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Response to: Selection bias and vitamin E and cystic fibrosis (Ronald J. Sokol, MD)

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To the Editor

We appreciate the comments in the letter entitled “Selection Bias and Vitamin E Status in Cystic Fibrosis” (CF) in response to our recent article regarding vitamin E status in preadolescent children with cystic fibrosis, pancreatic insufficiency (PI), and mild-to-moderate lung disease. (1). To address vitamin E status, we presented data using both serum vitamin E and vitamin E:cholesterol ratio in 7 to 10 year old children compared to healthy children of the same age from NHANES III. We agree with Dr. Sokol that vitamin E supplementation to prevent deficiency is essential in CF care, and is the reason for the low incidence of vitamin E deficiency in our preadolescent sample. We found that an unexpectedly high proportion of our sample of children had high vitamin E levels on currently routine supplementation. We suggested that future dose and response studies are warranted to determine a more optimal level of vitamin E supplementation in children with CF.

We will address the three issues that were raised: the generalizability of the data and concern for selection bias; different findings in our study from those of Feranchak et al (2); and the strengths and weakness of various vitamin E biomarkers. We suggest that the data presented are generalizable to school-age, preadolescent children with CF, PI and mild-to-moderate lung disease. Subjects within the inclusion/exclusion criteria from each center were sorted into a random order and approached to join the two year study of nutrition and lung function. Although we recruited a limited number of subjects from each center, for many of the 13 centers, these children represent a substantial proportion of children within this age range. Feranchak et al (2) presented important prospective, longitudinal data from one state/one center with 113 subjects in our age range of interest. The findings in the two studies are remarkably similar.

When the Feranchak et al (2) data are reviewed for children ages 7 to 10 years, the same proportion (4%) of children were deficient in their sample using their cut-point from the 1978 Farrell et al data (3) as in our sample using the 5th %ile cut-point from NHANES proposed in our report. Also, among children ages 7 to 10 years, 7% had low vitamin E:lipid ratios in the Feranchak et al study (2) and a comparable 4% or 13% of children in our study had low vitamin E:cholesterol ratios depending on the cut-point used. Thus, similar rates of deficiency were

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documented by both groups of investigators utilizing various approaches. Moreover, among children 7 to 10 years old, 48% in our study and up to 40% in the Feranchak et al study had serum vitamin E levels above the 95th %ile for healthy children from NHANES. Again, the two data sets appear comparable using the approaches we reported.

The issue of the optimal vitamin E biomarker for clinical care is a challenge. The vitamin E:total lipids ratio may be preferable, but it is rarely available in the clinical setting. We were interested in examining vitamin E status with measures that are widely clinically available. One of the strengths of our study is the presentation of vitamin E status, using both serum vitamin E and the vitamin E:cholesterol ratio, in children with CF compared with healthy children of the same age from the NHANES nationally representative reference set. This provides appropriate comparison values for children in our age group. We suggest our approaches have merit in routine CF clinical care and should be further investigated.

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