Methods and Clinical Usefulness. Clin Chen Lab Med 37, 381–388, DOI 10.1515/CCLM.1999.063
10 Stoneham SJ, Palmer L, Cash R, Rossdale PD (2010) Measurement of serum amyloid A in the neonatal foal using a latex agglutination immunoturbidimetric assay: determination of the normal range, variation with age and response to disease. Equine Vet J 33, 599–603, DOI 10.2746/042516401776563472
11 Witkowska-Pilaszewicz OD, Zmigrodzka M, Winnicka A, Miskiewicz A, Strzelec K, Cywinska A (2019) Serum amyloid A in equine health and disease. Equine Vet J 51, 293–298, DOI 10.1111/evj.13062
12 Hultén C, Gronlund U, Hirvonen J, Tulamo RM, Suominen MM, Marhaug G, Forsberg M (2002) Dynamics in serum of the inflammatory markers serum amyloid A (SAA), haptoglobin, fibrinogen and alpha2-globulins during induced noninfectious arthritis in the horse. Equine Vet J 34, 699–704, DOI 10.2746/042516402776250405
13 Satué K, Calvo A, Gardón JC (2013) Factors Influencing Serum Amyloid Type A (Saa) Concentrations in Horses. Open J Vet Med 03, 58–66, DOI 10.4236/ojvm.2013.31010
14 Jacobsen S, Jensen JC, Frei S, Jensen AL, Thoefner MB (2005) Use of serum amyloid A and other acute phase reactants to monitor the inflammatory response after castration in horses: a field study. Equine Vet J 37, 552–556, DOI 10.2746/042516405775314853
15 Busk P, Jacobsen S, Martinussen T (2010) Administration of perioperative penicillin reduces postoperative serum amyloid A response in horses being castrated standing. Vet Surg 39, 638–43, DOI 10.1111/j.1532-950X.2010.00704.x

16 Schliewert EC, Damhuis L, Swagemakers JH (2019) Serum amyloid A response post laparotomy in colic horses. Pferdehlk Equine Med 35, 492–497,,DOI 10.21836/pem20190601
17 Hulten C, Demmers S (2002) Serum amyloid A (SAA) as an aid in the management of infectious disease in the foal: comparison with total leucocyte count, neutrophil count and fibrinogen. Equine Vet J 34, 693–698, DOI 10.2746/042516402776250360
18 Yasushi Nunokawa, Toru Fujinaga, Tomoko Taira, Masahiro Okumura, Yamashita K, Nabuo Tsunoda, Hagio M (1993) Evaluation of Serum Amyloid A Protein as an Acute-Phase Reactive Protein in Horses. J Vet Med Sci 55 1011–1016, DOI 10.1292/jvms.55.1011
19 Hoeberg E, Sange A, Saegerman C, Bohlin A, Nostell K, Durie I, Husted L, Öhman A, Jacobsen S, Berg L, Hyldahl Laursen S, van Galen G (2022) Serum amyloid A as a marker to detect sepsis and predict outcome in hospitalized neonatal foals. J Vet Intern Med 36, 2245–2253, DOI 10.1111/jvim.16550
20 Passamonti F, Vardi DM, Stefanetti V, Marenzoni ML, Prato S, Cevese P, Coletti M, Pepe M, Casagrande Proietti P, Olea-Popelka F (2015) Rhodococcus equi pneumonia in foals: an assessment of the early diagnostic value of serum amyloid A and plasma fibrinogen concentrations in equine clinical practice. Vet J 203, 211–218, DOI 10.1016/j.tvjl.2014.08.033
21 Thomé R, Weber C, Rohn K, Venner M (2018) Serum amyloid A concentration in foals – Can it help when making a treatment decision in foals with pneumonia? Pferdehlk Equine Med 34, 61–67, DOI 10.21836/pem20180111
22 Lankenfeld A, Weber C, Rohn K, Venner M (2021) Kinetics of serum amyloid A during the treatment period of foals with pneumonia. Pferdeheilk Equine Med 37, 128–137, DOI 10.21836/pem20210204
23 Giguere S, Berghaus LJ, Miller CD (2016) Clinical Assessment of a Point-of-Care Serum Amyloid A Assay in Foals with Bronchopneumonia. J Vet Intern Med 30,1338–1343, DOI 10.1111/jvim.13978
24 Eckersall PD (2000) Recent advances and future prospects for the use of acute phase proteins as markers of disease in animals. Plen Lect 151, 577–584
25 Tomoko Taira, Toru Fujinaga, Masahiro Okumura, Kazuto Yamashita, Nobuo Tsunoda, Mizuno S (1992) Equine Haptoglobin: Isolation, Characterization, and the Effects of Ageing, Delivery and Inflammation on Its Serum Concentration. J Vet Med Sci 54, 435–442, DOI 10.1292/jvms.54.435
26 Cray C, Belgrave RL (2014) Haptoglobin Quantitation in Serum Samples from Clinically Normal and Clinically Abnormal Horses. J Equine Vet Sci 34, 337–340, DOI 10.1016/j.jevs.2013.05.007
27 Westerman TL, Tornquist SJ, Foster CM, Poulsen KP (2015) Evaluation of serum amyloid A and haptoglobin concentrations as prognostic indicators for horses with inflammatory disease examined at a tertiary care hospital. Am J Vet Res 76,882–888, DOI 10.2460/ajvr.76.10.882
28 Hassanpour A, Moghaddam S (2023) Evaluation of serum concentration of acute-phase proteins (haptoglobin and serum amyloid A) in the affected Arabian foals with rhodococcosis. Vet Med Sci 9, 144–149, DOI 10.1002/vms3.1005
29 Sarah Herrick, Olivier Blanc-Brude, Andrew Gray, Laurent G (1999) Fibrinogen. Int J Biochem Cell Biol 31, 741–746, DOI 10.1016/S1357-2725(99)00032-1
30 Borges AS, Divers TJ, Stokol T, Mohammed OH (2007) Serum Iron and Plasma Fibrinogen Concentrations as Indicators of Systemic Inflammatory Diseases in Horses. J Vet Intern Med 21, 489–494, DOI 10.1111/j.1939-1676.2007.tb02995.x
31 Russell EB, Courtman NF, Santos LL, Tennent-Brown BS (2021) Fibrinogen heterogeneity in horses. J Vet Intern Med 35,1131–1139, DOI 10.1111/jvim.16065
32 Belgrave RL, Dickey MM, Arheart KL, Cray C (2013) Assessment of serum amyloid A testing of horses and its clinical application in a specialized equine practice. J Am Vet Med Assoc 243,113–119, DOI 10.2460/javma.243.1.113
33 de Araujo Borba L , Wayne Nogueira CE, Pascoti Bruhn FP, Castro da Silva G, Soares Feijó L, Igor F, Canisso I, Curcio B (2020) Peripheral blood markers of sepsis in foals born from mares with experimentally ascending placentitis. Vet Rec 187,129, DOI 10.1136/vetrec-2017-104710
34 Newquist JM, Baxter GM, (2009) Evaluation of plasma fibrinogen concentration as an indicator of physeal or epiphyseal osteomyelitis in foals: 17 cases (2002–2007). J Am Vet MednAssoc 235, DOI 10.2460/javma.235.4.415
35 Giguère S, Hernandez J, Gaskin J, Miller C, Bowman JL (2003) Evaluation of white blood cell concentration, plasma fibrinogen concentration, and an agar gel immunodiffusion test for early identification of foals with Rhodococcus equi pneumonia J Am Vet Med Assoc 222, DOI 10.2460/javma.2003.222.775
36 Okumura M, Asano M, Tagami M, Tsukiyama K, Fujinaga T (1997) Serum Copper and Ceruloplasmin Activity at the early Growing Stage in Foals. Can J Vet Res 62,122–126, PMID 9553711
37 Gaware V, Kotade K, Dhamak K, Somawanshi S (2010) Ceruloplasmin its role and significance: A Review. Int J Biomed Res153–162, DOI 10.7439/ijbr.v1i4.69
38 Okumura M, Fujinaga T, Yamashita K, Tsunoda N, Mizuno S (1991) Isolation, characterization, and quantitative analysis of ceruloplasmin from horses. Am J Vet Res 52, DOI 10.2460/ajvr.1991.52.12.1979
39 Cecchini Gualandi S, Di Palma T, Boni R (2023) Analytical Validation of Two Assays for Equine Ceruloplasmin Ferroxidase Activity Assessment. Vet Sci 10, DOI 10.3390/vetsci10100623
40 Smith JE, Cipriano JE (1987) Inflammmation-Induced changes in Serum Iron Analytes and Ceruloplasmin of Shetland Ponies. Vet Pathol 24,356–359, DOI 10.1177/0300985887024004
41 Klöpping A, Werner S, Weber C, Müller SF, Müller E, Weiß M, Venner M, Vervuert I (2023) Comparison of serum iron status in healthy foals and foals with bronchopneumonia. Pferdehlk Equine Med 39, 448–457, DOI 10.21836/pem20230506