Statistical and psychobiological significance in developmental research\textsuperscript{1,2}

Ernesto Pollitt

Documentation of the adverse effects of highly prevalent nutritional deficiencies on growth and developmental outcomes in low-income countries has justified scientific research and programmatic interventions in different regions of the world (1–3). In the past decade or so, theory and empirical evidence have contributed to growing scientific and policy concern about zinc deficiency (4). Zinc deficiency has teratogenic effects in rodents, limits physical growth in children, impairs learning and behavior in monkeys, and may also affect motor activity and cognition in preschool children (4, 5). In low-income populations in some developing countries, zinc deficiency is as prevalent as is iron deficiency anemia (6). Nonetheless, zinc supplementation, particularly of pregnant women and young children, must proceed cautiously because the appropriate safety ranges of zinc intake have not yet been established.

Safety underscores the biological and programmatic importance of the findings reported by Hamadani et al (7) on Bangladeshi children in this issue of the Journal. These findings require careful scrutiny because of their potential public health implications. In the study by Hamadani et al, children were given a zinc supplement or a placebo for 5 mo beginning at 4 wk of age. At 13 mo of age, the children in the placebo group had a 3.3-point higher mean score on the mental development index (MDI) of the second edition of the Bayley Scales of Mental Development (8) than that of the group who received zinc (106.4 ± 9.3 compared with 103.1 ± 11.1; P < 0.05). This difference was the basis for the authors’ suggestion of “a possible risk of giving zinc alone for a prolonged period.” The authors also speculated that the “lower scores in the zinc-treated group…were caused by an imbalance of micronutrients.”

At issue is whether the 3.3-point intergroup difference is indicative of biological risk. The sample of subjects from 1 to 42 mo of age used to standardize the second edition of the Bayley Scales systematically excluded some age groups within that range. Therefore, it is necessary to extrapolate to determine the index scores of subjects whose age at testing falls within the excluded age groups. A change of a single point in the raw score of test items successfully completed is equivalent to changes of 2–3 points on the scale of index scores. For example, an MDI raw score of 106 at 13 mo, which is the rounded average MDI score of the placebo group, can be either 93 or 94 points, respectively, whereas the MDI raw score of 103, the rounded mean score of the zinc group, is 92 points. Therefore, the 3.3-point difference in index scores is reduced to 1 or 2 of the 28 test items listed for toddlers aged 13 mo. None of the 28 items is backed by either theoretical or empirical support for use as an indicator of a psychobiological difference in the 2 groups under consideration.

Another issue regards construct validity. Within the general research area of nutrition and psychobiological development, it was customary to use the first edition of the Bayley Scales of Infant Development (9) to assess the functional consequences of nutritional supplementation of infants and toddlers. This practice was generally accepted without an explanation of the concepts behind the method and without a reference to proven construct validity. The Bayley Scales were candidly considered to be a gold standard. However, the original version of this scale for infants and toddlers up to 24 mo of age has failed to show construct and predictive validity (10, 11). The edition of the Bayley Scales that became available in 1993 (8) incorporated a new standardization of the mental scale and changes in its construction and administration, but shed no new light on its construct validity up to the ages of 18–24 mo.

The very modest test-retest correlations of the MDI between 7 and 13 mo reported by Hamadani et al for the placebo (0.23) and zinc (0.46) groups indicate the presence of either methodologic (ie, large measurement errors) or conceptual (ie, the scale tested different constructs at 7 and 13 mo) inaccuracies of the mental scale. Regarding the latter, the coefficients suggest that the very nature of the concept “mental” has undergone significant transformations in 6 mo. But there is no way of going any further in our understanding of the intergroup differences in intragroup developmental changes with the information available either in this paper or in the Bayley Scales. The yellow flag raised by the authors regarding zinc supplementation must be viewed within the psychometric constraints noted. The potential adverse consequences of zinc supplementation among poorly fed infants remain an open question.

\textsuperscript{1}From the Department of Pediatrics, University of California, Davis.

\textsuperscript{2}Reprints not available. Address correspondence to E Pollitt, University of California, Department of Pediatrics, TB-139, One Shields Avenue, Davis, CA 95616. E-mail: epollitt@ucdavis.edu.
REFERENCES