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Zinc deficiency in young children[1,2]

K Michael Hambidge

As respect for the role of zinc in human nutrition grows, so does our appreciation of the practical importance of this micronutrient in infants and young children. Although not detracting from the considerable evidence that zinc deficiency can have a negative effect on pre- and postnatal development in North America and other more affluent societies, it is in the developing world that progress has been most rapid in the 1990s. Whatever the reasons for zinc deficiency in young children in the United States, and these are not always apparent, there are greater reasons for concern in the developing world. Notable among these are the lack of animal products in the diet, the use of low-zinc starchy roots and tubers as food staples, and/or intakes of phytate that are sufficient to negatively affect the bioavailability of dietary zinc (1). Excessive zinc losses associated with recurrent acute or persistent diarrhea increase the risk of deficiency.

It was in the developing world that the hypothesis of human zinc deficiency was first seriously entertained >30 y ago. What is different now that has attracted growing attention from the international nutrition scientific community? First is the greater appreciation of the public health importance of specific micronutrient deficiencies. Second is the rigorous application of state-of-the-art epidemiologic techniques to study design and implementation. This has been especially critical for zinc because of the notable lack of reliable, sensitive, and specific laboratory or functional indexes of zinc nutritional status. Hence, the role of carefully designed, randomized controlled studies of dietary zinc supplementation have been of paramount importance. Third is the multiplicity of recent studies covering a wide range of developing countries with widely varying cultures and food staples. Though results have varied, sometimes in ways that are not immediately explicable [as in the study by Rosado et al (2) reported in this issue of the Journal], more notable has been the overall concordance and the evidence for underlying zinc deficiency that has emerged from the results of these studies. This has been illustrated by the results of a recent meta-analysis of the effects of zinc supplementation on growth (3).

Fourth, there is growing evidence that zinc deficiency contributes to some of the major causes of morbidity among young children in the developing world as has been well illustrated by recent studies in New Delhi (4). Results of supplementation have included reductions in the prevalence, severity, and duration of diarrhea. Reductions in the incidence of persistent diarrhea and dysentery could have important implications for diarrhea-related morbidity and mortality. Concurrently, improvement in cell-mediated immune function has been documented. Though requiring additional careful research, there are indications that zinc deficiency may be partially responsible for impaired neurocognitive development that is associated with poor growth in young children in the developing world (5).

Rosado et al (2) provide further evidence of the favorable effect of zinc supplements on the incidence of infections, especially diarrhea. This and other recent studies have clearly illustrated the value of single nutrient intervention studies at this stage in our understanding of zinc nutriture. These studies have gone a long way to establish definitively a major role for zinc as a key micronutrient in the developing world. Rosado et al's study also, however, illustrates the additional need to undertake more complex studies. None of the features of zinc deficiency are specific to that element. Furthermore, zinc has well-known and complex interactions with other micronutrients, both minerals and vitamins. The negative results with respect to iron in this study are useful, but the possibility that one or more other nutrients may have been growth-limiting in these children, thus preventing a growth response to zinc, remains one plausible explanation for the lack of an increase in linear growth velocity. Whereas the reason that a growth response was not observed in this study remains speculative, one factor that cannot be questioned seriously is the adequacy of the zinc supplement that was known to have been administered. At this age, each centimeter of new linear growth, with proportional weight gain, requires the retention of ≈5 mg Zn or an average retention of an additional 14 μg Zn/d for an increase in growth velocity of 1 cm/y. Even at as little as 5% net (apparent) absorption, this would require only 2% of the supplement given.

Our cumulative experience from animal and human studies indicates that retarded growth velocity is an early and potentially reversible manifestation of even mild zinc deficiency (6). The increase is generally modest, however, and of little practical consequence to stature itself. Rather, the importance of poor linear growth velocity in young children in the developing world is its association with impaired cognitive development

[1] From the Section of Nutrition, Department of Pediatrics, and University of Colorado Center for Human Nutrition, University of Colorado Health Sciences Center.

[2] Address correspondence to KM Hambidge, Section of Nutrition, Department of Pediatrics, University of Colorado Center for Human Nutrition, University of Colorado Health Sciences Center, 4200 East Ninth Avenue, C-225, Denver, CO 80262. E-mail: michael.hambidge@uchsc.edu.

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and compromised host-defense mechanisms (5). This is not a cause-effect relation and measurements of physical growth velocity are being used primarily as a surrogate marker in studies of the effects of zinc supplementation in young children. Although the lack of a statistically significant growth response in Rosado et al's study (2) raises questions about the sensitivity of this surrogate marker, it does not detract from the apparent significant benefits of the zinc supplements on host defense mechanisms.

Relatively little is yet known about zinc homeostasis and metabolism, especially in young children. For example, Rosado et al (7) showed that net absorption of zinc was low in adults fed diets similar to those consumed by children in this study. Yet, this amount of absorption was sufficient to maintain balance and can, therefore, be assumed to be adequate. We do not know if they or children on similar diets can increase net absorption if needed, for example, to support catch-up growth. It appears that careful measurements of fecal excretion of endogenous zinc may be especially important in advancing our understanding of zinc homeostasis. The judicious application of stable-isotope techniques now available (8) should facilitate resolution of these questions and also provide a better basis for designing intervention studies, including identification of communities most at risk.

Although benefits of zinc supplementation in preschool-aged children were shown in several studies, it is noteworthy that the linear growth velocity of the control children in Rosado et al's study (2), in contrast with some other investigations, was a little greater than reference standards without zinc supplements. As is typical in the developing world (9), the period of poor linear growth had already passed. A strong argument can be made for starting intervention at an earlier age with the goal of either preventing the slowing of growth and associated functional deficits that are attributable to postnatal zinc deficiency or reversing these at a much earlier stage. Growth velocity in fully breast-fed infants in North America has been increased by providing a modest zinc supplement between 2 and 6 mo of age (10). It is at this age that growth typically falters in developing countries. Other studies have also documented responses to zinc supplementation in the first year or two of postnatal life. There is also evidence that benefits may accrue from prenatal zinc supplementation. It is conceivable that these are not necessarily limited to embryonic and fetal growth and development but could effect cross-generational genetic imprinting (11).

Though a wide range of research initiatives are essential to provide an adequate basis for effective measures to minimize the adverse effects of zinc deficiency on growth and development in young children globally, special attention should now be given to research that facilitates the design of effective community-based strategies to prevent zinc deficiency (12).

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