Lactate Clearance in the Acutely Traumatized Patient

HEN oxygen deliverv falls below a critical threshold, the anaerobic threshold, the amount of oxygen available for consumption is not able to meet the needs of cells. These imbalances result in cellular hypoxia, resulting in the failure of mitochondrial oxidative phosphorylation, and as a result energy metabolism becomes wholly dependent anaerobic glycolysis.1 on Anaerobic glycolysis sharply increases the production of cellular lactate, which diffuses into the blood during prolonged cell ischemia. Elevated circulating lactate concentration thus often indicates widespread inadequate tissue oxygenation due to inadequate oxygen delivery and/ or consumption.² In this issue of ANESTHESIOLOGY, Regnier et al.3 present a prospective cohort analysis of the utility



"Thus, lactate clearance ... provides more meaningful data about the overall adequacy of the resuscitative processes."

of lactate and lactate clearance measurements in the setting of the acutely traumatized patients.

Numerous previous studies have documented the utility of lactate as a prognostic indicator in shock states.^{2,4} The use of lactate measurements is gaining recognition in critical care settings as a potential indicator of tissue hypoperfusion.^{5,6} Furthermore, lactate screening as a method of risk stratification and prognosis has been shown to be beneficial in hemodynamically stable patients with suspected infection.^{5,7} Underscoring the importance of these data is the fact that point-of-care testing performed at the patient's bedside is becoming more common.8,9

There are many evidence based, data-driven, and logical arguments why lactate clearance monitoring is a superior therapeutic target than oxygen-derived variables. First, the published experimental (randomized trial) evidence

Photo: J. P. Rathmell.

supporting the use of lactate clearance as a therapeutic target is more robust in terms of the number of multicenter studies.^{10,11} Unlike oxygen-derived variables, the ability to clear lactate has consistently predicted better survival in published studies of resuscitation.12-15 Second, elevated lactate levels reflect the total picture of energy metabolism in the acutely stressed patient. Elevated blood lactate level has long been known to reflect anaerobic metabolism from tissue hypoxia in critically ill patients.2 However, besides these anaerobic processes, aerobic (metabolic) mechanisms that affect the host's efficiency of energy transfer also contribute to lactate production. Cytokine-mediated glucose uptake and catecholamine-stimulated Na-K pump overactivity both can

result in increased pyruvate production that eventually will overwhelm the catalytic capacity of pyruvate dehydrogenase and result in increased lactate due either to mass effect, sepsis-induced pyruvate dehydrogenase dysfunction, or both. In addition, reduced lactate clearance may reflect globally impaired metabolic function by the liver and kidney, both of which normally contribute to systemic lactate disposal through anaplerosis, a mechanism that carboxylates lactate and delivers it to the tricarboxylic acid cycle, independent of the action of pyruvate dehydrogenase.¹⁶ Thus, lactate clearance biologically reflects more of the general homeostasis of the host and provides more meaningful data about the overall adequacy of the resuscitative

Lactate clearance has previously been shown to be of value in monitoring several critically ill populations including those with sepsis^{10,12} and cardiac arrest.¹⁷ With the present publication by Regnier et al. we now have

processes.

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This Editorial View accompanies the following article: Régnier MA, Raux M, Le Manach Y, Asencio Y, Gaillard J, Devilliers C, Langeron O, Riou B: Prognostic significance of blood lactate and lactate clearance in trauma patients. ANESTHESIOLOGY 2012; 117:1276-88.

important evidence of the utility of lactate clearance in the acutely traumatized population.³ There are several important conclusions that can be drawn from this interesting report. First, the early clearance of lactate provides additional important prognostic information beyond what is available from just single lactate measurements or severity-of-illness scores, particularly in the setting of patients who died early deaths. This additional information can assist the clinician in understanding the adequacy of the resuscitative process that has been undertaken, the severity of the potentially ongoing insult, and the physiological responses to the insult-resuscitation interaction. Second, the data clearly support the paradigm of evaluating lactate clearance early in the clinical course, underscoring the rapidity with which the body identifies and reacts to lactate production. In fact, the reported data confirm that much of the clearance will take place in the first 2 h and that there seems to be a plateau of the clearance effect at later time points (2-4 h). This is likely due to the decrease in production with resuscitation and increase in clearance resulting in flattening of the relationship as depicted in Figure 2 of the report. Third, there seems to be an important threshold for achieving a lactate clearance of 20% per hour. This level is associated with a sharp drop in mortality, particularly among subjects with initial lactate levels between 2 and 10 mM/l. Identification of this threshold is important inasmuch as it provides a numeric target for clinicians to consider as an important target to achieve. In addition, this target is similar to those reported as important thresholds in other disease states.^{10,11} Fourth and finally, an important finding by Regnier et al. is that among normotensive subjects, neither initial lactate or lactate clearance contributed additional prognostic value beyond what was available in standard scoring systems. This suggests that lactate may have limited value in detecting occult hypoperfusion in the acutely traumatized patient. This finding is an important distinction to the established utility of lactate for identifying occult hypoperfusion in sepsis.^{5,6,18}

As with any report, the report by Regnier *et al.* has some important limitations that should be considered. First, this is an observational study and can only provide associative interactions rather than cause and effect interactions. Thus, the present observations are not adequate to change practice; however, they are important observations that could be carried forward in therapeutic experimental trials. And second, this study took place in France, which has a different organized prehospital medical care system as compared with many other regions of the world. This effect could not be controlled and thus it is not clear if this had a confounding effect on the reported results.

In conclusion, the report by Regnier *et al.* provides important new information suggesting that early lactate clearance in the setting of acute traumatic injury, particularly

clearance rates of 20% per hour, provides important additional prognostic information beyond what is presently available from single lactate measurements and scoring systems. These observations support the continually emerging evidence that clearing lactate is always good, probably never bad and should be strongly considered as important information in the armamentarium of caring for the critically ill and injured.

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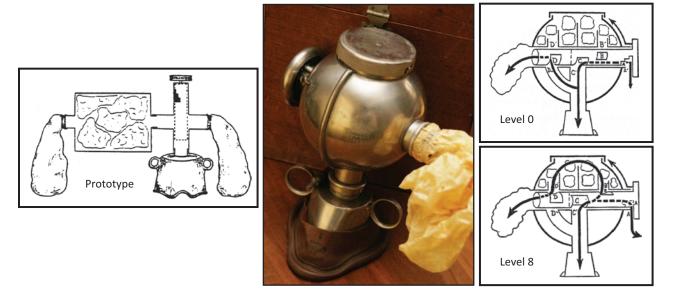
References

- 1. Watts JA, Kline JA: Bench to bedside: The role of mitochondrial medicine in the pathogenesis and treatment of cellular injury. Acad Emerg Med 2003; 10:985–97
- Weil MH, Afifi AA: Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation 1970; 41:989–1001
- Régnier MA, Raux M, Le Manach Y, Asencio Y, Gaillard J, Devilliers C, Langeron O, Riou B: Prognostic significance of blood lactate and lactate clearance in trauma patients. ANESTHESIOLOGY 2012; 117:1276–88
- 4. Huckabee WE: Abnormal resting blood lactate. I. The significance of hyperlactatemia in hospitalized patients. Am J Med 1961; 30:840–8
- Puskarich MA, Trzeciak S, Shapiro NI, Heffner AC, Kline JA, Jones AE; Emergency Medicine Shock Research Network (EMSHOCKNET): Outcomes of patients undergoing early sepsis resuscitation for cryptic shock compared with overt shock. Resuscitation 2011; 82:1289–93
- Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, Bellamy SL, Christie JD: Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med 2009; 37:1670–7
- Shapiro NI, Howell MD, Talmor D, Nathanson LA, Lisbon A, Wolfe RE, Weiss JW: Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 2005; 45:524–8
- Jones AE, Kline JA: Use of goal-directed therapy for severe sepsis and septic shock in academic emergency departments. Crit Care Med 2005; 33:1888–9; author reply 1889–90
- Sivayoham N: Management of severe sepsis and septic shock in the emergency department: A survey of current practice in emergency departments in England. Emerg Med J 2007; 24:422
- Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA; Emergency Medicine Shock Research Network (EMShockNet) Investigators: Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: A randomized clinical trial. JAMA 2010; 303:739–46
- 11. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, Willemsen SP, Bakker J; LACTATE study group: Early lactate-guided therapy in intensive care unit patients: A multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010; 182:752–61
- 12. Arnold RC, Shapiro NI, Jones AE, Schorr C, Pope J, Casner E, Parrillo JE, Dellinger RP, Trzeciak S; Emergency Medicine Shock Research Network (EMShockNet) Investigators: Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. Shock 2009; 32:35–9

- 13. Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, Tomlanovich MC: Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004; 32:1637–42
- Bakker J, Coffernils M, Leon M, Gris P, Vincent JL: Blood lactate levels are superior to oxygen-derived variables in predicting outcome in human septic shock. Chest 1991; 99:956–62
- Bakker J, Gris P, Coffernils M, Kahn RJ, Vincent JL: Serial blood lactate levels can predict the development of multiple organ failure following septic shock. Am J Surg 1996; 171:221–6
- Russell RR 3rd, Taegtmeyer H: Changes in citric acid cycle flux and anaplerosis antedate the functional decline in isolated rat hearts utilizing acetoacetate. J Clin Invest 1991; 87:384–90
- 17. Donnino MW, Miller J, Goyal N, Loomba M, Sankey SS, Dolcourt B, Sherwin R, Otero R, Wira C: Effective lactate clearance is associated with improved outcome in post-cardiac arrest patients. Resuscitation 2007; 75:229–34
- Howell MD, Donnino M, Clardy P, Talmor D, Shapiro NI: Occult hypoperfusion and mortality in patients with suspected infection. Intensive Care Med 2007; 33:1892–9

ANESTHESIOLOGY REFLECTIONS FROM THE PIERRE VIARS MUSEUM

Ombrédanne Inhaler 1908–1982(?)



In 1907, after a number of anesthetic fatalities, Pr. Auguste Nélaton gave his pupil Louis Ombrédanne the task of creating a safe anesthetic device. The prototype (*left*), made by Ombrédanne and his driver, consisted of a metal English sweet tin that acted as a reservoir and was fitted with felt to absorb ether, a graduated air inlet, and a respiratory reserve chamber. Modifications of the design followed quickly. The elliptical reservoir became spherical (*center*), the mask and the reservoir were separated, but the design hardly changed over many years of use apart from the addition of oxygen and carbon dioxide (Level 0: air only, no ether [*top right*]; Level 8: no air, ether full and rebreathing [*bottom right*]). It was sold by the Collins Company (more than 80,000) around the world. Thanks to Ombrédanne, inhalation anesthesia made great strides toward safety and allowed proper control. The simplicity of the device allowed its use by a large number of nonspecialists. This delayed the development of anesthesia as a medical specialty in France until the late 1940s. (Reproduced from Cazalaà JB, Cousin MT, Baker D. Apparatus for anesthesia and intensive Care. Paris, France, Glyphe, 2005, with authorization.)

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