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BIOMARKERS USED IN THE DETECTION OF INFECTIONS IN HORSES

Abstract

Early identification of infectious diseases in horses is crucial for accurate diagnosis, effective treatment, and improved clinical outcomes. However, distinguishing infectious conditions from non-infectious inflammatory processes remains challenging in equine practice due to overlapping clinical signs and nonspecific laboratory findings. Over recent years, a variety of hematological, biochemical, and acute phase biomarkers have been investigated to support the detection and monitoring of infections in horses.

This article reviews the most commonly used biomarkers applied in equine infectious disease diagnostics, including white blood cell indices, neutrophil-to-lymphocyte ratio, serum amyloid A, fibrinogen, serum iron, haptoglobulin, CRP and Neutrophil Gelatinase–Associated Lipocalin (NGAL). The biological basis, diagnostic performance, and clinical relevance of these biomarkers are discussed, with particular emphasis on their roles in differentiating inflammatory responses, assessing disease severity, and monitoring treatment response. While acute phase proteins such as serum amyloid A and fibrinogen demonstrate high sensitivity to inflammatory stimuli, their limited specificity highlights the need for careful interpretation in conjunction with clinical findings and other laboratory parameters.

Overall, current evidence suggests that no single biomarker is sufficient for the definitive diagnosis of infectious diseases in horses. Instead, a multimodal approach integrating clinical assessment with multiple biomarkers provides the most reliable diagnostic and prognostic information. Continued research is required to refine biomarker interpretation, establish standardized reference intervals, and improve their practical application in equine medicine.

Keywords: *Equine infections; Biomarkers; Acute phase proteins; Serum amyloid A; Fibrinogen; Inflammation; Hematological parameters*

1. Introduction

1.1 The Importance of Infections in Equine Health

Infections and the systemic responses they trigger play a critical role in equine health and survival. Sepsis—defined as organ dysfunction resulting from a dysregulated host response to infection—remains one of the leading causes of morbidity and mortality in adult horses and foals, representing a life-threatening condition (Blangy-Letheule et

al., 2023). Horses are predisposed to developing sepsis due to their extensive microbial exposure in natural environments and their particularly high sensitivity to bacterial endotoxins (Taylor, 2015). Gastrointestinal diseases (such as colic and enterocolitis) and pulmonary disorders constitute the most common causes of sepsis in horses (Blangy-Letheule et al., 2023).

Therefore, early detection of infections in equine medicine is a critical factor that directly influences not only disease severity but also treatment success and survival outcomes (Nocera et al., 2021). Accurate diagnosis of sepsis in animals is of great importance. Misdiagnosis or delayed diagnosis may lead to excessive use of antibiotics, which can in turn promote the spread of antimicrobial resistance (López-Martínez et al., 2022).

The Increasing Role of Biomarkers in Infection Diagnosis and the Limitations of Classical Methods

For many years, the diagnosis of infectious diseases in veterinary medicine has relied primarily on clinical examination findings, complete blood count (CBC), and monitoring of leukocyte parameters. However, these traditional methods remain limited due to their low sensitivity in early-stage infections, their inability to clearly identify the source of infection, and their overall lack of specificity (Jacobsen & Andersen, 2007). In light of these limitations, biomarker-based diagnostic approaches have gained increasing importance in veterinary medicine. Biomarkers assessed through the acute-phase response provide a more objective means of monitoring the presence and severity of infection as well as the response to treatment. Accordingly, considerable attention has been directed toward markers such as Serum Amyloid A (SAA), haptoglobin, fibrinogen, and serum iron concentrations (Crisman et al., 2008; Afsar & Şener, 2015).

One of the most significant advantages of biomarkers is their supportive role in the differential diagnosis of infections presenting with nonspecific clinical signs. These parameters also allow clinicians to follow whether the infection is localized or systemic, whether its severity is increasing or decreasing over time, and how the patient is responding to therapy through serial measurements (Belgrave et al., 2013). In particular, highly sensitive acute-phase proteins such as SAA rise and decline more rapidly than traditional markers, thereby providing earlier diagnostic information. When interpreted together with more slowly responding indicators such as fibrinogen, both diagnostic sensitivity and specificity are improved (Pihl et al., 2013; Nocera et al., 2021; Jacobsen, 2023).

2. Acute Phase Response and the Concept of Biomarkers

2.1 Pathophysiology of the Acute Phase Response

The acute phase response (APR) is a systemic physiological reaction of the organism to infectious and non-infectious inflammatory stimuli such as trauma, infection, toxins, or malignancy (Cray & Altman, 2009). This process begins with the release of pro-inflammatory cytokines and other mediators from damaged tissues (Eckersall & Bell, 2010). As a result, endocrine, hematological, immunological, metabolic, and neurological alterations develop, manifesting clinically as fever, anorexia, depression,

and leukocytosis—hallmark signs of systemic inflammation (Sevgisunar & Şahinduran, 2014). In response to this systemic activation, acute phase proteins (APPs) are synthesized primarily in the liver, although other tissues may also contribute (Jacobsen, 2023). The process is highly coordinated and encompasses numerous behavioral, biochemical, and metabolic changes (Ceciliani et al., 2012). The principal functions of APPs include pathogen elimination, restoration of homeostasis, and support of tissue repair (Tóthová et al., 2014). The cytokines responsible for initiating the inflammatory cascade are mainly IL-1, IL-6, and TNF-α. These cytokines are first released from macrophages and monocytes at the site of injury, after which they enter systemic circulation, disseminate to distant tissues, and trigger a widespread cytokine response (Sevgisunar & Şahinduran, 2014). Their stimulation of hepatocytes in the liver leads to increased APP synthesis, causing serum concentrations of these proteins to rise rapidly (Eckersall, 2000). APPs play crucial roles in initiating, regulating, and resolving the inflammatory process. Driven by proinflammatory cytokines, their serum concentrations typically change by more than 25%, enabling their use as biomarkers in disease diagnosis, prognosis, and monitoring of therapeutic response (Eckersall & Bell, 2010). However, despite their high sensitivity, their specificity remains limited, underscoring the need for careful clinical interpretation. Additionally, significant species-specific differences exist in the acute phase response.Cytokines also exert hypothalamic effects that lead to behavioral changes such as anorexia. This, in turn, may create a general suppression in hepatic protein synthesis (Sevgisunar & Şahinduran, 2014). However, it has also been reported that there is no clear linear correlation between systemic cytokine release and AFP levels (Kushner & Mackiewicz, 2020).

2.2 What is a biomarker?

Biomarkers are molecules or parameters that objectively and measurably reflect normal biological processes, pathological conditions, or responses to therapeutic interventions within an organism (Strimbu & Tavel, 2010). They can be detected in various biological materials such as blood, urine, or synovial fluid. In veterinary medicine, biomarkers are particularly used for the early diagnosis of infections, assessment of inflammation severity, prediction of disease prognosis, and monitoring of treatment response. Acute phase proteins (e.g., SAA, fibrinogen, haptoglobin), hematological parameters, and certain cytokines are among the most frequently utilized biomarkers in equine health (Jakobsen et al., 2024; Thurston et al., 2022).

2.2.1 Acute Phase Proteins (APPs)

Although the majority of acute phase proteins are synthesized in the liver, some can also be produced by extrahepatic sources such as plasma cells or endothelial cells (Hassanpour & Moghaddam, 2023). When exposed to an inflammatory stimulus, the plasma concentrations of these proteins either increase (positive APPs) or decrease (negative APPs) (Jacobsen, 2023). Positive APPs are proteins whose plasma levels rise during inflammation. This group includes haptoglobin (Hp), C-reactive protein (CRP), serum amyloid A (SAA), fibrinogen (Fb), ceruloplasmin (Cp), alpha-1-acid glycoprotein (α1-AGP), various protease inhibitors, and inter-alpha trypsin inhibitor

heavy chain 4 (ITIH4) (Jacobsen, 2023). Negative APPs, on the other hand, are proteins whose plasma concentrations decrease during the inflammatory process. For example, paraoxonase-1 (PON-1) levels decrease in many species, including horses, during the acute phase response (Ruggerone et al., 2020). Other negative APPs include transferrin, prealbumin, and retinol-binding protein (Aldred & Schreiber, 2020). Biomarker indices created by evaluating positive and negative APPs together have the potential to increase the sensitivity of inflammation assessment. However, this approach has not yet been sufficiently investigated in equine medicine (Jacobsen, 2023). Acute phase proteins are also classified according to the magnitude of their response as major, moderate, or minor responders. Major APPs are present at low levels in healthy individuals but can increase 100- to 1000-fold during inflammation, typically reaching their peak within 24–48 hours. Moderate responders increase approximately 5–10 fold and peak within 2–3 days before gradually returning to baseline. Minor APPs generally rise by about 50–100% above resting levels, and their changes remain relatively limited (Eckersall & Bell, 2010). Among the biomarkers used to monitor inflammatory processes in horses, serum amyloid A (SAA), a major acute phase protein, is considered one of the most sensitive indicators of inflammation due to its early and rapid response characteristics (Jacobsen, 2023). Among the moderate acute phase responders, haptoglobin (Hp) and fibrinogen hold particular importance (Crisman et al., 2008; Jacobsen & Andersen, 2007). In addition, several hematological and biochemical parameters—such as plasma iron concentration (Oliveira-Filho, 2012), total leukocyte counts and leukocyte fractions (Burkat et al., 2024), as well as C-reactive protein (CRP) (Hildebrandt et al., 2025), and neutrophil gelatinase–associated lipocalin (NGAL) (Winther et al., 2023)—provide valuable contributions to clinical decision-making in the assessment of inflammation and infectious processes. Evaluating these parameters collectively allows for a more comprehensive understanding of the severity, duration, and underlying etiology of the inflammatory response.

2.3 Sensitivity – Specificity – Clinical Utility Criteria in Biomarkers

The Biomarkers Definitions Working Group (BDWG), established by the U.S. National Institutes of Health (NIH), defines an ideal biomarker as an indicator that "provides rapid diagnosis, distinguishes between physiological and pathological processes, and offers information regarding responses to pharmacological or other therapeutic interventions" (Strimbu & Tavel, 2010). Sensitivity, specificity, and clinical utility are critical criteria in the evaluation of biomarkers. These parameters determine how accurately and effectively a biomarker can identify a disease or condition (Winther et al., 2023). Sensitivity and specificity are used to assess the diagnostic capacity or accuracy of a test or biomarker (Siwińska et al., 2021). Sensitivity is the proportion of truly diseased animals that test positive (Salciccia et al., 2013). A highly sensitive test is more suitable for ruling out disease (Jacobsen, 2023). Specificity, on the other hand, relates to whether the biomarker responds exclusively to the infectious process. A highly specific test is more appropriate for confirming disease (Laurberg, 2023). Clinical utility extends beyond sensitivity and specificity and

concerns the extent to which a biomarker contributes to decision-making in the veterinary field. A single parameter is often insufficient; instead, interpreting biomarkers alongside clinical examination, imaging, and other laboratory findings facilitates a more accurate diagnosis (Gómez-Laguna et al., 2011). It has been reported that the biomarkers currently used in the diagnosis of SIRS exhibit high sensitivity but limited specificity (Jacobsen & Andersen, 2007).

3. Commonly Used Biomarkers in Horses

3.1 Serum Amyloid A (SAA)

Serum amyloid A (SAA) is considered the major acute phase protein in horses. During the acute phase response, it is produced intensively in the liver, leading to a rapid increase in its circulating levels. In healthy adult horses, serum concentrations are reported to be <10–20 mg/L (Jacobsen, 2023). In neonatal foals (<19 hours old), mean serum SAA levels have been reported as 27.7 mg/L (Nieman & Chan, 2022). However, healthy foals are believed to have slightly higher serum concentrations than adult horses, with levels peaking up to 120 mg/L within 24–72 hours after birth (Duggan et al., 2007; Paltrinieri, 2008).

3.1.2 Use in Infectious Conditions

In studies conducted on colic, SAA has been evaluated for purposes such as determining prognosis, guiding decisions regarding surgical intervention, identifying postoperative complications, differentiating non-inflammatory causes of colic from inflammatory ones, and distinguishing strangulating colic cases from non-strangulating cases (Ludwig et al., 2023; Elsawaf et al., 2025). Measurement of serum SAA is suggested to improve the ability to differentiate between medically and surgically managed acute inflammatory colic cases by approximately 4%, thereby potentially reducing the risk of unnecessary or delayed surgical intervention (Pihl et al., 2016). However, Dondi et al. (2015) reported no significant differences in SAA levels between strangulating and non-strangulating colic lesions, nor between cases requiring medical versus surgical treatment.

In colic conditions, SAA levels in peritoneal fluid have also been reported to increase in a manner similar to serum concentrations (Pihl et al., 2013). Because SAA concentrations were found to be higher in colic cases associated with primary inflammatory etiologies—such as enteritis, colitis, peritonitis, and peritoneal abscesses—and in non-surviving horses, it has been suggested that SAA may serve as a parameter associated with survival outcomes (Vandenplas et al., 2005). In horses undergoing colic surgery, postoperative SAA levels were found to be elevated in all operated animals due to inflammation. However, no differences in SAA concentrations were detected between horses that developed postoperative infections and those exhibiting non-infectious postoperative complications (Aitken et al., 2019). SAA concentrations have been reported to increase most prominently in inflammatory diseases and in colic cases with a duration exceeding five hours (Pihl et al., 2016). Serum SAA concentrations were also shown to be significantly higher in cases of acute colitis and *Clostridium difficile*–associated enterocolitis compared with both healthy horses and those with obstructive intestinal lesions (El-Deeb et al., 2020; Ludwig et

al., 2023). Based on these findings, SAA does not appear to determine the anatomical localization of colic lesions in horses; however, it is useful in assessing prognosis, with higher concentrations being associated with lower survival rates (Ludwig et al., 2023). In equine respiratory diseases, Serum Amyloid A (SAA) has become a notable biomarker for distinguishing between infectious and non-infectious conditions and for monitoring treatment response. In bacterial pneumonia, SAA levels have been shown to decrease significantly during treatment in parallel with clinical improvement, whereas fibrinogen, neutrophil counts, and total leukocyte counts fail to adequately reflect this change (Hepworth-Warren et al., 2023). Additionally, in infections caused by bacterial agents such as *Streptococcus equi* subsp. *equi*, SAA levels have been found to be markedly higher compared with viral respiratory infections (Viner et al., 2017). This suggests that SAA may contribute to differential diagnosis based on the etiological agent in respiratory disease.

Experimental studies have demonstrated that SAA rises within 24 hours, peaks on day 3, and rapidly returns to baseline values with effective treatment (Hobo et al., 2007). Owing to this early and dynamic response, SAA serves as a practical tool particularly for monitoring disease progression and evaluating treatment efficacy in equine infectious respiratory conditions.

3.1.3 Use in Non-Infectious Conditions

In endurance horses, leukogram findings and SAA concentrations have been evaluated to assess overall physiological condition. Prior to the race, SAA concentrations were within reference intervals; however, horses that successfully completed the race had significantly lower SAA levels compared with those that were eliminated. Notably, SAA was the only laboratory parameter capable of identifying the majority (66.6%) of the horses that would subsequently be eliminated before the competition. Moreover, none of the horses with SAA levels exceeding 1000 ng/mL were able to finish the race. Therefore, serum SAA concentration may serve as an indicator of poor physiological status and could potentially predict elimination during an endurance event (Cywinska et al., 2010). Serum SAA concentrations have been reported to be significantly elevated in cases of Juvenile Idiopathic Arthritis (JIA), suggesting that SAA may serve as a reliable parameter for identifying JIA in affected humans (Dev & Singh, 2019). In a study conducted on horses with synovial penetration injuries that required surgical treatment, SAA levels were found to be higher in cases necessitating multiple surgical interventions compared with those requiring only a single procedure. Furthermore, serial measurements taken at 48-hour intervals showed a noticeable decline in SAA concentrations in parallel with clinical improvement. Therefore, serial SAA assessment has been proposed as a valuable tool for monitoring treatment progress in synovial penetration injuries (Haltmayer et al., 2017).

3.1.4 Advantages and Limitations

SAA is widely used in clinical practice for early detection of inflammation, monitoring its severity, and evaluating response to treatment because its serum concentration increases rapidly and markedly in the presence of an inflammatory stimulus and returns to baseline in parallel with clinical improvement (Belgrave et al., 2013). However,

SAA is a non-specific marker of inflammation and, because it does not provide etiological distinction, it cannot independently determine whether the cause of inflammation is infectious (bacterial or viral) or non-infectious (traumatic, surgical, immune-mediated) (Jacobsen, 2023). Although it has been suggested that viral diseases generally result in lower SAA concentrations compared with bacterial infections (Viner et al., 2017), substantial overlap in plasma values among different etiologies limits SAA's ability to definitively distinguish viral infections from bacterial ones (Jacobsen, 2023).

3.2 Iron

Iron is an essential element involved in fundamental biological processes such as hemoglobin synthesis, oxygen transport, cellular respiration, and DNA replication (Hentze et al., 2010). In blood, iron is transported bound to transferrin, a β-globulin primarily synthesized in the liver, and is stored within ferritin as well as in the macrophages of the reticuloendothelial system and hepatocytes (Hentze et al., 2010). Hepcidin, a hormone secreted by the liver, is the principal regulator of plasma iron concentration and overall iron homeostasis (Corradini et al., 2014). Hepcidin exerts its effects on ferroportin (FPN1), the cellular iron exporter located on enterocytes in the proximal duodenum and on macrophages. FPN1 is the only known transporter responsible for exporting iron from duodenal enterocytes into the bloodstream (Nemeth et al., 2004). Elevated hepcidin levels lead to ferroportin degradation via binding and internalization, resulting in reduced iron absorption from the intestine and decreased release of iron from macrophages into circulation. Consequently, serum/plasma iron concentrations fall rapidly ((Nemeth et al., 2004, Hentze et al., 2010). This mechanism represents a key host defense strategy during inflammation, limiting pathogen access to iron (Hentze et al., 2010). For this reason, iron concentrations decrease rapidly during systemic inflammation in many species, including horses (de Oliveira-Filho, 2012). Experimental studies in horses have shown a significant reduction in serum iron levels within the first 24 hours following induction of inflammation (Brosnahan & Brown, 2012).

3.2.1 Use in Infectious Conditions

Canola et al. (2024) reported that serum/plasma iron concentrations were significantly lower in horses with colic compared to healthy controls, and concluded that the combined assessment of iron-metabolism parameters and conventional acute phase proteins may enhance diagnostic accuracy and prognostic evaluation in horses with inflammatory colic. Similarly, Crisman et al. (2008) demonstrated that, although increased fibrinogen (Fb) concentrations are associated with poor prognosis, hypoferremia (low serum iron) more accurately reflects acute, subacute, and chronic inflammation in hospitalized horses older than two months. Lilliehöök et al. (2020) observed that serum iron decreased more rapidly and normalized earlier than serum amyloid A (SAA), a commonly used acute-phase protein. While SAA remained elevated 72 hours post-challenge, serum iron had already begun to return to normal levels, suggesting that iron concentrations change more rapidly than SAA, a phenomenon also noted in mares following experimentally induced endometritis.

Otsuka et al. (2025) reported that serum iron levels in horses with inflammatory diseases were significantly lower than in the control group, indicating that serum iron may serve as a reliable marker for detecting acute inflammation or disease. Its measurement is simple, cost-effective, and feasible in standard biochemistry laboratories, making it a practical option, particularly in clinical settings with limited resources. Moreover, serum iron assessment could be considered as an alternative or complementary tool to existing acute-phase protein tests. Corradini et al. (2014) found that, in horses with systemic inflammation (SI), plasma iron concentrations were significantly lower compared to both healthy controls and hospitalized horses without SI. Plasma iron predicted the presence of SI with an accuracy of 82.9% and demonstrated high sensitivity (87.9%) for SI detection. In nonsurviving horses, plasma iron concentrations either remained below the reference range or decreased relative to admission levels during follow-up, reflecting persistence of SI in these animals. In contrast, Sanmartí et al. (2020) showed that plasma iron concentration is not a useful marker for predicting SIRS or prognosis in neonatal foals. Foals meeting SIRS criteria did not show statistically significant differences in plasma iron concentrations compared to non-SIRS foals or healthy controls, and plasma iron was not associated with survival outcomes. These findings suggest that, unlike in adult horses, plasma iron is not a reliable early inflammatory marker or prognostic tool in neonatal foals, likely due to age-related rapid fluctuations and high natural variability. Brosnahan et al. (2012) demonstrated that a decrease in serum iron (sFe) concentration (hypoferremia) serves as an early and sensitive indicator of systemic inflammation in horses, which may result from tissue necrosis, bacterial infections, or endotoxemia. Following EHV-1 infection, sFe concentration decreased significantly in a biphasic pattern, suggesting that serum iron parameters may be useful for monitoring the clinical course of viral infections such as EHV-1.

3.2.2 Advantages and Limitations

Otsuka et al. (2025) reported that serum iron concentrations were significantly lower in the inflammatory disease group and suggested that its diagnostic capability may be comparable to existing acute phase proteins (APPs). Moreover, because iron measurement is inexpensive and easy to perform, it may contribute to routine inflammation assessment and serve as an alternative to costly or more complex APP testing (Otsuka et al., 2025).

Iron measurement is a practical and economical biomarker for the early detection of systemic infection and for monitoring treatment efficacy. However, factors such as nutritional status, age, hemolytic processes, and chronic diseases can influence iron levels; therefore, it is recommended that iron be interpreted not in isolation but in conjunction with other acute phase proteins and hematological indicators (Hentze et al., 2010; Jacobsen, 2023). When combined particularly with positive acute phase proteins such as SAA, iron provides complementary value in assessing the progression of infection and monitoring the response to treatment (Matur et al., 2017). Although Borges et al. (2007) reported that serum iron had 90% sensitivity for detecting systemic inflammation, its specificity for identifying the underlying cause is low; thus, iron

alone cannot differentiate etiology and should be used alongside other biomarkers. Age, hemolysis, liver disease, and iron supplementation are additional factors that may influence plasma iron concentrations (Borges et al., 2007).

3.3 Fibrinogen

Fibrinogen is a positive acute phase protein that plays a critical role in hemostasis and wound healing (Russell et al., 2021). Primarily synthesized by hepatocytes in the liver, this glycoprotein increases in production in response to pro-inflammatory cytokines such as IL-6 and IL-1β (Hildebrandt & Venner, 2024). Fibrinogen is one of the oldest and most commonly used biomarkers for monitoring inflammatory processes in horses (Crisman et al., 2008). Its plasma concentration rises in association with infection, trauma, tissue injury, or inflammation, and therefore it is classified as a positive APP (Crisman et al., 2008; Ko & Flick, 2016). Plasma fibrinogen concentrations typically begin to increase 24–48 hours after the onset of inflammation and reach peak levels within 3–5 days (Hildebrandt & Venner, 2024). In healthy horses, fibrinogen levels range between 2–4 g/L, and in response to an inflammatory stimulus, concentrations increase only two- to four-fold; therefore, fibrinogen is considered a moderate acute phase responder (Jacobsen & Andersen, 2007; Belgrave et al., 2013). In adult horses, the physiological upper limit is generally accepted as 4 g/L (Hildebrandt & Venner, 2024). During the early phase of the acute inflammatory response, thrombin cleaves fibrinogen to form fibrin, which limits blood loss, contains tissue damage, and restricts microbial spread (Luyendyk et al., 2019). Fibrinogen also plays an active role in host defense by promoting leukocyte recruitment and activation (Ko & Flick, 2016; Luyendyk et al., 2019). As in humans, horses possess three major forms of fibrinogen—high, low, and very low molecular weight forms—derived from proteolytic cleavage of the C-terminal region of the Aα chain (Russell et al., 2021). Increased fibrinogen levels are commonly observed in both surgical trauma and infectious conditions (Daniel et al., 2016). However, because of its slow kinetics, fibrinogen is considered more useful for monitoring chronic infections than for early diagnosis (Luyendyk et al., 2019; De Cozar et al., 2020).

3.3.1 Use in Infectious Conditions

Fibrinogen also functions as an antimicrobial host defense factor that limits bacterial growth and prevents dissemination. Fibrin/fibrinogen matrices physically entrap bacterial foci, thereby restricting microbial spread (Ko & Flick, 2016). In foals, fibrinogen levels have been reported to increase particularly in cases of bacterial infection, septicemia, and postoperative inflammation. However, physiologically elevated concentrations may also be observed during the first days after birth (Hildebrandt & Venner, 2024; Stoneham et al., 2001). Levels ≥9 g/L in neonatal foals are considered predictive for osteomyelitis or physitis (Hildebrandt & Venner, 2024). In horses with systemic inflammation, non-survivors have been shown to have significantly higher fibrinogen concentrations, suggesting that this parameter may be associated with mortality risk (Corradini et al., 2014; Taylor, 2015). Taylor (2015) also reported that elevated fibrinogen levels were associated with intrauterine infections and may indicate infection in the fetus or neonate. However, fibrinogen is a non-specific

marker of inflammation and may also increase in a variety of non-infectious conditions. Popelka (2015) suggested that weekly monitoring of fibrinogen might assist in the early diagnosis of *Rhodococcus equi* infections. Nonetheless, the author emphasized that reference intervals in foals vary with age and therefore results must be interpreted cautiously. The sensitivity of fibrinogen for detecting systemic inflammation has been reported as 82%, and persistent elevation during hospitalization has been associated with poor prognosis (Borges et al., 2007). De Cozar et al. (2020) further demonstrated that high preoperative fibrinogen levels in horses undergoing emergency surgery increased the risk of postoperative complications, a finding that may reflect underlying chronic inflammation or a predisposition to hypercoagulability.

3.3.2 Advantages and Limitations

In equine medicine, fibrinogen is one of the most frequently used positive acute phase proteins due to its simplicity and rapidity of measurement (Hildebrandt & Venner, 2024). Corradini et al. (2014) reported that fibrinogen alone demonstrated moderate accuracy (66.7%) and low sensitivity (54.2%) for detecting systemic inflammation; however, its diagnostic performance increased markedly when interpreted together with serum iron concentrations. Due to its slow kinetics, fibrinogen is a limited marker in the early stages of acute inflammation but is highly valuable in prolonged and chronic conditions (Crisman et al., 2008; Hildebrandt & Venner, 2024). Nonetheless, certain bacteria—such as *Staphylococcus aureus*—can exploit fibrinogen as a virulence factor to manipulate host defense mechanisms (Ko & Flick, 2016). In foals, fibrinogen is considered a complementary marker for understanding the kinetics of the acute phase response, but it is not sufficient as a standalone indicator for early diagnosis (Hildebrandt & Venner, 2024; Crisman, 2008). Its sensitivity is limited in some conditions, and fibrinogen does not respond as rapidly as SAA or haptoglobin during the early inflammatory phase (Crisman, 2008). Fibrinogen concentrations are influenced by numerous factors, including the location of infection, the severity of inflammation, changes in coagulation, and the overall condition of the horse. In severe sepsis, fibrinogen levels may be reduced due to consumption (Taylor, 2015). Age, breed, and assay differences can also complicate interpretation in foals (Popelka, 2015). Therefore, fibrinogen monitoring alone is insufficient, and more reliable diagnosis is achieved through combined assessment with clinical examination, ultrasonography, and other biochemical parameters (Corradini et al., 2014; Popelka, 2015; Hildebrandt & Venner, 2024). Because fibrinogen levels change more slowly than clinical signs, it remains limited for early detection (Thurston et al., 2022). This delayed response has been attributed to consumption of fibrinogen during coagulation (Daniel et al., 2016). Additionally, variability among measurement methods and clinically insignificant increases restrict its reliability for postoperative monitoring (Daniel et al., 2016). Given the presence of different molecular fractions of fibrinogen, measurement accuracy may be negatively affected—particularly in samples collected using EDTA—potentially leading to heterogeneity in interpretation (Russell et al., 2021). Moreover, individual factors such as breed and physiological status may

influence reference intervals, thereby reducing the clinical reliability of fibrinogen (Fonteque et al., 2015).

3.4 Haptoglobin

Haptoglobin is classified as a moderate acute phase protein (APP) in horses and may increase up to 1- to 10-fold above the reference interval (reference range: 2–10 g/L) during the acute phase response (APR) (Crisman et al., 2008). Haptoglobin (Hp) is a glycoprotein synthesized in the liver and is included among the positive acute phase proteins (Cray et al., 2009). Its primary function is to bind free hemoglobin, thereby preventing the oxidative toxicity of hemoglobin and reducing iron loss. Through this mechanism, haptoglobin acts as both an antioxidant and an immunomodulatory molecule (Cray, 2009). In horses, Hp concentrations rise markedly in association with bacterial infections, tissue injury, inflammation, and trauma (Crisman et al., 2008).

3.4.1 Use in Infectious Conditions

Haptoglobin typically begins to increase 24–48 hours after the onset of infection and may remain elevated during the chronic stages of the inflammatory process. Therefore, haptoglobin measurement is particularly useful for monitoring chronic infections and assessing response to treatment (Jakobsen, 2024). In a study by Cray and Belgrave (2014), serum Hp concentrations in clinically abnormal horses (showing signs of infection or inflammation) were reported to be, on average, 3.3 times higher than in healthy horses. This increase demonstrates the clinical value of Hp in evaluating the presence and severity of inflammatory processes. Increases in Hp concentrations are observed in bacterial infections, tissue injury, trauma, and postoperative inflammation; however, Hp elevation is generally limited in acute and short-duration infections (Cray & Belgrave, 2014).

3.4.2 Advantages and Limitations

Because Hp responds more slowly but more persistently than serum amyloid A, it is particularly useful for monitoring residual inflammation or prolonged infectious processes following treatment. Owing to these characteristics, Hp is considered a complementary biomarker for both diagnosis and prognosis. For this reason, Hp is recommended as a more suitable parameter for monitoring chronic or subacute inflammatory conditions and for evaluating treatment response (Jakobsen et al., 2024).

3.5 Leukocyte Count

Leukocytes (white blood cells, WBCs) are cells that protect the body against foreign invaders and abnormal cells (Chmielewski & Strzelec, 2018). Through their ability to exit blood vessels (diapedesis) and to engulf foreign substances (phagocytosis), they defend the host against numerous pathogens including bacteria, viruses, fungi, parasites, and helminths. They also play roles in recognizing and eliminating tumor cells or other foreign materials (Chmielewski & Strzelec, 2018).

In horses, changes in leukocyte count and in the distribution of leukocyte subpopulations (neutrophils, lymphocytes, monocytes, eosinophils, basophils) in the presence of systemic or local infection provide valuable information regarding the stage, type, and severity of disease (Overmann, 2017; Burkat et al., 2024). An increase in leukocyte count (leukocytosis) is generally associated with bacterial infections,

inflammatory conditions, or stress responses (Moore & Vandenplas, 2014). In lymphoid neoplasms such as lymphoma, extreme elevations in blood leukocyte counts may occur. These increases are not merely a simple rise in normal lymphocytes but may consist of atypical or abnormally differentiated cell types (Meichner et al., 2017).

3.5.1 Neutrophils

Neutrophils are the most abundant nucleated cells in the blood, comprising approximately 60–70% of all circulating leukocytes (Chmielewski & Strzelec, 2018). They represent a fundamental component of the innate immune defense mechanisms in horses (Donovan et al., 2007; Ryan et al., 2010). Also referred to as polymorphonuclear leukocytes (PMNLs), neutrophils are the first immune cells activated in response to infection (Ulgen et al., 2014). During inflammation, large numbers of neutrophils migrate rapidly to the affected site (Chmielewski & Strzelec, 2018). The primary function of neutrophils is to eliminate microorganisms through phagocytosis (Satué et al., 2014). These cells are specialized in the production of proteolytic enzymes—such as elastase, cathepsins, and matrix metalloproteinases (Salciccia et al., 2013)—and reactive oxygen species (ROS) (Faleiros & Belknap, 2017). In addition, they can produce pro-inflammatory cytokines (IFN-γ, TNF-α, IL-12, IL-6, IL-8, and IL-23p19) when stimulated by pathogens such as *Rhodococcus equi* (Ryan et al., 2010). Myeloperoxidase (MPO), released during neutrophil degranulation, plays a critical role in innate immune defense. MPO catalyzes the reaction between hydrogen peroxide (H_2O_2) and chloride ions to form hypochlorous acid, a potent microbicidal agent (Ulgen et al., 2014). The circulating half-life of neutrophils is approximately 10.5 hours, and once they migrate into tissues, they remain functional for 1–2 days (Satué et al., 2014). Before returning to peripheral circulation, neutrophils are eliminated through apoptosis (programmed cell death) or, in certain conditions, necrosis (Donovan et al., 2007; Chmielewski & Strzelec, 2018).

Neutropenia, Neutrophilia, and Morphological Changes

Neutropenia (Decrease)

Because mature neutrophil storage pools are limited in horses, neutrophil counts can decline rapidly during severe inflammation (Lester et al., 2015). Neutropenia is typically associated with severe bacterial processes, particularly septicemia in neonatal foals and gastrointestinal disorders in adults such as endotoxemia, strangulating obstructions, peritonitis, and salmonellosis (Satué et al., 2014).

Neutrophilia (Increase)

Neutrophilia may occur under physiological conditions (stress response, splenic contraction) or pathological conditions (inflammation, infection, neoplasia). Following the initial decline during acute inflammation, neutrophil numbers increase once the bone marrow response begins—typically within 4–5 days (Lester et al., 2015).

Morphological Changes (Toxic Change)

Accelerated bone marrow production can lead to toxic changes in neutrophils. These alterations are commonly associated with systemic bacterial infections and severe acute inflammatory lesions (Satué et al., 2014). Toxic changes include Döhle bodies,

increased cytoplasmic basophilia, and cytoplasmic vacuolization (Lester et al., 2015; Chmielewski & Strzelec, 2018).

Left Shift

Left shift refers to the release of less mature neutrophil forms into circulation due to increased tissue demand (Lester et al., 2015). The presence of band neutrophils and toxic neutrophil changes has been found to be significantly associated with SIRS (Systemic Inflammatory Response Syndrome) and with poor prognosis (higher mortality risk) (Lambert et al., 2016). Therefore, evaluating neutrophil count alone is insufficient; assessment of morphological quality is also essential (Chmielewski & Strzelec, 2018). During infection, large numbers of neutrophils are required to eliminate microorganisms. Thus, changes in the ratio of non-segmented (immature) to segmented (mature) neutrophils provide a more accurate indication of infection severity than relying solely on total granulocyte count (Honda & Littman, 2016).

3.5.2 Lymphocytes

Lymphocytes constitute 20–40% of all white blood cells. B lymphocytes produce antibodies, T lymphocytes regulate and coordinate the immune response, and natural killer (NK) cells directly destroy pathogens and abnormal/infected cells through cytotoxic mechanisms (Chmielewski & Strzelec, 2018). After neutrophils, lymphocytes (LYM) are the second largest WBC population in circulation and represent a major component of the immune system. Their average transit time through the bloodstream is approximately 30 hours, and they possess the ability to recirculate between blood, lymphatic channels, and peripheral tissues (Satué et al., 2014). Viral infections (e.g., EHV-1) and certain systemic infections often present with lymphopenia. Lymphopenia may be associated with suppression of the immune response or migration of lymphocytes into tissues. Although lymphocyte count can provide prognostic information in SIRS/sepsis cases, it is not decisive on its own. Lymphocytes serve as the principal regulators of cellular and humoral immune responses. Lymphopenia is commonly observed during acute inflammation and in cortisol-mediated stress responses (Overmann, 2017). Conversely, viral infections, immunodeficiency syndromes, and certain chronic diseases may present with lymphocytosis. Clinical observations in horses indicate that the combination of neutrophilia and lymphopenia during acute bacterial infections is one of the early indicators of SIRS (Bonelli et al., 2015).

Lymphopenia, Lymphocytosis, and Hematologic Ratios

Lymphopenia (Decrease in Lymphocytes)

Lymphopenia is the most frequently observed alteration in acute bacterial infections. This occurs due to redistribution of lymphocytes into lymphoid tissues and apoptosis of a subset of cells, driven by increased cortisol and catecholamines during the systemic inflammatory response (Chmielewski & Strzelec, 2018). Lymphopenia is commonly observed during acute inflammation and cortisol-mediated stress responses (Overmann, 2017). In addition, in endotoxemic shock or sepsis, lymphopenia often occurs concurrently with neutrophilia, a combination that has been proposed as an indicator of severe systemic infection (Bonelli et al., 2015).

Lymphocytosis (Increase in Lymphocytes)

Lymphocytosis may be observed in chronic infections or lymphoproliferative diseases (e.g., lymphosarcoma). It may also occur due to physiological stress (adrenaline release), viral diseases (e.g., EHV-1, EIA), immune stimulation, chronic antigenic exposure, and, more rarely, in lymphoid neoplasms (Satué et al., 2014).

Hematologic Ratios (NLR, MLR, Leukocyte Stress Index)

Recent studies have shown that parameters such as the neutrophil-to-lymphocyte ratio (N/L), monocyte-to-lymphocyte ratio (M/L), and leukocyte stress index may help assess the degree of systemic inflammation in horses (Burkat et al., 2024). In a study by Migliorisi et al. (2025), NLR and TNCC (total nucleated cell count) measured at admission in adult horses with non-infectious gastrointestinal colic were evaluated for their association with the need for surgery and survival outcomes. TNCC did not show significant differences between groups; however, NLR was significantly higher in cases requiring surgical intervention, particularly in horses with small intestinal lesions. Furthermore, horses that did not survive had significantly higher admission NLR values compared with survivors. These findings suggest that NLR may serve as a prognostic biomarker in colic cases, although overlapping values indicate that it should not be used as a sole decision-making parameter (Migliorisi et al., 2025).

3.5.3 Monocytes

Monocytes are cells that differentiate into macrophages within tissues, undergoing ultrastructural, metabolic, and receptor-mediated changes during this transformation. The half-life of macrophages varies from several days to several months (Satué et al., 2014). As precursors to tissue macrophages, monocytes play important roles in both innate and adaptive immune responses (Lester et al., 2015).

Monocytosis (Increase in Monocytes)

An increase in peripheral blood monocytes may occur during intense phagocytic activity such as in cases of tissue necrosis, intravascular hemolysis, or chronic suppurative diseases. Monocytosis frequently occurs alongside neutrophilia due to cytokine stimulation (Satué et al., 2014; Lester et al., 2015). It may also appear during the post-acute or recovery phase of viral infections. Persistent monocytosis suggests that the inflammatory process may be becoming chronic (Lester et al., 2015).

Monocytopenia (Decrease in Monocytes)

A decrease in circulating monocyte count is not considered clinically significant. Because the reference interval includes zero, monocytopenia generally carries no diagnostic value (Lester et al., 2015).

3.5.4 Eosinophils and Basophils

Eosinophils are associated with parasitic infections and allergic reactions. In horses, eosinophilia is particularly common in gastrointestinal parasitic infestations and hypersensitivity disorders. Basophil elevation is less frequent but may hold diagnostic value in cases of systemic allergic reactions and immune dysregulation (Moore & Vandenplas, 2014).

3.5.5 Advantages and Limitations

Leukocyte count and differential analysis provide a rapid, economical, and clinically valuable method for the early diagnosis and monitoring of infections in horses. These measurements can be performed within minutes using routine hematology analyzers, making leukocyte assessment a first-line diagnostic tool when infection is suspected (Moore & Vandenplas, 2014). However, because of its low specificity and susceptibility to physiological influences, leukocyte data should be interpreted alongside other biomarkers (Jacobsen & Andersen, 2007; Bonelli et al., 2015). In addition, severe infections may present with neutropenia or even normal leukocyte counts, which reduces the diagnostic sensitivity of total leukocyte measurements alone (Lester et al., 2015). In conclusion, although leukocyte count is a fast, cost-effective, and useful method for detecting inflammation, accurate interpretation requires simultaneous evaluation of the differential cell distribution, clinical findings, and other laboratory parameters.

3.6 C-Reactive Protein (CRP)

C-reactive protein (CRP) is an acute phase protein synthesized in the liver during inflammatory conditions and belongs to the pentraxin family (Biondi et al., 2022). In human medicine, CRP is well-established as a biomarker of infection and inflammation. In humans, CRP can increase up to 1,000-fold within hours during the acute phase of sepsis (Zabrecky et al., 2015; Jacobsen, 2023). In horses, however, CRP is considered a moderate acute phase protein because its concentrations rise more slowly—typically within 3 to 5 days after an inflammatory event—and increase to a lesser extent compared with many other species (Hildebrandt et al., 2025). During inflammation, CRP concentrations in horses increase approximately 3- to 6-fold above baseline values (Biondi et al., 2022). This contrasts with major acute phase responders such as dogs, in which CRP can increase more than 100-fold (Hildebrandt et al., 2025). Because CRP has a short half-life (19 hours) and the timing of sample collection may be insufficient to detect acute changes, it is thought that more frequent measurements may be required to determine its diagnostic or prognostic value in horses (Hildebrandt et al., 2025).

3.6.1 Reasons for Limited Use in Horses

In horses, CRP has been considered an acute phase protein (APP) of limited value because baseline concentrations tend to be relatively high, and increases during inflammatory or infectious conditions are minimal or altogether absent (Jacobsen, 2023). Current literature indicates that the clinical utility of CRP in horses remains limited and inconsistent. Hildebrandt et al. (2025), in a study conducted on foals, reported that CRP concentrations were not significantly affected by respiratory disease (subclinical or clinical bronchopneumonia) at any age. Therefore, in this study, CRP concentrations were not regarded as suitable predictors for subclinical or clinical bronchopneumonia in foals (Hildebrandt et al., 2025). Zabrecky et al. (2015), in a study on critically ill neonatal foals, found that CRP increased in the presence of inflammation; however, it did not specifically indicate the presence of sepsis. Moreover, a single CRP measurement did not prove to be a useful biomarker for predicting survival in critically ill foals. CRP was positively associated with age and

was found to be lower in premature foals or foals born after dystocia (Zabrecky et al., 2015). In healthy horses vaccinated against EHV-1, mean CRP values were elevated above baseline on day 7 post-vaccination (D1); however, no statistically significant differences were detected across different sampling time points (Biondi et al., 2022). CRP has been shown to increase in association with toxic changes in neutrophils, enterocolitis, colic, rib fractures, and septic arthritis in foals (Zabrecky et al., 2015). Measurement of CRP concentrations has not been found useful for aiding in the diagnosis of equine protozoal myeloencephalitis (EPM), as affected horses exhibit low or undetectable CRP concentrations in both serum and cerebrospinal fluid (CSF) samples (Mittelman et al., 2018).

3.7 Neutrophil Gelatinase–Associated Lipocalin (NGAL)

Neutrophil gelatinase–associated lipocalin (NGAL) is a protein identified within activated neutrophil granulocytes (Winther et al., 2023). NGAL is secreted by various cell types, including neutrophil granulocytes, renal tubular epithelial cells, hepatocytes, adipocytes, and tissues exposed to microbial agents (Jacobsen et al., 2022). The protein exists in monomeric, dimeric, or metalloproteinase-9–bound complex forms (Frydendal et al., 2021). Circulating NGAL consists of a dimer released by neutrophils and a monomer secreted by the tubular epithelial cells of the distal nephron (Lo et al., 2022). NGAL is involved in multiple physiological and pathological processes, including apoptosis, fatty acid transport, metabolic homeostasis, and modulation of inflammation (Jacobsen et al., 2022).

3.7.1 Clinical Applications

NGAL is widely used in both human and veterinary medicine primarily as a biomarker of acute kidney injury (AKI) (Winther et al., 2023). It has been demonstrated that NGAL serves as a novel biomarker for renal injury and inflammation in horses (Frydendal et al., 2021). In horses with AKI, serum and urinary NGAL concentrations are significantly higher than in healthy controls (Siwińska et al., 2021). In a study by Lo et al. (2022), serum and urinary NGAL concentrations were found to be significantly elevated in horses with dehydration (mild, moderate, and severe) compared with controls. NGAL remains necessary as a marker for the early detection of renal injury. Urine NGAL and urinary cystatin C concentrations are higher in horses with colic that are at risk of AKI compared with healthy horses, suggesting that these parameters may be suitable for identifying subclinical renal dysfunction (Siwińska et al., 2021; Lo et al., 2022). Because NGAL is expressed not only in renal tubules but also in other organs, concurrent diseases may influence NGAL concentrations. Horses with both renal and inflammatory disease exhibit higher serum NGAL levels than those with renal disease alone (Winther et al., 2023). This may render serum NGAL less sensitive as a stand-alone biomarker for detecting renal pathology (Siwińska et al., 2021). In contrast, urinary NGAL appears to be more specific for predicting AKI when systemic inflammation is present (Lo et al., 2022). Winther et al. (2023) reported significantly higher serum and peritoneal fluid NGAL concentrations in horses with inflammatory abdominal disease and non-strangulating intestinal infarction compared with horses with simple or strangulating intestinal obstruction. Peritoneal fluid NGAL

concentrations were highest in horses with non-strangulating intestinal infarction, suggesting that NGAL may be useful for identifying this condition, which is otherwise difficult to distinguish from other forms of peritonitis. Frydendal et al. (2021) demonstrated that NGAL concentrations increase in synovial fluid (and to a lesser extent in serum) in response to experimentally induced and naturally occurring joint inflammation. These findings suggest that NGAL may serve as a useful biomarker for joint inflammation and infection in horses (Frydendal et al., 2021). Jacobsen et al. (2022) reported that NGAL demonstrates excellent diagnostic accuracy for distinguishing synovial fluid from horses with septic synovitis from that of non-septic cases. NGAL displays a rapid rise-and-fall pattern; synovial fluid (SF) NGAL concentrations peaked 8 hours after experimental LPS injection. This rapid response may make NGAL particularly suitable for the early diagnosis and monitoring of joint inflammation (Frydendal et al., 2021). In accordance with this, SF NGAL concentrations decreased over time in response to treatment (Jacobsen et al., 2022). Hansen et al. (2024) investigated whether NGAL could serve as a potential biomarker in equine asthma (EA). Bronchoalveolar lavage (BAL) fluid NGAL concentrations were significantly higher in horses with EA compared with controls, and BAL NGAL concentrations increased proportionally with disease severity. Furthermore, BAL NGAL concentrations differed significantly between controls and horses with mild–moderate EA (MEA), and between MEA and severe EA (SEA). BAL NGAL concentration was significantly positively correlated with BAL neutrophil counts. No differences in serum NGAL concentrations were identified among EA groups, and serum NGAL showed no correlation with BAL NGAL concentrations or BAL neutrophil counts. Thus, measurement of NGAL concentrations in BAL fluid may serve as a meaningful biomarker for diagnosing EA and assessing disease severity (Hansen et al., 2024). Laurberg et al. (2023) suggested that serum NGAL concentrations may serve as a potential adjunct marker for diagnosing sepsis and predicting outcome in neonatal foals. In their study, serum NGAL concentrations were significantly higher in septic foals compared with non-septic foals, with a reported sensitivity of 71.4% and specificity of 100%. Serum NGAL concentrations were also significantly lower in surviving foals compared with non-survivors. For predicting non-survival, a sensitivity of 39.3% and specificity of 95.2% were determined. Due to its high specificity, serum NGAL may be useful as a *rule-out* biomarker for sepsis or for excluding non-survival in critically ill foals. Serum NGAL showed a statistically significant correlation with Serum Amyloid A (SAA), but not with creatinine. This finding supports the hypothesis that NGAL functions as a marker of inflammation independent of renal disease (Laurberg et al., 2023).

3.7.2 Advantages and Limitations

NGAL has been reported to possess excellent diagnostic accuracy for distinguishing synovial fluid from horses with septic synovitis from that of non-septic cases (Jacobsen et al., 2022). NGAL exhibits a rapid rise-and-fall pattern in response to inflammation. This fast kinetic profile may make NGAL suitable for the early detection and monitoring of inflammatory processes, representing a potential advantage over

traditional biomarkers that respond more slowly (Frydendal et al., 2021). However, due to its rapid kinetics, more frequent sampling may be required to detect acute changes. Because NGAL concentrations can change substantially within a few hours during an inflammatory response, accurate interpretation requires a thorough understanding of its kinetic behavior (Winther et al., 2023). Serum and urinary NGAL concentrations have shown potential for detecting early renal injury in dehydrated horses, outperforming conventional renal biomarkers such as creatinine and BUN (Lo et al., 2022). Nevertheless, NGAL is expressed in multiple tissues—including neutrophils and renal tubular cells—meaning that concurrent diseases may influence NGAL concentrations (Siwińska et al., 2021). NGAL also increases in systemic inflammatory conditions independent of renal injury. For example, dehydrated horses meeting SIRS criteria showed significantly higher serum NGAL concentrations than horses without SIRS. This suggests that serum NGAL may be a less sensitive standalone biomarker for identifying renal disease (Siwińska et al., 2021). The ELISA formats commonly used in NGAL studies are not designed for rapid single-sample analysis and are more suited to research settings requiring batch processing. In situations requiring immediate clinical decision-making—such as equine colic—the usefulness of NGAL would depend on the availability of an assay capable of fast individual-sample processing (Winther et al., 2023). Additionally, the absence of established reference intervals for NGAL in horses remains a limiting factor in its clinical application (Winther et al., 2023).

4. Conclusion

Early and accurate identification of inflammatory processes in horses is crucial for determining appropriate treatment strategies and predicting prognosis. The biomarkers reviewed in this article are complementary, as they reflect different stages and pathophysiological aspects of the inflammatory response. The studies evaluated consistently indicate that no single biomarker provides absolute diagnostic accuracy; however, appropriate combinations can significantly strengthen clinical decision-making.

Serum Amyloid A (SAA) is the major acute phase protein in horses, showing the fastest and most sensitive response to inflammation. Its rapid increase within the first hours after the onset of inflammation, followed by a quick decline as inflammation resolves, makes SAA one of the most valuable biomarkers for the early diagnosis of acute infections. Its rapid kinetics offer a major advantage in clinical conditions such as colic, pneumonia, and synovial infections. However, despite its high sensitivity, its limited etiological specificity restricts its standalone use for differentiating bacterial from viral infections.

Moderate acute phase proteins such as fibrinogen and haptoglobin (Hp) provide valuable information in more slowly developing or chronic forms of inflammation. The fact that fibrinogen increases typically 48–72 hours after the onset of inflammation makes it useful for monitoring subacute and chronic infectious processes. Hp, on the other hand, often remains elevated even after inflammation has resolved, offering a clinical advantage for evaluating residual inflammation. In contrast, C-reactive protein

(CRP) holds limited clinical value in horses due to physiologically high baseline concentrations and a relatively low response to inflammation.

Serum iron, a biochemical parameter exhibiting a negative acute phase response, is notable for its marked decline in systemic inflammatory conditions. Its low cost and ease of measurement make it a practical complementary biomarker; however, its diagnostic specificity is limited by physiological influences such as age, nutrition, and hemolysis. Neutrophil gelatinase–associated lipocalin (NGAL), a more recently investigated biomarker in equine medicine, is considered promising for detecting localized infections because it reflects neutrophil activation.

Hematological indicators—particularly total leukocyte count, neutrophilia, lymphopenia, and the neutrophil-to-lymphocyte ratio (NLR)—are among the fastest and most economical measures of inflammation. However, their diagnostic specificity is limited because they are easily influenced by non-infectious factors such as stress, exercise, and cortisol release. Therefore, interpreting hematologic findings alongside acute phase proteins provides more accurate results both for early diagnosis and for monitoring the clinical course of disease.

Overall, SAA stand out as early-phase biomarkers providing high sensitivity while fibrinogen and Hp serve as valuable complementary indicators for understanding the duration and severity of inflammation. The limited clinical utility of CRP, the low specificity of serum iron despite its affordability, and the still–investigational nature of NGAL indicate that these biomarkers function best as supportive tools. The leukocyte profile, meanwhile, provides the fundamental hematologic framework within which all biomarker results must be interpreted.

In light of these findings, the most accurate diagnostic approach to inflammation in horses is not reliance on a single parameter, but rather the use of integrated biomarker panels that combine acute phase proteins (SAA, Hp, fibrinogen), hematologic indicators (WBC count, NLR), negative APPs (iron), and, when necessary, pro-inflammatory cytokines. Future studies should focus on refining species-specific reference intervals, developing rapid and economical point-of-care assays, and validating the diagnostic performance of biomarker combinations. Such advances will substantially strengthen the management of inflammatory diseases in equine medicine.

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