Review Article

Diagnostic and prognostic use of L-lactate measurement in equine practice

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Keywords: horse; lactate; prognosis; diagnosis

Summary

Lactate concentrations can now be measured rapidly and inexpensively in equine hospitals or in the field with a degree of accuracy that is acceptable when compared to laboratory analysers. Arterial or venous blood samples can be used. Short-term storage of samples for up to 4 h at room temperature does not appear to affect the result. Taking a sample in the field and returning to the practice to analyse it is therefore feasible.

Lactate measurement is useful in horses with colic to aid in the diagnosis of an ischaemic lesion and to determine the probability of a successful outcome if surgery is undertaken. Lactate concentrations are also useful as an indicator of hypoxia and/or circulatory disturbances associated with *intra-*, or *post partum* abnormalities including dystocia, prematurity, dysmaturity, neonatal encephalopathy, sepsis, systemic inflammatory response syndrome or enteritis. Measuring lactate concentrations may assist in determining the severity of these conditions and the need for intensive care. Initial lactate concentration and increases or decreases in blood lactate concentration following a period of treatment can provide useful prognostic information. Lactate may also be measured during training to monitor fitness and performance.

Introduction

Lactate measurements have been used in the human intensive care setting since the 1960s (Broder and Weil 1964; Schlag 1967; Koch and Wendell 1968). In equine practice, L-lactate was first assessed as a diagnostic and prognostic indicator in colic cases in the 1970s (Donawick *et al*. 1975; Moore *et al*. 1976). The prognostic value of lactate in sick neonates, horses with renal disease, and focal bacterial infections was reported by Gossett *et al*. (1987). The purpose of this article is to review the published data and clinical applications relating to measurement and interpretation of L-lactate concentrations in equine practice.

Lactate production and metabolism

Under normal, anaerobic conditions, pyruvate produced by glycolysis enters the citric acid cycle, resulting in the generation of carbon dioxide, water and ATP. However, during anaerobic conditions, pyruvate is converted to lactate. Lactate production occurs predominantly in skeletal muscle and intestine (Arief and Graf 1987) with smaller quantities being generated in the brain, integument, erythrocytes, leucocytes and platelets (Park and Arief 1980).

Lactate must be converted back to pyruvate once aerobic conditions are restored, or eliminated (**Fig 1**). The majority of lactate metabolism occurs in the liver, with renal excretion being responsible for removal of approximately 30% of the daily lactate load (Leal-Pinto *et al*. 1973). Large quantities of lactate are produced in the physiological situation under anaerobic conditions of intense exercise (Margaria *et al*. 1964). As the intensity of the exercise increases, the requirement for ATP exceeds the aerobic capacity and anaerobic energy production becomes important. Over a 400 m Quarter Horse sprint race, anaerobic metabolism may provide approximately 60% of the energy utilised, whereas over a mile or longer distances in Thoroughbred or Standardbred racing, only 10–30% of energy production is anaerobic (Eaton 1994). Lactate can be used as an oxidisable substrate for cardiac and skeletal muscle and studies of lactate kinetics during exercise have shown enhanced lactate clearance during repeated bouts of maximal or submaximal exercise (Birks *et al*. 1991).

Hyperlactataemia occurs due to decreased oxygen delivery when tissue perfusion is inadequate (*type A*) or increased lactate production in the face of normal tissue perfusion (*type B*) (Cohen and Woods 1976).

Specific causes of *type A* hyperlactataemia include cardiogenic, hypovolaemic or septic shock, hypoxaemia, anaemia, and seizures. *Type B1* hyperlactataemia occurs secondary to neoplasia, alkalaemia, diabetes mellitus, sepsis, hepatic disease, thiamine deficiency, renal failure, iron deficiency and short-bowel syndrome. *Type B2* hyperlactataemia is caused by a variety of drugs or toxins (Cohen and Woods 1976), including epinephrine, norepinephrine, salicylates, bicarbonate, halothane and terbutaline, which may be encountered in equine practice. An increase in circulating adrenaline in various disease states is associated with hyperlactataemia (Clutter *et al*. 1980; McCarter *et al*. 2001). *Type B3* hyperlactataemia is a result of genetic metabolic abnormalities, such as glycogen storage disease (Cohen and Woods 1976).

Although hepatic metabolism plays a major role in lactate clearance, research in human medicine suggests that hepatic failure alone does not cause hyperlactataemia and that a significant reduction in hepatic blood flow would be necessary to reduce lactate clearance (Kruse *et al*. 1987).

Measurement of lactate

Site of sample collection

Arterial lactate concentrations reflect global lactate production and homeostasis. Variation between arterial and jugular venous lactate concentrations is dependent on lactate production and uptake by different organs. Corley (2002a) measured lactate concentrations in dorsal metatarsal

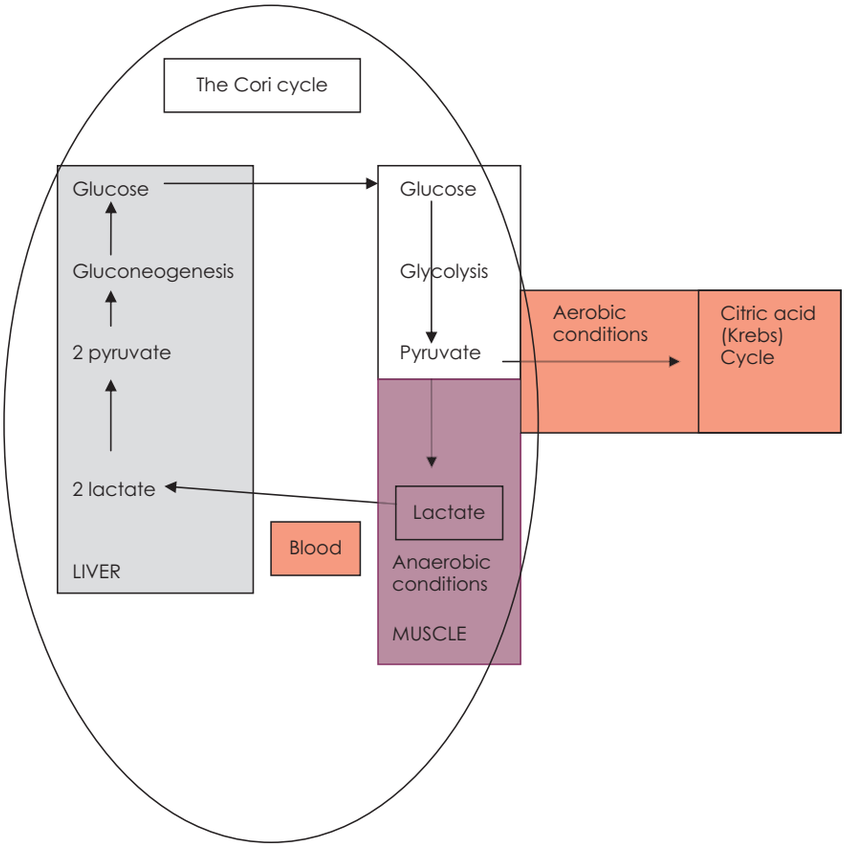

Fig 1: The Cori cycle.

arterial and jugular venous samples in normal foals and found the difference to be very small (mean lactate concentrations of 2.12 ± 0.49 and 2.18 ± 0.35 mmol/l, respectively). In pathological states, greater variation between sampling sites may be expected, particularly in intestinal ischaemia, when venous drainage from the affected organ occurs into the hepatic portal vein. The author is unaware of any published studies in horses discussing variation in lactate concentration according to sampling site in different pathological conditions. Donati *et al*. (2004) identified a significant increase in portal venous blood lactate concentrations in human patients developing complications related to gut hypoxia compared to patients without complications following clamping of the aorta. Wotman *et al*. (2009) reported no significant difference between dorsal metatarsal arterial samples and umbilical vessels, suggesting that umbilical cord samples may be of use in neonatal foals born following a high-risk pregnancy. Amniotic fluid lactate concentrations were found to be higher in mares delivering healthy foals than sick foals (Pirrone *et al*. 2012). A negative correlation between amniotic fluid lactate and blood lactate concentration of foals at delivery and positive correlation between amniotic fluid lactate and Apgar score was identified, suggesting that reduced amniotic fluid lactate concentration may be an indicator of placental impairment.

Sample storage

Storage of whole blood in lithium heparin anticoagulant for 4 h at room temperature or 5ºC did not result in a significant increase in lactate concentrations; however, storage for 24 h at room temperature caused a mean increase in lactate of 2.9 mmol/l (Evans and Golland 1996).

Effect of different anticoagulants

Several studies have found no or minimal effect of the addition of anticoagulants to blood samples (Lindner 1996; Williamson *et al*. 1996; Tennent-Brown *et al*. 2010). Manufacturer instructions for the lactate monitoring device 'Accusport'[1] advise that fluoride should not be present in assayed blood. If there is a delay in testing, however, erythrocytes in heparinised blood samples metabolise glucose, producing lactate which will artificially increase the sample lactate concentration (Luft 2001). Sodium fluoride anticoagulants will inhibit glycolytic enzymes, preventing a significant increase in lactate occurring (Astles *et al*. 1994; Ferrante and Kronfeld 1994). Tennent-Brown *et al*. (2010) found no significant changes over 6 h when blood samples collected into sodium fluoride/potassium oxalate anticoagulant and refrigerated were compared with immediate analysis on a laboratory analyser. The use of a sodium fluoride anticoagulant is therefore recommended if there may be a delay in the analysis of the sample.

Lactate monitors

Point of care or 'stable-side' lactate analysers are practical for use in equine clinics, allowing a result to be obtained rapidly and cheaply. Various studies have evaluated the use of hand-held lactate meters under standard environmental

conditions (Evans and Golland 1996; Lindner 1996; Williamson *et al*. 1996; Saulez *et al*. 2005; Tennent-Brown *et al*. 2007; Sloet van Oldruitenborgh-Oosterbaan *et al*. 2008; Castagnetti *et al*. 2010). These studies support the use of portable 'stable-side' lactate meters as a means of achieving results that are comparable with those obtained on wet chemistry laboratory analysers. When measuring serial lactate concentrations, however, it is important to use the same meter as correlation and repeatability between different hand-held meters has not been determined.

Normal lactate concentrations in horses

A number of studies have reported normal lactate concentrations in mature horses and foals. In neonatal foals, the normal lactate concentration decreases from birth over the first 48 h (see **Table 1**). Measurement techniques vary between different laboratories and normal ranges should be established for individual laboratories and populations.

Clinical use of lactate measurement

Blood lactate concentrations may be measured for diagnostic, prognostic and monitoring purposes or in the context of training and exercise physiology. The remainder of this article will focus on the use of lactate in clinical cases.

Gastrointestinal disorders

One of the earliest uses of lactate in a clinical case setting was as a diagnostic and prognostic aid in colic cases (Donawick *et al*. 1975; Moore *et al*. 1976). The need for intestinal resection was significantly associated with an increase in plasma lactate concentration (Delesalle *et al*. 2007). Blood lactate concentration was identified as a useful parameter in the prediction of survival by Svendsen *et al*. (1979), Orsini *et al*. (1988), Ebert (1994), Furr *et al*. (1995) and Johnston *et al*. (2007). Mean lactate concentrations in survivors were reported as 1.92 mmol/l and 2.0 ± 2.0 mmol/l, compared to 4.26 mmol/l and 6.1 ± 4.8 mmol/l in nonsurvivors (Parry *et al*. 1983; Southwood *et al*. 2010). More recently Radcliffe *et al*. (2012) reported significantly higher plasma lactate concentrations in nonsurviving horses undergoing emergency abdominal surgery at admission and 24 and 72 h post operatively (median lactate concentrations of 7.56 mmol/l, 1.35 mmol/l and 2.30 mmol/l respectively in nonsurvivors compared to 3.00 mmol/l, 0.75 mmol/l and 0.82 mmol/l in survivors). Tennent-Brown *et al*. (2010) measured sequential plasma lactate concentrations in adult equine emergencies, of which the majority (80.4%) were colic cases. In horses with large intestinal strangulating lesions, median lactate concentrations were significantly higher at admission, 48 and 72 h in

TABLE 1: Normal lactate concentrations*

Horse	Sample type	Lactate concentration mmol/l	References	Testing conditions
Normal, mature	Whole blood	<0.7	Williamson *et al*. (1996)	Jugular venous samples in EDTA sodium fluoride were below the limits of detection of the hand-held analysers
Normal foal age 0 min 20–140 min	Whole blood	3.8 ± 1.9 2.38 ± 1.03	Castagnetti *et al*. (2010) Magdesian (2003, research abstract)	Jugular venous samples collected into sodium fluoride/potassium oxalate anticoagulant, frozen at -20°C and analysed on a Chemistry Analyser AU400[4]. Jugular venous samples were collected into fluoride anticoagulants, stored on ice and measured on a commercial analyser.
Normal foal age 12 h	Whole blood	2.8 ± 1.3	Castagnetti *et al*. (2010)	Jugular venous samples collected into sodium fluoride/potassium oxalate anticoagulant, frozen at -20°C and analysed on a Chemistry Analyser AU400[4].
Normal foal age 24 h	Whole blood	1.24 ± 0.33 2.1 ± 0.8	Magdesian (2003, research abstract) Castagnetti *et al*. (2010)	Jugular venous samples were collected into fluoride anticoagulants, stored on ice and measured on a commercial analyser. Jugular venous samples collected into sodium fluoride/potassium oxalate anticoagulant, frozen at -20°C and analysed on a Chemistry Analyser AU400[4].
Normal foal age 48 h	Whole blood	1.08 ± 0.27 1.7 ± 0.6	Magdesian (2003, research abstract) Castagnetti *et al*. (2010)	Jugular venous samples were collected into fluoride anticoagulants, stored on ice and measured on a commercial analyser. Jugular venous samples collected into sodium fluoride/potassium oxalate anticoagulant, frozen at -20°C and analysed on a Chemistry Analyser AU400[4].
Normal foal age 72 h	Whole blood	1.9 ± 0.7	Castagnetti *et al*. (2010)	Jugular venous samples collected into sodium fluoride/potassium oxalate anticoagulant, frozen at -20°C and analysed on a Chemistry Analyser AU400[4].
Normal foal 1–6 months	Whole blood	0.9–1.65	Lumsden *et al*. (1980)	Jugular venous samples in sodium fluoride oxalate samples stored at -70°C

nonsurvivors compared to survivors. In horses with colitis, nonsurvivors had the highest admission lactate concentrations of all the diagnosis groups and significantly higher lactate concentrations than survivors at all time points (median lactate concentrations of 5.35 mmol/l at admission and 2.35 after 72 h in nonsurvivors, compared to 1.75 mmol/l at admission and 0.75 mmol/l at 72 h in survivors). A larger study of 110 horses with colitis by Hashimoto-Hill *et al*. (2011) found no significant difference in lactate concentration between survivors and nonsurvivors at admission, however, 4–8 h lactate concentration, 24 h lactate concentration and the percentage reduction in lactate concentration (≥30% at 4–8 h and ≥50% at 24 h) were significantly associated with survival. These results suggest that measurement of lactate concentrations may be particularly helpful in assessing progress and prognosis when treating horses with colitis.

Peritoneal fluid lactate

Lactate has been measured in peritoneal fluid samples in cases of colic, both as a diagnostic and prognostic indicator. Latson *et al*. (2005) reported normal peritoneal fluid lactate concentrations of 0.60 ± 0.19 mmol/l for samples collected into lithium heparin anticoagulant and analysed on a laboratory analyser (ABL 700 series)[2].

Saulez *et al*. (2005) assessed the accuracy of the iSTAT[3] hand-held device for measuring peritoneal fluid lactate. These authors found that the iSTAT slightly underestimated peritoneal fluid lactate concentrations when compared to a laboratory analyser, but concluded that readings obtained by both the hand-held and laboratory method would be interpreted similarly in the clinical context. Delesalle *et al*. (2007) determined that the Accusport analyser is reliable for measuring peritoneal fluid lactate concentrations up to 20 mmol/l.

Peritoneal fluid lactate concentrations may be elevated in relation to peripheral blood lactate concentrations in cases with strangulating lesions, peritonitis, anterior enteritis and colitis. In contrast, in healthy horses, peritoneal fluid lactate concentrations are lower than those in peripheral blood (Moore *et al*. 1977). Parry *et al*. (1983) demonstrated a significant association between peritoneal fluid lactate and survival in equine colic cases. Hjortkjaer and Svendsen (1979) reported increased peritoneal fluid lactate concentrations in experimentally induced small-intestinal volvulus. Latson *et al*. (2005) found that a peritoneal fluid to peripheral blood lactate ratio exceeding one was associated with a high probability of a strangulating obstruction. Delesalle *et al*. (2007) found that each 1 mmol/l increase in either peritoneal fluid or peripheral blood lactate was associated with a 1.23 (blood) and 1.58 (peritoneal fluid) increase in the odds ratio (OR) for requiring abdominal surgery. An increase in the availability of surgical facilities and recognition of the importance of early referral in achieving a successful outcome has led to more horses being admitted for monitoring at referral centres early in the course of disease, when the requirement for surgical treatment may not be immediately obvious. Peloso and Cohen (2012) monitored serial peritoneal fluid samples and found that an increase in peritoneal fluid lactate to >4 mmol/l within 1–6 h after admission was significantly associated with the presence of a strangulating lesion (OR 62, 95% sensitivity, 77% specificity). The sensitivity and specificity of a peritoneal fluid lactate concentration of >4 mmol/l at admission for prediction of a strangulating lesion was 27% and 91% respectively, OR 3.8, 95% confidence interval 1.1–9.0, P = 0.027). Some owners may not wish to go ahead with surgical treatment if there is likely to be a considerable amount of aftercare, which can significantly increase the total cost. In these situations, identifying the presence of a strangulating lesion that is likely to require resection and may increase the likelihood of complications such as post operative ileus, rather than a simple obstruction or displacement, can help owners to make the appropriate decision. In cases where surgical treatment is not a financially viable option, a single, high blood and peritoneal fluid lactate result on arrival, in conjunction with clinical and ultrasonographic findings may assist in determining that the horse is highly likely to have a surgical lesion. In cases that are less clear cut on arrival and are admitted for monitoring, sequential measurements showing an increasing peritoneal fluid and/or blood lactate concentration may be very helpful in making the decision that medical management is insufficient and that the horse requires euthanasia.

Blood loss

Magdesian *et al*. (2006) showed a significant increase in the mean blood lactate concentration from 0.7 mmol/l to 2.2 mmol/l (P<0.05) following experimental removal of 16 ml/kg of blood and an associated decrease in central venous pressure. The lactate concentration decreased immediately after replenishment of the circulating blood volume. Castagnetti *et al*. (2010) reported a lactate concentration of 36.6 mmol/l in a foal with haemorrhagic shock, which responded to treatment and survived.

Pleural fluid

Brumbaugh and Benson (1990) compared pleural fluid lactate concentration in horses with nonseptic pleural disease and pleuropneumonia. There was no difference between venous blood lactate and pleural fluid lactate in nonseptic pleural disease, however, cases of pleuropneumonia had higher pleural fluid lactate concentrations (mean 11.63 mol/l) when compared to cases of nonseptic pleural disease (mean 3.24 mmol/l).

Synovial fluid

A study of experimentally induced septic arthritis in horses by Tulamo *et al*. (1989) found that synovial fluid lactate concentrations were significantly increased in septic joints by 24 h after inoculation (6.9–11.9 mmol/l compared to 0.42–3.9 mmol/l initially). Considerable variation (2.3–22.9 mmol/l) occurred in septic joints from 24 h onwards, suggesting that lactate concentrations are less reliable in the diagnosis of chronic septic arthritis. A significant increase in synovial fluid white blood cell count occurred by 8 h in all horses, indicating that cellular changes allow an earlier diagnosis and are therefore more useful than an increase in synovial fluid lactate concentration.

Critical care of mature horses

Tennent-Brown *et al*. (2010) recently evaluated the prognostic value of sequential lactate measurements in mature horses admitted to an emergency referral centre in a prospective study. The majority of cases were presented due to colic (see above) with the remaining admissions being due to disorders of the reproductive tract, guttural pouch mycosis, end-stage liver disease, septic peritonitis, severe puncture wounds and

acute exacerbations of recurrent airway obstruction. The study identified significant differences in lactate concentrations in nonsurvivors compared to survivors at all time-points (admission, 6, 12, 24, 48 and 72 h). For every 1 mmol/l increase in admission lactate concentration, the odds of nonsurvival increased by 29%. Persistence of the hyperlactataemia to 72 h after admission was associated with a further increase in the odds of nonsurvival to 49.90 (95% confidence interval 6.47–384.82) for every 1 mmol/l increase in lactate concentration The decrease in lactate concentration over time was initially larger in nonsurviving adult patients, in contrast to findings in nonsurviving neonates (Wotman *et al*. 2009, retrospective study). A larger decrease in lactate initially suggests that, in the earlier stages of disease, lactate metabolism mechanisms are unaffected and a decrease in lactate concentrations is seen in response to therapeutic interventions to improve tissue perfusion and oxygenation, even in horses which did not go on to survive. Between 24 and 72 h, and 48 and 72 h, however, lactate concentrations were increased in nonsurvivors. Sequential lactate measurements may be very helpful in this situation in deciding whether to continue treatment, as the daily costs of intensive care, particularly in an adult horse, can be very high.

Neonatal intensive care

Use of lactate measurement for prediction of prognosis and survival

Several studies have identified a significant association between lactate concentrations and survival in neonatal foals. Corley *et al*. (2005) investigated the association of blood lactate concentration with survival to hospital discharge, cardiovascular parameters, metabolic acid base status, sepsis and systemic inflammatory response syndrome (SIRS). The mean admission lactate concentration was significantly higher in nonsurvivors than survivors at admission and at 18–36 h (4.37 ± 0.55 mmol/l in survivors and 9.31 ± 0.86 in nonsurvivors at admission and 3.23 ± 0.53 mmol/l in survivors and 9.12 ± 0.71 in nonsurvivors at 18–36 h, P<0.001). Similar findings were reported by Henderson *et al*. (2008) (median admission and 18–36 h lactate concentrations respectively of 3.50 mmol/l and 1.9 mmol/l in survivors and 11.30 mmol/l and 6.24 mmol/l in nonsurvivors) and Wotman *et al*. (2009), with foals surviving to discharge having a median admission and 24 h lactate concentrations respectively of 3.4 mmol/l and 1.9 mmol/l, compared to 8.4 mmol/l and 3.9 mmol/l in nonsurvivors (P<0.001). A recent, larger study including 588 foals, by Borchers *et al*. (2012) reported mean admission lactate concentrations of 4.6 ± 3.7 mmol/l in survivors and 7.4 ± 5.6 mmol/l in nonsurvivors. Henderson *et al*. (2008) found that an admission cut-off point of 6.9 mmol/l had a sensitivity of 60%, specificity of 93%, positive predictive value of 71.4% and negative predictive value of 88.9% and allowed correct classification of 85.6% of case outcomes. After 24 h of treatment, a cut-off lactate concentration of 3.2 mmol/l had a sensitivity of 76.9%, specificity of 97.2%, positive predictive value of 71.4% and negative predictive value of 88.9% and allowed for correct classification of 94.1% of cases. Wotman *et al*. (2009) identified a similar cut-off point of 5.5 mmol/l at admission for foals surviving to discharge (sensitivity 77%, specificity 72%).

This information could be useful in helping owners decide whether to pursue treatment, particularly as the cost of intensive care can be high, with a significant proportion occurring within the first few hours, e.g. due to the costs of over-the-wire catheter placement, haematological and biochemical data collection, plasma transfusions and oxygen supplementation.

Change in lactate over time

If the decision is made to embark on intensive treatment, it is useful to be able to monitor the foal's response to therapy as objectively as possible, both for welfare reasons and due to the ongoing financial commitment on the part of the client. In the studies by Corley *et al*. (2005), and Henderson *et al*. (2008), the change in lactate concentration between the 2 time points was not significantly associated with survival. In contrast, Wotman *et al*. (2009) identified a significant association (P = 0.043) between the change in lactate from admission to 48 h and survival to discharge. This study suggests that foals with impaired lactate metabolism, and/or a continued increase in lactate production have a poorer prognosis compared to foals with a rapid decrease in lactate concentration. Castagnetti *et al*. (2010) defined the time to reach a normal lactate concentration as 'lactime'. Classifying foals according to a lactime of 24, 48 or >72 h gave a useful indication of prognosis for survival. All foals in the 24 and 48 h lactime subgroups survived whereas the mortality rate was 100% in the foals that failed to reach a normal lactate concentration by 72 h.

Lactate concentrations in foals with different diagnoses

A number of retrospective studies have reported lactate concentrations in neonatal foals with different diagnoses (Corley *et al*. 2005; Henderson *et al*. 2008; Castagnetti *et al*. 2010; Borchers *et al*. 2012). Admission lactate concentrations were found to differ between the different diagnostic categories. It was therefore suggested that the accuracy of the use of lactate concentrations for prognostic purposes may be improved by considering the different, common neonatal presentations separately.

Sepsis and SIRS

In the study by Corley *et al*. (2005), foals aged <7 days with a positive blood culture were found to have a higher mean admission lactate concentration than those with a negative blood culture. The difference between these 2 groups became more marked at the second time point. Contrasting results were obtained in recent studies by Henderson *et al*. (2008) (foals up to 96 h), which identified a significantly lower mean admission lactate concentrations in foals with a positive blood culture; however, both studies involved a small number of foals (26 and 13 respectively) with positive blood culture results. It is possible that differences in the study populations, such as time to referral, may contribute to these contrasting findings. Wotman *et al*. (2009) found no significant difference in lactate concentrations between positive and negative blood culture groups in foals aged 1–30 days. These results are in agreement with those of a much larger study by Borchers *et al*. (2012), where no significant difference in lactate concentrations was found between 346 foals with negative blood cultures and 120 foals with positive blood cultures. Although this study was performed on sick neonates aged 0–35 days, one explanation for the lack of correlation between blood culture and lactate concentration may be attributed to

the findings of Hackett *et al*. (2010), who reported positive blood culture results on one or more occasion in normal foals sampled within the first 12 h, and Hollis *et al*. (2008) who found no correlation between blood culture status and survival in neonatal foals presenting with diarrhoea, suggesting that bacteraemia may not always be associated with disease severity.

Corley *et al*. (2005) found that foals with SIRS had higher admission and 18–36 h lactate concentrations than those without SIRS. Foals classified as being in septic shock at admission had the highest median lactate concentrations (11.34 mmol/l). Median lactate concentrations for foals with bacteraemia were 7.65 mmol/l, and for local bacterial infections, 2.0 mmol/l. Castagnetti *et al*. (2010) also found higher lactate concentrations in foals with SIRS than those without. Both these retrospective studies included foals aged ≤7 days, but the definition of SIRS differed slightly. The sampling site was also different, with arterial blood samples used for lactate measurement by Corley *et al*. (2005) and venous samples collected by Castagnetti *et al*. (2010), making a direct comparison difficult.

Neonatal encephalopathy, prematurity and other diagnoses

Henderson *et al*. (2008) found that in premature or dysmature foals (analysed collectively) and foals with neonatal encephalopathy (NE), the OR for nonsurvival increased by 55% and 52% respectively for each 1 mmol/l increase in admission lactate concentration. In contrast, in foals with enteritis the OR for nonsurvival increased by 115% per mmol/l increase in admission lactate concentration. In foals with other diagnoses including colic, neonatal isoerythrolysis and uroperitoneum, the OR for nonsurvival increased by 247% per mmol/l increase in admission lactate concentration. These results were supported by a larger study by Borchers *et al*. (2012) in which foals with a major diagnosis of sepsis, enterocolitis, colic, trauma, immune related (other than failure of passive transfer) or respiratory disease had a significant increase in the odds of nonsurvival per mmol/l increase in admission lactate, whereas foals with a major diagnosis of prematurity and perinatal asphyxia syndrome did not. This suggests that premature or dysmature foals and foals with NE may respond more favourably to treatment in spite of higher admission lactate concentrations. However, in the study by Henderson *et al*. (2008) at 24 h, it was notable that foals with NE had a greater increase in the odds of nonsurvival of 245% per mmol/l increase in lactate concentration, whereas in foals with enteritis, the increase in the odds of nonsurvival was only 24% for a 1 mmol/l increase in lactate concentration. In the clinical situation, this would suggest that some foals with NE have high admission lactate concentrations and show a rapid response to therapy over a 12–36 h period, but a persistently high lactate concentration at this stage is a poor prognostic indicator. In a foal with enteritis, a slightly higher lactate concentration after 12–36 h of treatment may be of less concern.

Interpreting lactate concentrations in relation to the age of the foal

Corley *et al*. (2005) reported that mean admission lactate concentration decreased with age in foals referred for intensive care, from 7 mmol/l for foals aged 0–12 h at the time of hospital admission, to 4.69 mmol/l in foals aged >36 h at the time of admission. Henderson *et al*. (2008) also found a significant negative association between age at admission and lactate concentration in clinical cases, although this may be due to more severe cardiovascular disturbances present in conditions such as prematurity and NE, for which younger foals tend to be referred. As discussed above, the normal range for lactate concentration in foals decreases during the first few hours after birth, suggesting that the age of the foal should be taken into consideration when interpreting lactate concentration and a slightly higher lactate concentration of approximately 3–4 mmol/l may be normal within the first few hours of life.

Using lactate as a predictor of other clinicopathological data and cardiovascular disturbances

Studies examining blood lactate concentrations are frequently performed in referral centres where it is possible to carry out detailed monitoring of cardiovascular and respiratory parameters such as arterial blood pressure and arterial blood gas measurement. For the practitioner in the field, however, the hand-held lactate meter may be the only practical and affordable option for initial assessment and on-going monitoring in cases where referral is not an option. Castagnetti *et al*. (2010) found significant negative correlations between admission lactate concentrations and bicarbonate concentration, pH and base excess. Arterial blood pressure values of 95 ± 13 mmHg (Franco *et al*. 1986) and 80.5 ± 12.4 mmHg (Hollis *et al*. 2006) are reported in healthy, conscious, neonatal foals. Borchers *et al*. (2012) found a small, but significant correlation between mean arterial blood pressure and admission lactate concentration. Castagnetti *et al*. (2010) found that in 14/16 foals, a mean arterial blood pressure of ≤60 mmHg was associated with a lactate concentration of ≥6 mmol/l, suggesting inadequate tissue perfusion. Corley *et al*. (2005) found that all foals with a mean arterial lactate concentration of ≤60 mmHg had a high lactate concentration of >7 mmol/l. In contrast, Wotman *et al*. (2009) were unable to demonstrate a similar correlation between mean arterial blood pressure and lactate concentration. All 3 centres employed indirect blood pressure monitoring techniques using a tail cuff placed over the coccygeal artery and therefore it is unlikely that the method of blood pressure measurement contributed to the different results. Further analysis of the data collected by Wotman *et al*. (2009) to investigate the effect of possible population differences between studies was carried out after removal of 24 foals with lactate concentrations <5.5 mmol/l (the cut-off point for predicting survival) and mean arterial blood pressure <60 mmHg. This allowed a significant, if small, association between mean, systolic and diastolic blood pressure and lactate concentration to be recognised. It is possible that factors, such as time to referral, may have contributed to the differences between the 2 studies. An earlier paper by Corley (2002b) suggests that arterial blood pressure in neonatal foals should be maintained over 60 mmHg to ensure adequate perfusion of vital organs; however, this figure is based on work carried out in other species. It is interesting that Wotman *et al*. (2009) found that the foals with a lactate concentration of <5.5 mmol/l and blood pressure of <60 mmHg had a 92% survival rate. These authors suggest that some foals with an arterial blood pressure of <60 mmHg that appear to be clinically well-perfused and have a lactate concentration of <5.5 mmol/l may not need intervention to raise the arterial

blood pressure. Further studies to ascertain the acceptable minimum mean arterial blood pressure for equine neonates with various conditions are required.

Corley *et al*. (2005) found that admission lactate concentration was also significantly associated with other parameters including creatinine concentration, presence of bacteraemia, anion gap, the presence of SIRS and the lactate concentration at 18–36 h post admission. Interestingly, Castagnetti *et al*. (2010) found no correlation between arterial partial pressures of oxygen and carbon dioxide and lactate concentrations, suggesting that lactate concentrations are not markedly affected by respiratory insufficiency in neonatal foals.

In summary, lactate concentration can be readily and cheaply measured in the neonatal intensive care unit or when assessing foals in the field, when other biochemistry tests or monitoring systems are not available. Lactate concentrations >5.5 mmol/l generally give greater cause for concern. The age of the foal and differential diagnosis should be taken into consideration when interpreting the initial lactate measurement. A higher lactate concentration in a foal aged <2 h, a premature or dysmature foal or foal with suspected neonatal encephalopathy may be viewed more favourably than a high lactate concentration in older foals or foals suffering from other conditions. Failure to restore lactate concentration to values approaching normal (less than approximately 3 mmol/l) within 48 h is associated with a more guarded prognosis. A persistently increasing lactate concentration in a foal in spite of intensive treatment is usually very a poor prognostic sign.

The current literature supports the use of point of care 'stable-side' lactate meters for measurement of blood lactate concentrations in horses and demonstrates the potential usefulness of lactate measurement for diagnostic, prognostic and monitoring purposes.

A high blood and peritoneal fluid lactate concentration at admission in a colic case suggests a surgical lesion is likely, while sequential measurements may be helpful in monitoring the response to treatment in horses with colitis. Future, prospective studies to validate cut-off points for predicting survival and nonsurvival identified in retrospective studies and further evaluation of serial measurements in patients with different diagnoses and of varying age may help to improve the monitoring, management and prognostication in intensive care patients.

Author's declaration of interests

No conflicts of interest have been declared.

Manufacturers' addresses

[1]Boehringer Mannheim Australia Ltd, Sydney, Australia.

[2]Radiometer Copenhagen, Bronshoj, Denmark.

[3]Heska, Loveland, Colorado, USA.

[4]Olympus Diagnostica GmbH, Center Valley, Pennsylvania, USA.

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Continued from page 485

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