at pragmatically arranged visits instead of standardized weekly follow-ups. We thus cannot rule out that unintended selection bias occurred. A larger confirmatory study is needed, now that the potential for the *Mp*-IgM-ASC ELISpot assay has been shown. Improving the early diagnosis of *Mp* infection in patients with CAP by the *Mp*-IgM-ASC ELISpot assay may help future interventional studies assessing the effect of antimicrobial treatment in the management of *Mp* CAP (5, 6). ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Acknowledgment: The authors thank the children and their parents who contributed to this study. They also recognize the emergency department staff, the outpatient clinic staff, and the short-stay department staff for recruiting participants; the microbiology laboratory staff for processing samples; and the primary care physicians and pediatricians (Brigitta Bircher, Angelika Broidl, Jörg Ersch, Helen Hauser, Regula Neidhardt, Bruno Piva, and Jacqueline Schneiter) for participating in out-of-hospital follow-up visits. They are grateful to Michael Buettcher (Division of Pediatric Infectious Diseases, Children's Hospital Lucerne, Switzerland) for participating in follow-up visits. Annette Oxenius and Ute Greczmiel (Institute of Microbiology, Swiss Federal Institute of Technology [ETH] Zürich, Switzerland), and Jop Jans (Radboud University Medical Center, Nijmegen, the Netherlands) assisted in developing the *Mp*-IgM-ASC ELISpot assay. They also thank Jacqueline Minder (RUWAG Diagnostics, Switzerland) and the immunology laboratory staff for assistance with ELISA, and Jürg Böni and Jon Huder (Institute of Medical Virology, University of Zurich, Switzerland) for performing the multiplex PCR assay.

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Understanding Hyperlactatemia in Sepsis: Are We There Yet?

To the Editor:

High plasma lactate is a useful indicator of shock, a canary in the coal mine, that is associated with increased mortality in sepsis.

Originally Published in Press as DOI: 10.1164/rccm.201905-0962LE on June 17, 2019

However, instead of being a harmful molecule *per se*, lactate is a central molecule in the intra- and interorgan exchange of carbon and redox potential (1). The study by Gattinoni and colleagues, who used a novel approach to analyze data from the ALBIOS (Volume Replacement with Albumin in Severe Sepsis) study, adds to the required change of paradigm concerning lactate metabolism in sepsis (2). The authors nicely demonstrate that there are multiple reasons for hyperlactatemia in sepsis, and that the increased snapshot value we measure reflects an imbalance between increased production and reduced consumption.

By introducing the term "alactic base excess," the authors also elegantly demonstrate that there is no causal relationship between elevated lactate and metabolic acidosis. We would add that, in fact, lactic acidosis *per se* is a misnomer, a construct that doesn't exist, because there is no lactic acid present in the human body (3). Similarly, we agree that current fluid resuscitation strategies should be modified and perhaps concentrate on organ perfusion rather than targeting hyperlactatemia (4).

We would, however, question the conclusion that impaired tissue oxygen use is the most likely causative factor for hyperlactatemia. Although we are unable to perform correlations without access to the raw data, if we chart the means shown in Table E2 in the online supplement of Reference 2, there seems to be a relationship between lactate levels and epinephrine dose but not between lactate and any variable related to oxygen use (oxygen extraction ratio, Pv_{O_2}, or central venous oxygen saturation). Therefore, we would suggest that exogenous (and likely endogenous) epinephrine via its stimulation of Na^+-K^+ ATPase and glycolysis is likely responsible for the hyperlactatemia in sepsis, rather than impaired tissue oxygen use (5). The possible association of a change in the mean lactate value with the mean P_{CO_2} gap, from Table E2 in the online supplement of Reference 2, also raises the possibility that increased (not decreased) Krebs cycle activity is associated with hyperlactatemia. Epinephrine-associated hyperlactatemia has also been observed in a prospective randomized trial in septic shock (6). ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Understanding Hyperlactatemia in Human Sepsis: Are We Making Progress?

To the Editor:

We have significant concerns about the interpretation of the data presented by Gattinoni and colleagues (1). The reminders that lactic acidosis commonly coexists with renal acidosis and that metabolic acidosis does not necessarily mean acidemia are welcome. Indeed, one should dissociate hyperlactatemia from acidosis because hyperlactatemia can be of hypoxic origin even in the absence of acidosis, and of nonhypoxic origin even when there is acidemia (2). Although we agree with Gattinoni and colleagues that a pH measurement can be misleading, and that lactate concentrations should be measured directly, neither the presence or absence of metabolic acidosis nor the central venous oxygen saturation (Scv_{O_2}) value can help identify the origin of hyperlactatemia.

Gattinoni and colleagues also reemphasize the well-known fact that hyperlactatemia can coexist with any value of $\dot{V}o_2$/oxygen delivery ($\dot{V}o_2/Do_2$) (or $S[c]v_{O_2}$). This is in part related to timing, because an increase in Do_2 as a result of resuscitative efforts may result in a rapid increase in Sv_{O_2} but a much slower decrease in blood lactate levels. More importantly, a normal or high Scv_{O_2} does not necessarily indicate that tissue perfusion is adequate. It is well known that a high Sv_{O_2} can be a sign of disease severity and worse prognosis (3). However, a high Sv_{O_2} does not always imply a significant alteration in cellular metabolism, as high Sv_{O_2} values can be the result of microcirculatory alterations. In our early study demonstrating the occurrence of microvascular alterations in sepsis (4), Sv_{O_2} values were identical in patients with sepsis and in other ICU patients, but hyperlactatemia was observed only in patients with septic shock (4). Accordingly, it may be erroneous and even potentially harmful to limit resuscitation efforts in a patient with hyperlactatemia just because his or her Scv_{O_2} values are normal or

Originally Published in Press as DOI: 10.1164/rccm.201905-1024LE on June 17, 2019