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Title:
The importance of applying physiological principles of hyperlactataemia to the study of human disease

Date:
2021-03-01

Citation:
See, E. J. & Bellomo, R. (2021). The importance of applying physiological principles of hyperlactataemia to the study of human disease. Journal of Physiology, 599 (6), pp.1933-. https://doi.org/10.1113/JP281371.

Persistent Link:
https://hdl.handle.net/11343/298211

To the Editor

The Journal of Physiology

January 16, 2021

As practicing critical care clinicians, we read the article on the anaerobic threshold by Poole et al. (Poole *et al.* 2020) with great interest. Its relevance extends well beyond exercise physiology since this work has major implications for clinical medicine, especially in the field of critical care.

In critically ill patients, lactate often increases in a way that resembles the changes seen during intense exercise. The interpretation of hyperlactatemia in the critical care setting is flawed because of the canonical concept that "anaerobic metabolism" is the dominant cause of hyperlactatemia. Clinicians continue to believe that elevated lactate levels must reflect "tissue hypoperfusion/hypoxia". This evidence-free and self-referential paradigm has been and continues to be perpetuated in Emergency and Intensive Care Medicine (Gomez-Ramos *et al.* 2018). Moreover, it has led to trials aimed at increasing "lactate clearance" as though lactate was some kind of toxin that has to be removed, a strategy which may increase mortality (Kattan E, *et al.* 2020).

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1113/JP281371.

Previous work has called attention to the concept of stress hyperlactatemia in sepsis (Garcia-Alvarez *et al*. 2014) and in critical illness in general (Garcia-Alvarez *et al.* 2014) and to the dangers associated with applying incorrect physiological paradigms from 60 years ago to modern Intensive Care Medicine (Hernandez *et al.* 2019). However, the sophisticated methodology of exercise physiology now needs to move to the clinic. We need exercise physiologists to start studying metabolism in sepsis (another important issue for mankind) and to investigate the effects of actually giving lactate in situations of physiological stress. We need physiologists to break the silos that confined so much of modern medicine to the physiological past and so many world-class physiologists to animal models not focused on human disease.

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