Reply to Hambridge et al.

Dear Editor:

We appreciate the comments by Hambridge et al. in their letter about our publication “Accuracy of Simple Techniques for Estimating Fractional Zinc Absorption in Humans” (1). These investigators take issue with our conclusion that the fecal monitoring technique with “English correction” (FM-E) (2) for estimating fractional zinc absorption (FZA) using a single oral tracer has serious theoretical limitations. They argue that their determinations of FZA with the FM-E technique do not differ significantly from those using the double isotope tracer ratio (DITR) technique, the latter being a technique that we prefer for theoretical as well as “ease-of-use” reasons. They also argue that our evaluation of the FM-E technique does not reflect the manner in which this technique is used in their laboratory. We disagree with this last assertion in that the FM-E technique we analyzed in our report is exactly that explained in their report by Krebs et al. (2).

Our main criticism of the FM-E technique is the same criticism of fecal monitoring techniques provided by Wastney and Henkin (3), i.e., the result is dependent on colonic transit time and timing of sample collection. The FM-E technique provides an overestimate of FZA early in the course of fecal tracer collection due to incomplete excretion of unabsorbed colonic tracer. Later in the course of cumulative fecal tracer collection, the technique leads to an underestimate of FZA resulting from the faulty hypothesis that the rate of endogenous secretion of absorbed tracer back into the gastrointestinal tract is constant and can be described by a linear response in the accumulation of fecal tracer after all of the unabsorbed tracer has exited the colon. Contrary to the statement by Hambridge et al., this hypothesis is simply not true. In fact the slope of the fecal accumulation response is constantly diminishing over time and eventually reaches zero asymptotically when all of the orally administered tracer has left the body. At that time, the slope of this zero slope equals the fraction of unabsorbed tracer plus the fraction of absorbed tracer (FZA) multiplied by the fraction of absorbed tracer exiting the body by the colon compared with all other routes of exit. Given the model parameters in our paper, this slope amplitude (or $t = 0$ intercept) is 0.975, yielding an FZA of 0.025, clearly a gross underestimate of the FZA from the model that equals 0.279. Changing the delay characteristics of the model that are used to describe the passage of tracer through the colon does not solve this theoretical problem. Additional problems with the FM-E technique are the influence of prolonged colonic transit time and incomplete tracer recovery in the feces. As we showed in our report (1), each of these occurrences can lead to significant additional errors in the FM-E technique.

All of these criticisms notwithstanding, there is a particular interval of time in the cumulative fecal tracer response (albeit variable from subject to subject) during which the FM-E technique provides an accurate estimate of FZA (Fig. 5 of our report) (1). Hambridge et al. have found that in their hands the results of FZA by FM-E and DITR (also an approximation of FZA but with a much smaller range of error) agree closely. We have not had such success experimentally using these two techniques and prefer the DITR technique performed on a spot urine sample a few days after tracer administration because of its simplicity, robustness and lack of requirement for stool samples. Nevertheless, if a group has found that FM-E estimates of FZA are similar to estimates provided by more accurate techniques such as DITR (likely the result of the cancellation of opposite errors), then it is reasonable for the FM-E technique to be used in that group of subjects (e.g., the pediatric population) as long as careful attention is paid to possible errors likely to occur from prolonged colonic transit time and incomplete fecal tracer recovery.

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