J Appl Physiol 126: 264, 2019;
doi:10.1152/japplphysiol.00782.2018.

LETTER TO THE EDITOR

Supramax exercise testing in cystic fibrosis: not ready for prime time

Dan M. Cooper

Pediatric Exercise and Genomics Research Center, University of California at Irvine, California

Submitted 5 September 2018; accepted in final form 24 September 2018

TO THE EDITOR: I read with interest the careful study of Causer's group (1). While the results are encouraging, caution must be used in recommending any new procedure as "safe" based on *1*) a retrospective study whose pediatric cohort consisted of 15 children with only 5 girls and *2*) a test that can cause hypoxia in patients with lung disease. The validity of "supramaximal verification" (Smax) is also problematic. Causer suggests that practitioners routinely "wrongly" accept an "inaccurate" $\dot{V}O_{2max}$ derived from incremental testing and that the perceived inaccuracy can be "corrected" by an additional test in which the participant exercises to exhaustion at a supramaximal constant work rate. The Smax approach assumes that the incremental test had no impact on the subsequent test, and this may be untrue. In cystic fibrosis, for example, peak exercise improves subsequent pulmonary function (3). High-intensity exercise in healthy volunteers speeds $\dot{V}O_2$ kinetics in subsequent tests (2). I simulated the effect of a 10% reduction in time constant (τ) and 10% increase in gain ($\Delta\dot{V}O_2/\Delta WR$) on $\dot{V}O_2$ obtained from Smax. I used the mean duration (76 s for children) reported by Causer. These modest changes in gain and τ led to a 10.5% increase in $\dot{V}O_2$. In the simulation, I did not test the effect of a 10% increase in work rate, prescribed by Smax, which would have led to an even greater $\dot{V}O_2$. The simulation shows that Smax $\dot{V}O_2$ higher than those achieved in the preceding progressive test does not necessarily indicate wrong or inaccurate tests. Rather, there are plausible physiological reasons for higher Smax $\dot{V}O_2$. The Nobel laureate A.V. Hill postulated in the 1920s the existence of volitional, maximal levels of $\dot{V}O_2$ (rapidly followed by cessation of exercise before any physiologic catastrophe had occurred) and wondered about physiologic and cognitive mechanisms. Fundamental issues such as exactly how to determine $\dot{V}O_{2max}$ and its clinical utility are still unresolved after a century of heated debate. Many factors influence the results obtained from testing to the-limit-of-tolerance and contribute to $\dot{V}O_{2max}$ ambiguity [e.g., exercise modalities (treadmill vs. cycle ergometer), rates of work rate increment, and the patient's cognitive state]. Adding uncomfortable procedures to an already challenging and time consuming test is not likely to advance CPET in clinical research or practice. Two of Causer's pediatric patients failed to complete the protocol for reasons encountered in clinical exercise laboratories: time restrictions and unwillingness to exercise. Technology has advanced, permitting us to address Hill's seminal questions in new ways. We can, for example, use modern data analytics to target the rich and voluminous data engendered in breath-by-breath testing and design protocols that more closely mimic real activities encountered in the daily lives of patients and research volunteers. Research talents and clinical expertise of our community might best be harnessed to develop testing strategies that are engaging to participants and patients, truly feasible and cost-effective, and informed not only by the investigators and practitioners' questions, but by the kind of information that the patients themselves will find useful in managing their daily life activities and benefiting their health.

Address for reprint requests and other correspondence: D.M. Cooper, PERC, University of California at Irvine, Irvine, CA 92697 (e-mail: dcooper@uci.edu).

GRANTS

This work was funded by National Center for Advancing Translational Sciences (NCATS) Grants UL1 TR001414100006108 and U01 TR00200410-0006108 and National Institute of Arthritis and Musculoskeletal and Skin Diseases Grant U01 AR071158100000069.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author.

AUTHOR CONTRIBUTIONS

D.M.C. drafted manuscript; approved final version of manuscript.

REFERENCES

1. **Causer AJ, Shute JK, Cummings MH, Shepherd AI, Bright V, Connett G, Allenby MI, Carroll MP, Daniels T, Saynor ZL.** Cardiopulmonary exercise testing with supramaximal verification produces a safe and valid assessment of $\dot{V}O_{2max}$ in people with cystic fibrosis: a retrospective analysis. *J Appl Physiol (1985)* 125: 1277–1283, 2018. doi:10.1152/japplphysiol.00454.2018.
2. **do Nascimento PC, de Lucas RD, de Souza KM, de Aguiar RA, Denadai BS, Guglielmo LGA.** The effect of prior exercise intensity on oxygen uptake kinetics during high-intensity running exercise in trained subjects. *Eur J Appl Physiol* 115: 147–156, 2015. doi:10.1007/s00421-014-3000-0.
3. **Tucker MA, Crandall R, Seigler N, Rodriguez-Miguelez P, McKie KT, Forseen C, Thomas J, Harris RA.** A single bout of maximal exercise improves lung function in patients with cystic fibrosis. *J Cyst Fibros* 16: 752–758, 2017. doi:10.1016/j.jcf.2017.05.011.