REFERENCES


REPLY: Perhexiline, Cardiac Energetics, and Heart Failure
Lessons From the First Law of Thermodynamics

We thank Drs. Davogustto and Taegtmeyer for their interest in our recent work (1) and for stressing the importance of the First Law of Thermodynamics. We concur that our data do not completely exclude a shift in the dominant substrate use as a mechanism; however, when considered in light of the previous study by Unger et al. (2), we nevertheless contend that it raises the possibility of an alternative or additional mechanism of action of perhexiline. Several of these were discussed in the paper, but these may include an increase in the efficiency of generation of energy from the same substrates, for example through reduced mitochondrial uncoupling. In heart failure, a reduction in CK activity has previously been reported (3) that appears in part as a result of increased oxidative stress, and partially corrected acutely by allopurinol (4). Perhexiline has been reported to reduce NADPH oxidase activity and to reduce cardiac TxNIP levels. Either or both of these mechanisms might contribute to a shift in the ratio of PCr to ATP.

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http://dx.doi.org/10.1016/j.jchf.2015.04.008

Please note: Prof. Frenneaux is an inventor of a method of use patent for perhexiline in heart muscle disease. Dr. Beadle has reported that he has no relationships relevant to the contents of this paper to disclose.

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