Nutrition in early life and cognitive functioning

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In this issue of the Journal, Alderman et al (1) report on the long-term follow-up of a cohort of individuals whose mothers participated in a randomized nutrition supplementation trial. One group of mothers received a protein-energy supplement, in the form of baked biscuits, from week 20 of gestation through parturition, whereas the control group received the same biscuits for 6 mo starting at delivery. The intervention was effective at increasing mean birth weight. In previous research, no long-term benefits of prenatal supplementation on growth, body composition, or cardiometabolic risk were seen; and in this study, no differences were seen between the groups in several measures of cognitive development measured at the mean age of 19 y. The usual concerns of differential attrition, masking/confounding, and power are all addressed adequately and cannot explain the null result. What we are left with is the conclusion that the 2 groups indeed did not differ.

As discussed by the authors, the primary concern with this design is that it is not possible to distinguish between 2 conclusions: 1) the interventions were each equally effective or 2) neither of the interventions was effective.

The former possibility is at least partially addressed by Maluccio et al (2) [and in related work by Stein et al (3)], who analyzed the impact of nutrition supplementation provided throughout pregnancy and the first 2 y of postnatal life in a cohort of rural Guatemalans. They reported substantial positive impacts on schooling (in girls, among whom schooling levels were lower than those of boys) and on performance on cognitive tests (in both males and females) as adults, even accounting for the differences in schooling, compared with those who were in a comparison village or who were exposed to the study intervention at other ages. So we can conclude (subject to the usual caveat that this is a single study conducted in one context) that interventions sustained over this entire age range indeed have positive benefits to the children.

The second concern is addressed in the seminal studies of the Dutch famine by Zena Stein et al (4). The circumstances of the Dutch famine, a 5-mo period in which food rations fell below 1000 kcal/d, facilitated the differentiation of the consequences of exposure to acute food shortages in various stages of pregnancy (5). Exposure in late gestation (but not exposure in early gestation) was associated with a large (~250 g) reduction in mean birth weights, compared with those without famine exposure. Stein et al used the Dutch military conscription database to relate performance at age 18 y on a variant of the Ravens Progressive Matrices to place and month of birth, a proxy for maternal exposure to famine, and found no impact of the famine on performance, after adjusting for the employment class of the recruit’s father. (Of note, the famine did result in a marked decrease in fertility, especially among the working classes, so failure to adjust for paternal employment status results in an apparent increase in mental performance among males exposed to famine in early pregnancy, a group in which children from the professional classes are overrepresented.) Subsequent work has followed 2 independent subsets of individuals exposed to the Dutch famine through to later adulthood, again finding little or no suggestion of any impact of exposure to famine on cognitive functioning (6, 7).

So what can we learn from these studies? The putative benefits of prenatal supplementation with specific nutrients on brain development are as yet not fully defined. There is ongoing work related to DHA, a major constituent of brain tissue (8). By and large, the results suggest little impact of prenatal supplementation; where impacts have been shown, the studies have continued the supplementation postnatally, whether by supplementing the mother or, for children who were not breastfed, by fortifying formula. The timing of prenatal interventions, most of which were implemented in the second half of pregnancy, may be suboptimal: data from the Dutch famine suggest that epigenetic changes consequent to undernutrition are apparent only when exposures occur periconceptionally (9). It is unlikely that we will identify a “magic bullet” of a single intervention at a single stage of development that will help all children reach their genetically endowed potential. The critical window of efficacy is likely to be nutrient- and context-specific, because a nutrient that is rate-limiting in one setting might not be so in another.

The benefits of early cognitive stimulation are often stressed (10, 11). It is here that nutritional interventions may have their role—in ensuring that the developing child has the strength and health to explore his or her environment and benefit from this stimulation. Child growth in the first 2 y predicts schooling attainment (12), and stunting at age 2 is related to a wide range of measures of human capital in adulthood (13). Thus, ensuring...
adequate child growth in early childhood remains the challenge. Supplementation of the mother may provide her with the energy she needs to interact with her child, and supplementation of the child provides energy for growth and exploration and micronutrients to enhance the immune response to the inevitable infections. Sustained, balanced, optimal nutrition of the mother before and during the pregnancy and through lactation, and of the child once breast milk is no longer adequate at ~6 mo, is likely to provide maximal benefit. This message is not new, and of course the challenges of delivery remain.

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REFERENCES