Interpreting Lactate Measurement in Critically Ill Horses: Diagnosis, Treatment, and Prognosis

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Abstract: In hospitalized horses, hypovolemia and the resulting decrease in tissue perfusion is the most common cause of hyperlactatemia. Therefore, measurement of blood lactate concentration can be a useful tool for guiding fluid therapy. Similarly, measuring blood lactate concentration can be used to assess the need for and adequacy of transfusions in horses receiving whole blood. Inflammatory leukocytes within closed body cavities consume glucose and produce lactate. Simultaneous measurement of blood lactate concentration and lactate concentration of peritoneal, pleural, or synovial fluid has been used to help differentiate septic from nonseptic effusions. A fluid lactate concentration higher than the blood lactate concentration provides evidence for a bacterial cause of the effusion. In horses evaluated for colic, a peritoneal lactate concentration higher than the simultaneously measured blood lactate concentration is indicative of intestinal strangulation and ischemia. Veterinary studies have suggested that serial blood lactate measurements might be a more useful prognostic indicator than a single lactate measurement. In hospitalized adult horses and foals, blood lactate concentration is higher at all time points in nonsurvivors compared with survivors, although the differences tend to be subtle. Measuring the rate at which lactate concentrations return to normal might also prove useful in equine medicine, but this requires further investigation.

For more information, please see the companion article, “Lactate Production and Measurement in Critically Ill Horses” (December 2011).

Blood lactate concentration has long been recognized as a useful indicator of disease severity in humans and has received attention as a prognostic indicator in horses with colic and in critically ill equine neonates. Although numerous studies in human and veterinary medicine have identified associations between hyperlactatemia and both morbidity and mortality, blood lactate concentration at hospital admission is not always strongly correlated with outcome. Furthermore, there is often considerable overlap in blood lactate concentrations among survivors and nonsurvivors. Although disappointing, the inability of a single laboratory value to discriminate between survivors and nonsurvivors should not be surprising when clinicians consider the multitude of factors involved in the pathophysiology of disease in critically ill patients. This article reviews the interpretation of lactate concentration measurements in blood and other body fluids.

Using Lactate Concentration in Diagnosis and Treatment
Lactate as a Resuscitation End Point

The most common and important cause of an increase in blood lactate concentration in hospitalized horses is decreased tissue perfusion and oxygen delivery with subsequent anaerobic metabolism. In adult horses, decreased tissue perfusion is most often due to hypovolemia, but inappropriate vascular tone during severe sepsis may also contribute to hyperlactatemia. In septic equine neonates, hypovolemia, inappropriate vascular tone, and decreased cardiac output have all been implicated as causes of hyperlactatemia. The half-life of lactate is approximately 20 minutes in humans and is probably similar in veterinary species. Consequently, lactate has been suggested to be an ideal resuscitation end point to guide fluid and vasopressor or inotrope therapy. As evidence of this, people with reduction in lactate concentration of >5% in the first hour or 10% in the first 6 hours after initiation of resuscitation had improved survival rates compared with patients in whom lactate concentration did not decrease over the same time period. However, in many human studies, particularly those examining septic patients, in whom causes of hyperlactatemia...
may be numerous, blood lactate concentration lacks precision as an acute resuscitation end point and concentrations may remain increased despite restoration of tissue oxygenation. In contrast, in a large group of adult horses admitted to a university emergency service, mean lactate concentration decreased to within normal range within 12 hours after presentation in most patients, suggesting that blood lactate concentration may be a useful end point for acute resuscitation in such patients. Because blood lactate concentration in healthy neonatal foals is increased for the first 48 to 72 hours of life, defining an appropriate resuscitation “target” value for these animals is more difficult; nevertheless, there should be a consistent decrease in blood lactate concentration in foals that are adequately volume resuscitated.5–7

**Lactate as a Transfusion Trigger**

Some have suggested that an increase in blood lactate concentration could serve as a “trigger” for initiating blood transfusions and that blood lactate concentration should be monitored to determine when adequate oxygen delivery is restored. Lactate concentrations are uncommonly described as transfusion triggers for human patients, in whom hemoglobin concentrations form the basis for most recommendations. In horses, blood lactate concentration appears to be a sensitive indicator of blood loss, although changes may be relatively subtle after mild to moderate hemorrhage. In one study, mean lactate concentrations increased significantly from a baseline of 0.7 ± 0.2 mmol/L to 2.2 ± 1.0 mmol/L after approximately 16 mL/kg of blood (15% to 26% of blood volume) was removed from healthy mares, although there was some overlap in the ranges of blood lactate concentrations measured before and after hemorrhage (0.4 to 1.1 mmol/L versus 0.5 to 6.7 mmol/L). In 17 horses requiring whole blood transfusion, mean lactate concentration was increased (consistent with inadequate oxygen delivery) before transfusion, although the increase in some horses was mild. Mean blood lactate concentrations returned to normal after autologous transfusion or after blood transfusion in horses with hemorrhagic anemia. Thus, blood lactate concentration appears to be useful for assessing the adequacy of transfusion. However, blood lactate concentrations remained increased after transfusions in horses with hemolytic anemia or anemia attributable to erythropoietic failure, suggesting that other mechanisms may be responsible for hyperlactatemia in these patients.

**Lactate in Septic Effusions**

The presence of bacterial (or fungal) infections in a closed body cavity has been associated with an increase in lactate concentration and, usually, a decrease in glucose concentration in effusions from the affected cavity. Lactate concentration within these effusions increases independently of the blood lactate concentration in these cases. The concentrations of lactate and glucose in these effusions may be determined in an attempt to rapidly characterize the nature of the fluid, particularly when other findings are equivocal or delayed. The cause of the increased lactate concentration in the effusion is unclear, but it may be due to tissue anoxia subsequent to impaired blood flow (secondary to tissue swelling) or increased glucose metabolism with subsequent lactate production by inflammatory leukocytes.

**Peritoneal Lactate Concentration**

Human studies have suggested that peritoneal lactate concentrations may be used to establish a diagnosis of septic peritonitis and differentiate it from other conditions that may cause an exudative effusion. Studies in small animals have shown that peritoneal lactate concentrations are increased in dogs with septic peritoneal effusions compared with dogs with nonseptic effusions. However, Nester et al reported that peritoneal fluid lactate concentrations were also increased in dogs with neoplastic effusions compared with dogs with nonneoplastic (and nonseptic) effusions. Calculation of the difference between abdominal fluid and peripheral blood lactate concentrations may improve the ability to discriminate between septic and nonseptic effusions. Although these findings are interesting and consistent with human reports, they should be interpreted with caution, as they have involved a small number of animals and the inclusion criteria (presence of bacteria on cytology and/or positive culture results) of the studies comparing septic and nonseptic effusions may have resulted in misclassification of some patients. Furthermore, in studies examining differences between septic and nonseptic effusions, neoplastic conditions were included in both patient groups and could have limited the ability to differentiate between septic and nonseptic effusions. Despite these shortcomings, increased lactate concentrations (>2.5 mmol/L) in peritoneal fluid should prompt consideration of a septic or neoplastic process. In horses, peritoneal fluid lactate concentration has been more commonly used to identify ischemic bowel lesions (see below) and, to my knowledge, has not been formally evaluated for diagnosing septic peritonitis.

**Pleural Lactate Concentration**

Increased lactate concentrations have been documented in human patients with malignancy and infections of the pleural cavity. In horses with nonseptic pleural effusion, there was no significant difference in mean lactate (and glucose) concentration between venous blood and pleural fluid. In contrast, horses with septic pleural effusions (defined as the presence of bacteria on cytology and/or positive culture results) had a significantly higher lactate (and lower glucose) concentration in their pleural fluid than in their venous blood. Because four horses with pleural effusions secondary to lymphosarcoma were included in the nonseptic group, concentrations of lactate and glucose in pleural fluid may help rule out neoplastic processes in this species. It is important to note that this would be in stark contrast to the situation in human and small animal studies, and additional studies with greater numbers of horses are needed.

**Synovial Lactate Concentration**

Based on the results of studies in human patients in the late 1970s and early 1980s, it was suggested that measurement of synovial fluid lactate concentration could be a useful tool to rapidly differentiate septic from nonseptic arthritis. In those studies,
lactate concentration in the synovial fluid appeared to be a more sensitive diagnostic indicator of sepsis than the results of Gram staining, particularly if antimicrobials had been administered before collection of synovial fluid. In addition, lactate concentration could be determined even when the synovial fluid was too thick for a cell count to be performed. It was often possible for a clinician to obtain the synovial fluid lactate concentration before synovial fluid cell counts and differentials were available. However, more recently, it was concluded that there is insufficient evidence to support the use of lactate measurements for diagnosing septic arthritis in humans. In six horses with septic arthritis induced by intraarticular injection of Staphylococcus aureus, synovial fluid lactate concentrations had increased from a baseline value of 2.02 ± 0.76 mmol/L to >6.9 mmol/L at 24 hours; mean synovial fluid lactate concentrations in control joints (injected with saline) never exceeded 4.0 mmol/L. Between 24 hours and 8 days after bacterial inoculation, synovial fluid lactate concentration in septic joints varied considerably (i.e., 2.3 to 22.9 mmol/L). Thus, synovial fluid lactate concentration may be useful for diagnosing septic arthritis, particularly in the acute phase, but results may be more difficult to interpret in chronic conditions.

**Pericardial Lactate Concentration**

Lactate concentration in pericardial fluid was assessed in 41 dogs in an attempt to identify parameters that distinguish between neoplastic and nonneoplastic effusions. Pericardial fluid lactate concentration was significantly higher than blood lactate concentration in all dogs with pericardial effusion. Most dogs with neoplastic pericardial effusions had masses associated with the heart. Lactate concentrations were significantly greater in pericardial fluid from dogs with neoplasia (n = 28) than in fluid samples from dogs without neoplasia (n = 13); however, the considerable overlap between the two groups precluded clinical usefulness. Because of a low glucose concentration in neoplastic effusions, the difference between glucose concentrations in peripheral blood and pericardial fluid was significantly greater in dogs with neoplasia; however, this difference was not present for lactate concentrations, perhaps because 61% of all dogs with pericardial effusion were hyperlactatemic. To my knowledge, lactate concentrations in pericardial effusions have not been evaluated in horses.

**Cerebrospinal Fluid Lactate Concentration**

Measurement of lactate concentrations in the cerebrospinal fluid (CSF) of human patients allows accurate differentiation of bacterial (septic) and nonseptic (commonly viral) meningitis. Increases in CSF lactate concentration reportedly occur with bacterial infections, but not with nonseptic meningitis. Unfortunately, increases in CSF lactate concentration may also occur with any condition that results in reduced brain oxygenation and/or increased intracranial pressure. Normal CSF lactate concentrations in horses vary slightly depending on the site of collection, with values reported for samples collected from the atlanto-occipital space being slightly lower (0.21 ± 0.01 mmol/L) than those for samples collected from the lumbosacral space (0.26 ± 0.01 mmol/L). Increased lactate concentrations in CSF have been reported for horses with brain abscesses, Eastern equine encephalomyelitis, and head trauma. Increased lactate concentration may be the only CSF abnormality in horses with brain abscesses, although lactate concentration appears to be less useful for distinguishing bacterial from viral brain infections in horses than in other species.

**Lactate as a Diagnostic Indicator of Intestinal Ischemia**

The reliability of several point-of-care monitors has been demonstrated for measuring peritoneal lactate concentration in horses. This has allowed rapid and simultaneous measurement of venous blood and peritoneal fluid lactate concentrations. In healthy horses, the peritoneal fluid lactate concentration is approximately 0.7 mmol/L and is always lower than the plasma lactate concentration; however, peritoneal fluid lactate concentration increases rapidly with intestinal ischemia. In one study, horses with strangulating intestinal obstructions had higher mean peritoneal fluid lactate concentrations (8.45 ± 5.52 mmol/L) than horses with nonstrangulating obstructions (2.09 ± 2.09 mmol/L). Furthermore, because lactate concentrations in peritoneal fluid appear to increase more rapidly than concentrations in plasma, measuring lactate in paired peritoneal fluid and plasma samples may provide more prognostic insight than either measurement alone. In horses with strangulating lesions, peritoneal lactate concentrations are consistently higher than plasma lactate concentrations, although this difference diminishes with onset of systemic shock as plasma lactate concentration increases.

**Using Lactate Concentration for Prognosis**

Numerous studies have demonstrated an association between blood lactate concentration at hospital admission and patient outcome (usually survival or hospital discharge) in both human and veterinary medicine. However, blood lactate concentration at hospital admission does not always correlate well with prognosis, and there is often considerable overlap between values obtained from survivors and nonsurvivors. The relationship between blood lactate concentration at admission and prognosis is almost certainly influenced by the underlying disease condition. Additionally, lactate metabolism is a dynamic process, and the time point at which lactate concentration is measured in the course of disease is likely an important confounder in interpreting this parameter. For example, in human studies, lactate concentration may be measured at admission to an intensive care unit after brief resuscitation in the emergency room and may not, therefore, accurately reflect disease severity. Additionally, blood lactate concentration and acid-base status are not always strongly correlated, which may reflect either the underlying disease process or the patient's ability to compensate for an acid-base disturbance.

More recently, blood lactate has been measured serially to determine the rate at which lactate concentration returns to normal. In human critical care medicine, this approach appears to provide data that more accurately predict outcome or identify the need for more aggressive therapy than a single measurement. Persistent hyperlactatemia despite treatment has been
associated with lower survival rates and a higher incidence of multiple organ failure in human patients. Therefore, serial lactate measurement may be valuable for guiding therapy and indicating prognosis in veterinary medicine.

**Hospital Admission Lactate Concentration in Foals**

The results of three recent studies indicate that hospital admission lactate concentration is significantly higher in nonsurviving equine neonates than in survivors. Although there was considerable overlap in the ranges of lactate concentrations in these three studies, by using an admission lactate concentration of 6.9 mmol/L as a cutoff, Henderson and colleagues determined that the outcome could be predicted in more than 85% of cases. Two of these studies also detected significant differences in admission lactate concentration when the foals were divided into different diagnostic groups; septic or bactereemic foals and foals with hypoxic-ischemic (neonatal) encephalopathy had higher admission lactate concentrations than foals with enteritis/colitis or a localized bacterial infection (e.g., septic arthritis, an infected umbilical remnant). In one of these studies, there was a moderate inverse correlation between lactate (and creatinine) concentration and mean arterial blood pressure, suggesting that the hyperlactatemia was at least partially due to tissue hypoperfusion (although there was no association between lactate concentration and either heart rate or packed cell volume). In that same study, a correlation was also found between lactate concentration and evidence of systemic inflammatory response syndrome. This latter finding and the modest associations between lactate concentration and blood pressure support the contention that an inflammatory reaction is important in the pathogenesis of hyperlactatemia in some sick foals.

**Hospital Admission Lactate Concentration in Adult Horses**

Several studies examining horses with colic have shown a solid association between hospital admission blood lactate concentration and outcome. The authors of a recent study measured lactate concentration in 250 horses that presented for emergency evaluation (including 152 horses with colic) and showed that the odds ratio for a poor outcome (death or euthanasia) increased by 29% for every 1 mmol/L that admission plasma lactate concentration increased. However, as in earlier studies, there was considerable overlap between the admission lactate concentrations of nonsurvivors and survivors. Furthermore, although the prognosis probably worsens considerably once blood lactate concentration exceeds 8 to 10 mmol/L, there is no concentration beyond which death is certain.

**Serial Measurement of Lactate Concentration in Foals**

In equine neonates in which blood lactate concentrations were serially measured, mean concentrations were consistently higher in nonsurvivors than survivors at all time points. In a large retrospective study examining blood lactate concentration in foals, Wotman et al. reported that the odds ratio for survival decreased for every day that lactate concentration remained increased. Despite these results, two of three studies have been unable to detect a significant relationship between the rate at which blood lactate concentration decreases and patient outcome. However, when changes in lactate concentration over time were used to approximate lactate clearance, the rate of decline in blood lactate concentration was lower in nonsurvivors. Although the mechanism for the delay in achieving normolactatemia in these foals is unknown, these findings suggest that serial measurement of lactate concentration in foals may be a useful predictor of outcome.

**Serial Measurement of Lactate Concentration in Adult Horses**

In a retrospective study of adult horses with large colon volvulus, postoperative mean blood lactate concentrations were lower than preoperative values in survivors and nonsurvivors; however, although lactate concentrations returned to normal in survivors, nonsurvivors remained hyperlactatemic. Mean blood lactate concentration was significantly higher in nonsurvivors than survivors preoperatively, and at 24 hours after surgery. Measurement of blood lactate concentrations at 6, 12, 24, 48, and 72 hours after hospital admission also appears to be of value in predicting outcome in adult horses presented for emergency evaluation and treatment. In this report, lactate concentration was significantly higher in nonsurvivors at all time points, and the odds ratio for nonsurvival increased the longer that lactate concentration remained increased. In contrast to results reported for equine neonates, there were temporal changes in the rate of lactate clearance (also estimated from changes in lactate concentration between sampling points). Initially, the change in lactate concentration tended to be positive and higher in nonsurvivors than survivors (i.e., lactate concentration tended to decrease more rapidly in nonsurvivors, suggesting that lactate clearance mechanisms were intact), although this difference did not reach statistical significance. However, between 24 and 48 hours after admission, the change in lactate concentration in nonsurvivors became negative (i.e., lactate concentration increased) and was significantly different from that in survivors.

Additional studies are required to determine whether this decrease in lactate clearance represents impaired metabolism or increased production. Further, although serial measurement of lactate concentration appears to be a promising tool in large animal critical care, optimal sampling times and duration as well as the appropriate patient populations to be monitored need to be defined. Another point to recognize is that changes in lactate concentration in nonsurvivors are relatively subtle. For example, when all cases were considered at 72 hours after admission, mean blood lactate concentration was 0.83 ± 0.21 mmol/L in survivors and 1.59 ± 0.68 mmol/L in nonsurvivors.

**Conclusion**

Blood lactate concentration is a useful indicator of disease severity in veterinary medicine and appears to be a useful guide for fluid resuscitation, particularly in adult horses. Blood lactate concentration may also be used as an indicator for the need for blood transfusion and to determine the adequacy of erythrocyte replacement in horses with blood loss anemia. Only limited information is
available to determine the value of measuring lactate concentrations in effusions in horses; however, an increased lactate (and decreased glucose) concentration should prompt consideration of a septic or neoplastic process. Further, increases in peritoneal lactate concentration (compared with peripheral blood concentration) in horses with colic support a diagnosis of intestinal ischemia and the need for surgery. Increased blood lactate concentrations are associated with mortality, but measurement at a single time point often does not distinguish survivors from nonsurvivors. Lactate concentrations measured serially over the first several days of hospitalization appear to provide better prognostic information in human critical care medicine and may have use in equine patients. Determining lactate clearance rates may also be of value, although more studies are required to determine whether decreases in fractional clearance represent impaired metabolism or increased production of lactate.

References

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1. In adult horses, increases in blood lactate concentration are most often due to:
   a. decreased cardiac output.
   b. volume maldistribution secondary to decreased venous tone.
   c. hypovolemia and decreased tissue perfusion.
   d. severe systemic inflammation.

2. The measurement of blood lactate concentrations has been suggested as a resuscitation end point. Which of the following statements is incorrect regarding the suitability of lactate as a guide for resuscitation?
   a. Similar “target” values can be used in foals and adult horses.
   b. Lactate has a relatively short half-life in vivo.
   c. Increases in blood lactate concentration primarily occur with hypoperfusion in equine patients.
   d. Lactate concentrations may be rapidly and accurately measured using a stall-side or point-of-care monitor.

3. Hemoglobin concentrations form the basis of most recommendations for blood transfusions in human medicine; in horses, blood lactate concentration:
   a. usually increases dramatically even in cases of mild anemia.
   b. appears to be a fairly sensitive indicator of clinically significant blood loss.
   c. typically remains increased after adequate red blood cell replacement in hemorrhagic anemia.
   d. is of no value in determining the need or adequacy of a blood transfusion.

4. The measurement of lactate concentration has been suggested for rapidly characterizing the nature of synovial fluid, particularly when the findings of other tests are equivocal or delayed. Which of the following statements is accurate regarding the measurement of lactate concentration in experimental septic arthritis in horses?
   a. In chronic disease, synovial fluid lactate concentrations are consistently higher in septic joints than control joints.
   b. Lactate concentrations are initially similar in infected and control joints, but lactate concentrations tend to increase in chronically infected joints.
   c. In the acute phase of disease, synovial fluid lactate concentrations are higher in septic joints than control joints.
   d. There is considerable overlap between synovial fluid lactate concentrations in infected and control joints, so measurement has no value.

5. In human medicine, the measurement of CSF lactate concentration has been suggested for differentiating bacterial from viral meningitis. In equine medicine, CSF lactate concentration:
   a. is increased only in horses with brain abscesses.
   b. is not increased in horses with head trauma.
   c. is higher in samples collected from the atlanto-occipital space than in the lumbosacral space.
   d. may be increased in bacterial and viral infections.

6. The measurement of peritoneal lactate concentration has some use in horses with colic. Peritoneal lactate concentration:
   a. is consistently higher than plasma lactate concentration in horses with strangulating intestinal lesions.
   b. must be determined on laboratory-based analyzers; therefore, measurement is impractical for most practitioners.
   c. is highly variable, even in normal horses, so little additional information is gained from measuring this parameter.
   d. remains higher than plasma lactate concentration with the onset of systemic shock.

7. Admission blood lactate concentrations in hospitalized foals are:
   a. strongly correlated with arterial blood pressure, although there is no correlation between heart rate or packed cell volume.
   b. higher in diseases with systemic effects compared with diseases with localized pathology.
   c. not different between survivors and nonsurvivors because neonates normally have higher blood lactate concentrations.
   d. strongly correlated with indicators of SIRS, and hypoperfusion plays only a small role in hyperlactatemia in foals.

8. Regarding serial blood lactate measurement in critically ill foals, mean lactate concentrations are:
   a. initially higher in nonsurviving foals but decrease more rapidly in nonsurvivors.
   b. initially similar in survivors and nonsurvivors but increase in nonsurviving foals.
   c. initially similar in survivors and nonsurvivors but decrease more slowly in nonsurviving foals.
   d. higher at all time points in nonsurviving foals compared with survivors.

9. Regarding serial blood lactate measurement in adult horses assessed on an emergent basis, mean lactate concentrations are higher in nonsurvivors at admission and then:
   a. remain higher than in survivors over the first 72 hours of hospitalization.
   b. decrease to concentrations identical to those in survivors within 12 hours of hospitalization.
   c. tend to remain at the same level throughout hospitalization.
   d. tend to increase throughout hospitalization.

10. In a study that serially measured lactate concentrations in adult horses after hospital admission, blood lactate concentrations increased between 24 and 72 hours in nonsurvivors. What was the mechanism for this increase?
    a. The mechanism was impaired lactate metabolism by the liver due to decreased hepatic perfusion.
    b. The mechanism was increased lactate production due to severe gastrointestinal inflammation.
    c. The mechanism was inconclusive; further studies, including clearance measurements, are required.
    d. The mechanism was decreased venous capacitance vessel tone, causing general tissue hypoperfusion.