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The Nutrition CRSP: What Is Marginal Malnutrition, and Does It Affect Human Function?

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This review of the Nutrition Collaborative Research Support Program (Nutrition CRSP) describes the results of a longitudinal study of the effects of marginal malnutrition on human function in Egypt, Kenya, and Mexico. Growth-stunting occurred soon after birth and was associated with cognitive and behavioral deficits in infancy and childhood. Maternal nutritional status was implicated in this phenomenon. All three population groups had poor dietary quality and multiple micronutrient deficiencies, which were associated with poor function. Energy deficiency was a problem only in Kenya.

Introduction

It is well accepted that marginal malnutrition is highly prevalent in developing countries and more common than severe malnutrition, which presents as starvation, marasmus, or kwashiorkor. In 1977, Study Team IX (Nutrition) of the National Academy of Sciences' World Food and Nutrition Study gave the highest priority to determining whether mild-to-moderate malnutrition affects the functional capacity of individuals.[1] In the late 1970s, it had gradually become apparent that neither the supply nor the quality of dietary protein was the world's main nutritional problem. Rather, it was thought that persons in poor countries generally suffered from a chronically low intake of energy because of lack of food. However, if chronic energy deficiency were the main problem, it was difficult to understand how most persons in poor countries avoided constant weight loss and eventual death from undernutrition. It was possible that they "adapted" to a low energy intake by reducing their basal metabolic rate or utilizing energy more efficiently[2] or by becoming less physically active. Some researchers were prompted by the possibility of such adaptive phenomena to suggest that it was normal and perhaps desirable to be "small but healthy."[3]

These proposed explanations did not stem from a lack of concern on the part of those who made them. Rather, they reflected our almost complete lack of understanding about what marginal malnutrition is and whether it affects human function. Study Team IX suggested that functions most likely to be impaired were growth, psychological development, immune function (morbidity), reproductive competence, and social competence. Based on these concerns, in 1980 the US Agency for International Development funded the Nutrition Collaborative Research Support Program (Nutrition CRSP).

The main purpose of the Nutrition CRSP was to determine whether there were any relationships between energy (food) intake and important functions, including growth, psychological development, pregnancy and lactation outcomes, behavior, and morbidity. The basic study design was to observe individuals and their households at frequent intervals for one year. There were no nutritional or other interventions because it was deemed more useful to describe the relationship between the existing food situation and nutritional status and human function.

The research was a collaborative effort between universities in the United States and institutions in developing countries. The University of Connecticut collaborated with the Instituto Nacional de la Nutrición in Mexico; the University of California, Los Angeles, with the University of Nairobi, Kenya; and Arizona, Kansas, and Purdue universities with the Nutrition Institute in Cairo, Egypt. The University of California, Berkeley, provided financial and technical oversight. After two years of recruiting and training staff, building community

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relations, and developing and testing methods in the field, data collection started in early 1984 and continued until mid-1986. After a two-year hiatus in funding, there was support for additional data analysis between 1990 and 1992. The final reports of each project were published in 1992.[4–7] In this review we attempt to summarize the main findings of this massive project and to discuss its policy implications. More details are available in the project reports and in numerous publications, of which only a few are referenced here.

The Research Locations

The Egyptian field location was Kalama, a periurban community in the Nile delta near Cairo. The density of housing was higher, and sanitary conditions and morbidity were subsequently worse, than in the other research sites. The Kenyan study took place in three rural agrarian locations in Embu, near Mount Kenya. The research in Mexico was conducted in six similar communities located at the edges of the Solís Valley, 170 km northwest of Mexico City. Each project studied about 300 households. To be eligible for participation, households had to include a lead male and female who were parents of children aged approximately 18 months or between seven and eight years, or the lead female had to be in an early stage of pregnancy. The adults and their children were each followed for one year. The pregnant women were followed from no later than five months of pregnancy and, with their infant, through six months (eight months in Mexico) of lactation. Approximately 100 "target" persons in each age/sex/physiological status group were studied longitudinally.

The diets were different in the three locations. In Egypt, the staples were wheat bread, rice, and legumes. Locally produced foods included cheese, milk, eggs, and vegetables. Staples, sugar, tea, and oil were subsidized so that food availability in Kalama was the best of the three locations. Using preschoolers as the basis of comparison, animal products supplied an average of 18% of energy compared to approximately 40% for children in the United States. The Kenyan households produced cash crops, such as coffee and cotton, and food, including maize, legumes, and vegetables. Productivity was seriously handicapped by inadequate rainfall so that the nutritional situation in Embu was the poorest of the three. Only about 8% of preschoolers' energy intake came from animal products. The Mexican communities were also predominantly agrarian, with production limited to one maize crop per year and relatively small amounts of beans and squash. The dietary staples were maize tortillas, which supplied about 60% of dietary energy, and smaller amounts of pasta, beans, and rice. Of the preschoolers' energy intake, 12% came from animal products.

Methods

An important aspect of the Nutrition CRSP is that the methods used in each of the countries were as similar as possible, although none of the test batteries could be completely replicated in exactly the same way because of cultural and logistical reasons. For example, in Egypt, the wearing of long outer garments made it almost impossible to obtain skinfold measures on the trunk, and observers were not permitted during every meal in Egyptian or Mexican households. In addition, the quantity and quality of food composition data varied greatly. Notwithstanding these types of problems, the collection of similar types of data across staple diets and geographical locations was invaluable in making the results of the Nutrition CRSP more generalizable.

Households included in the study were identified on the basis of the presence of target individuals, and information was obtained about each household's socioeconomic status, education levels, literacy, and variables such as land ownership, agricultural and other employment, and involvement in community activities. Anthropometric measures were collected monthly during pregnancy and lactation and in children, and every three months in adults. Food intake was measured at the household level (food prepared and consumed inside and outside the home) and more accurately for target individuals. Each project used the best method feasible in that community.

Morbidity information was collected from all household members by interviewers who went to the household weekly inquiring about illness on that day and during the past week. Fecal and/or blood measures of parasites were made routinely. Blood samples were collected at intervals throughout pregnancy and lactation, and on exit from the study. Hemoglobin and ferritin were measured by all projects, whereas other micronutrient status measures tended to be project-specific, with Egypt focusing on zinc and vitamin B_6 status; Kenya on iodine, zinc, and vitamin B_{12}; and Mexico on folate and vitamin B_{12}.

Tests of cognitive and behavioral development were made on infants at three and six months of age; on preschoolers at 18, 24, and 30 months; and on school-aged children at their entry and exit from the study. Women were studied more intensively during pregnancy, birth, and lactation. During lactation, breast milk samples were collected as was information on infant intake of supplemental foods for two days each month.

Adequacy of Dietary Energy and Protein

Several lines of evidence indicate that energy intake was adequate in Egypt and Mexico and that protein and essential amino acid intakes were adequate in all three countries. Average energy intake met or exceeded the estimated requirements of children and adults in Egypt and Mexico. Energy intake increased with socioeconomic status only in Kenya, indicating that intake was not constrained by resources in the other two countries.

In general, adults did not change weight during the year that they were studied. Kenyan adults lost weight during the drought but regained it later. Energy intakes met the requirements for light activity in Egypt (where more labor-saving devices were used and some occupations were characteristically urban), were adequate to support heavy activity in Mexico (where there was more agricultural work), but failed to meet even light activity requirements in Kenya even though this population was involved in agriculture and other energy-intensive activities. In Egypt and Mexico, women in particular were relatively fat, and the body mass index (BMI) of both sexes tended to increase with age; in Kenya, adults were lean and their BMI did not change with age. In Egypt, access to adequate amounts of staple foods was improved by government subsidies, and in Mexico, field staff who collected food intake information always found some tortillas (but often little else) in the households. Beaton et al.[8] used the probability approach to estimate the risk of low protein and essential amino acid consumption in each region. There was a negligible risk of total protein or essential amino acid intakes being inadequate, for both children and adults.

Examining Relationships Between Diet and Function

To examine relationship between dietary intake and functional outcomes, dietary data were expressed in several ways. Dietary quality, expressed, for example, as a percent of energy (or other nutrients) derived from animal products, was included as a dietary variable. Given that poorer households depended more on staple foods that are generally lower in quality, while wealthier families consumed fewer of these but included more animal products, fruits, vegetables, and other foods that are richer in bioavailable micronutrients,[9] "dietary patterns" were constructed using various analytical strategies.[7] Relationships between functions and specific micronutrients were often explored, although these are difficult to interpret because the intake of single nutrients covaries with that of many others. In general, most associations between functional outcomes and other factors were explored in multiple regression analyses with control for logical confounders. For various reasons, the results are presented here in general terms. The actual analyses are described in more detail in the final reports and publications from each project.

Reproductive Outcomes

Maternal Diets

The average daily intake of energy by nonpregnant, nonlactating women in Egypt was 2224 kcal, but this group included many women who did not become pregnant. In pregnancy, mean intake was 2059 kcal/day, with only a small increase to 2224 kcal/day during lactation. Intakes less than two-thirds the RDA for vitamin A, vitamin B_6, riboflavin, calcium, iron, and zinc occurred during pregnancy or lactation or both.

Kenyan women clearly consumed less energy than those in the other countries. Average intakes (kcal/day) were 1762 for nonpregnant, nonlactating women, 1442 for pregnant women, and 1749 for those who were lactating. During pregnancy and/or lactation, most women consumed less than two-thirds of the RDA for riboflavin, niacin, vitamins A, B_6, and B_{12}, calcium, iron, and zinc. Goiter (iodine deficiency) was apparent in 24% of pregnant women and 15% of nonpregnant, nonlactating women. Compared to the post-food-shortage period, during the drought women consumed about 200 and 400 fewer kcal/day during pregnancy and lactation, respectively.

On average, nonpregnant, nonlactating women in Mexico ingested 2455 kcal/day, compared to 2415 kcal/day during gestation and 2648 kcal/day in lactation. Many in the nonpregnant, nonlactating group, however, were older women who did not become pregnant. During pregnancy and lactation, Mexican women consumed only one-third to two-thirds the RDA for vitamin C, iron, zinc, riboflavin, niacin, vitamin B_{12}, retinol, and vitamin E.

Thus, the general picture is one of very low intakes of energy by Kenyan women, especially during the drought, and a high prevalence of low intakes of numerous micronutrients by women in all three locations.

Maternal and Infant Size

The average age of pregnant and lactating women was about 30 years in each country, and parity was four to six, since many of the households were selected because of the presence of existing children. The average birth interval ranged from 2.0 years in Mexico to 2.5 years in Egypt and Kenya, with partial breast-feeding typically extending into the second year. The median BMI of these women was 25.2 in Egypt, 23.4 in Mexico, and 21.2 in Kenya, reflecting the general pattern of energy intake in the populations. In Egypt, 45% of women had a high BMI (>26) compared to 7% in Kenya; in addition, 32% of Kenyan women had a low BMI (<20), while this was true for only 2% of Egyptian women. Median maternal height was similar, with Mexican women being slightly shorter than the others.

Despite the differences in maternal energy intake and body composition across projects, anthropometric changes during pregnancy and lactation, as well as the size of the infant at birth, were remarkably similar. Pregnancy weight gain in each project was about 6–7 kg on average. This is only half that recommended in the United States but is typical of developing countries. The reason that this situation persists even in the absence of dietary energy shortage is not understood. In both Kenya and Mexico, a strong inverse relationship was observed between maternal BMI early in pregnancy and subsequent weight gain; that is, fatter women gained less weight during pregnancy. This pattern is also seen in women in wealthier countries (although less strongly) and is part of the rationale for basing current pregnancy weight gain recommendations on maternal BMI.[10] Although the reasons for this are not completely understood, pregnancy weight gain alone is clearly not a valid indicator of current maternal nutritional status.

Although there was a negative relationship between maternal BMI and weight gain in Kenya and Mexico, maternal BMI and weight were strongly positively correlated with birth weight in all three countries and with birth length in Egypt and Kenya. Thus, thinner women were at greater risk of having smaller infants; in such cases, a greater pregnancy weight gain might be protective against low birth weight.[10] Median birth weights were 3.1 kg in Kenya, 3.2 kg in Mexico, and 3.3 kg in Egypt, surprisingly similar across locations and not far below the National Center for Health Statistics (NCHS) reference values. Birth lengths were also similar and about -0.5 to 1.0 Z below the reference. Perhaps the greatest difference among pregnancy outcomes in the three countries was that 10% of the Kenyan women delivered low birth weight (<2500 g) infants, compared to 7% in Mexico and 2.5% in Egypt. In a logistic regression analysis, the strongest predictors of low birth weight in Kenya were low maternal BMI, parity greater than three, low maternal hemoglobin concentration, and poor socioeconomic status; these factors correctly identified 86% of the cases. The risk of low birth weight outcome was ten times higher for those women whose weight was in the lowest quartile before pregnancy and during all trimesters. During the period of food shortage, the proportion of birth weights between 2500 and 2800 g rose from 16 to 28% and the main prenatal problem was intrauterine growth retardation, not prematurity.

In the Kenyan group as a whole, maternal energy intake, size upon entering pregnancy, and severe illness (negative) were the best predictors of birth weight, explaining 28% of the variance. Dietary quality, in addition to quantity, promoted weight gain and birth weight. Iodine deficiency (low T_4 levels) and lack of iodized salt use predicted lower fat gain in pregnancy and lactation, lower birth weight, and an increased number of stillbirths and miscarriages. Vitamin B_{12} status was extremely poor in pregnant and lactating women, and those with macrocytic anemia (8%) had more miscarriages and stillbirths.

In the Egyptian population, early pregnancy weight, weight gain in the second and third trimesters, and length of gestation explained 45% of the variance in birth weight.[11] Maternal plasma zinc in midpregnancy and vitamin B_6 concentration in breast milk (a proxy for vitamin B_6 status during pregnancy) were also significant predictors of birth weight. Gestational age (assessed by the Dubowitz exam) of Egyptian infants was positively predicted by maternal consumption of animal products and by maternal body weight in early pregnancy.

The strongest predictors of birth weight in Mexico were also maternal weight, BMI, and fat-free mass. Neither pregnancy weight gain nor maternal dietary variables were significantly related to birth weight or length.

Neurobehavioral Development of the Infant

The neurobehavioral development of the infants at birth was assessed by the Brazelton Neonatal Assessment Scale, an additional measure of pregnancy outcome. Maternal nutritional status during pregnancy appeared to affect the neurobehavioral development of infants in Egypt and Mexico; equivalent analyses for Kenya are not yet available.

Intakes of animal products, vitamin B_6, iron, and zinc during pregnancy were significant predictors of Egyptian infants' habituation scores on the Brazelton scale, while orientation was best predicted by maternal weight and fatness in early pregnancy. Available zinc was associated with infant autonomic stability and motor behavior. Maternal milk levels of vitamin B_6, which were low in about one-third of the women, were associated with lower birth weight and an infant who was more difficult to console and more likely to cry; it was the strongest predictor of neonatal behavior of all other explanatory variables tested.[12]

Similar relationships between maternal micronutrient status and the behavior of the newborn were seen in Mexico, where the mother's prepregnancy weight was associated with autonomic stability of the infant, and her dietary quality was a strong predictor of infant habituation. As in Egypt, infants born to mothers with better iron intake and status had better neurobehavioral performance at birth. Vitamin B_{12} and ferritin levels also appeared to be important although the sample size was low.

The Nutrition CRSP results indicate that maternal energy intake was inadequate to support optimal pregnancy outcome in Kenya and that maternal micronutrient deficiencies were prevalent in all three locations. These were associated with low birth weight and poor infant neurobehavioral development at birth. Intervention trials are clearly needed to confirm that maternal micronutrient status during pregnancy affects the neurobehavioral development of the infant in utero.

Predictors of Children's Growth

One of the most important observations in the Nutrition CRSP was the timing and type of early postnatal growth-faltering. Figure 1 combines longitudinal data from infants (followed from birth to six or eight months), preschoolers (followed between 18 and 30 months), and school-aged children (followed for a year between seven and nine years) with data from children of other ages. The latter were obtained by a cross-sectional measure of siblings in the same households.

Although the Nutrition CRSP was certainly not the first project to describe the almost universal experience of early growth-faltering in developing countries,[13] the data have altered our perspective on this problem in several ways. First, growth-faltering occurred even earlier than was expected, starting at about three months postpartum. Second, most growth-faltering had occurred prior to about 22 months of age, after which growth rate was relatively normal. As described in the INCAP experience in Guatemala,[14] little catch-up growth occurs at later ages. Third, because both length and weight were affected, the assumption that normal weight-for-length signifies currently adequate nutritional status must be rejected. Fourth, the Nutrition CRSP was relatively unique in that the extensive information enabled us to search for associations between growth-faltering and other variables with the aim of better understanding this common phenomenon. These are described here at some length, given the universal occurrence of early growth-faltering and its strong impact on later size and functional competence.

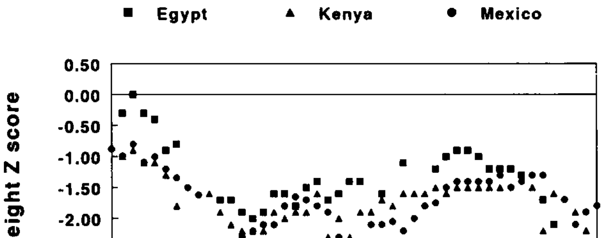

Figure 1. Longitudinal data from infants (followed from birth to six or eight months), preschoolers (followed between 18 and 30 months), and school-aged children (followed for a year between seven and nine years) combined with data from children of other ages. The latter were obtained by a cross-sectional measure of siblings in the same households.

Infants

Although the nonintervention design of the Nutrition CRSP does not permit us to infer causality, several factors were consistent predictors of infant size at six months and growth from birth to six months. Table 1 summarizes the predictors for weight. In all three projects, birth weight was a strong predictor of infant weight and length at six months. However, infants who weighed more at birth did not necessarily grow faster during early lactation; in Egypt, those with heavier birth weights grew more slowly between birth and six months than those who weighed less at birth. In Mexico and Kenya, birth weight was unrelated to subsequent growth rate, although in Mexico longer birth length predicted faster linear growth between birth and three months. Heavier, fatter mothers in Kenya and Mexico had babies who grew faster and were heavier at six months.

The general prevalence of morbidity was highest in Egypt and lowest in Mexico; infant morbidity was unrelated to the size and growth of Mexican infants. In Kenya, infants grew more slowly if they had more fever (including malaria) and respiratory illness, but diarrhea had no effect. In contrast, the duration of diarrheal events was the strongest (negative) predictor of weight change in Egyptian infants between three and six months.

The use of foods other than breast milk during infancy was uncommon in all three locations. In Egypt, however, liquids such as sugar water and rice water were fed to most infants from birth. In this unsanitary environment, the practice was associated with more diarrhea, which impaired growth. In Kenya, early infant supplementation was also

Table 1. Factors Associated with Infant Weight and Growth[a]

Factor	Egypt		Kenya		Mexico	
	Weight	Growth	Weight	Growth	Weight	Growth
Birth weight	+	—	+	0	+	0
Maternal weight	—	0	+	+	+	+
Maternal BMI	—	0	+	+	+	+
Morbidity	—	—	—[b]	—[b]	0	0
Amount of supplemental feedings	—	—	(—)[c]	(—)[c]	0	0
Maternal energy intake[d]	+	+	+	+	+	0[e]
Maternal diet quality[d]	+	+	+	+	+	+

[a] Weight at six months and weight gain from birth to six months. "+" signifies positive association; "—" negative; "0" none; "( )" weak.
[b] Related to fever and malaria, not diarrhea.
[c] Only associated with length, not weight.
[d] During lactation.
[e] Positively associated with infant growth from six to eight months.

common; by three months of age, 90% were receiving supplemental feedings of cow's milk and maize or millet gruels. Supplementation did not increase the prevalence of diarrhea but was associated with a slight increase in febrile illness and had a slight negative effect on growth. Two-thirds of the Mexican infants were still exclusively breast-fed at four to five months, and supplementation was unrelated to growth or morbidity. Overall, across projects, even infants who received no or few complementary foods still faltered in growth.

Maternal diet was related to infant growth. Lactating Egyptian and Kenyan women who consumed more energy had infants who grew faster between birth and six months; in Mexico, this was true for growth between six and eight months. It is difficult to determine cause and effect here because faster-growing infants and those exclusively breast-fed may consume more breast milk and thereby stimulate maternal energy intake.

The quality of the women's diets was consistently important for the growth of their infants. In Egypt, maternal intake of iron, thiamin, and vitamin B_6 predicted infant growth between birth and three months of age. In Mexico, infants of mothers who consumed more animal products grew more rapidly. In Kenya, growth was positively associated with maternal dietary quality and vitamin B_{12} intake during lactation. Maternal milk levels of vitamin B_{12} were low in the majority of women in both Kenya and Mexico. In Kenya, where marginal iodine deficiency was prevalent, household use of iodized salt and maternal iodine status were also strong predictors of infant weight and length at six months.

These factors were also entered into multiple regression models, which can be summarized as follows. The heaviest Egyptian infants at six months weighed more at birth, had mothers who consumed more energy and B vitamins during lactation, were of higher socioeconomic status, and had less diarrhea between birth and six months of age. These four factors explained 46% of the variance in weight at six months. Higher growth rate was associated with weighing less at birth and having a mother who ate more food and a better quality diet. Especially between three and six months, children who had more diarrhea grew less. These factors explained about half the variance in growth rate.

In Kenya, the strongest predictor of infant size at six months was again birth weight, followed by maternal fatness and socioeconomic status. Intake of supplemental foods had a weak negative impact. These variables together accounted for 27% of the variance in weight and 41% of the variance in height at six months. Growth rate between birth and six months was most strongly associated with maternal size and the amount and quality of food she consumed during pregnancy and lactation. Infant supplementation and morbidity had a weak negative influence.

In Mexico, about one-third the variation in infant weight at six months was explained by birth weight, maternal weight, and socioeconomic status. Likewise, almost half the variation in infant length was explained by birth length and maternal BMI. The rates of weight and length gain were strongly predicted by maternal size and fatness and weakly associated with the quality of the mother's diet. Unlike the situation in Egypt, diarrhea did not affect growth, perhaps because the prevalence was much lower.

Overall, data from the three projects demonstrate the importance of maternal size and fatness in determining infant size and growth rate. Growth failure is more severe in infants born to small, thin women, who also tend to have poorer quality diets, and to consume less food in the Kenyan situation. Some of the growth failure may be attributable to supplemental feeding, particularly in Egypt, where the amount of these foods is greater and the risk of infection higher, and to some extent in Kenya; this association could not be detected in Mexico, however, where there is less complementary feeding and less infection. A major question that needs further investigation is whether the micronutrient content of breast milk is adequate to support infant growth and function if maternal diet quality is poor.

Predictors of Size and Growth in Preschool- and School-Aged Children

The investigators at the University of California, Berkeley, performed cross-project analyses of child anthropometry.[7] Although each project performed its own analyses as well, the results from Berkeley are presented here because similar variables were used across the three projects. Factors associated with the children's weight and growth are summarized in Table 2.

Although the majority of growth faltering had occurred well before the age of 18 months, considerable variability was still observed during the later growth of children, especially at 18- to 30-months of age. Higher socioeconomic status predicted larger anthropometric measures in Kenyan and Mexican (but not Egyptian) toddlers and school-aged children. Better household sanitary conditions were associated with children's size but not with their growth. In all three projects, taller women had taller children and heavier women had heavier children, associations that were strongest in school-aged children.

Larger size or faster growth was unrelated to higher energy intake in Egyptian and Mexican preschoolers. In Kenya, all food intake variables, including energy but especially intake of animal products and available iron, related positively to toddlers' attained weight and length at 30 months and weight gain from 18 to 30 months. Energy intake remained a significant predictor when controlled for socioeconomic status, maternal anthropometry, child gender, and sanitary conditions.

Dietary quality was a determinant of growth of Kenyan and Mexican but not Egyptian children of this age. Principal component analysis identified two main food groups in each project. For Kenya, the first group, including milk, cereals, fat, potatoes, and sugar, was positively correlated with attained length and weight at 30 months and weight growth between 18 and 30 months. This group of foods was associated with higher socioeconomic status and provided more animal protein, fat, and vitamins A and B_{12} but less fiber, iron, zinc, thiamin, niacin, and folate. In contrast, the group of foods associated with low socioeconomic status included more maize, sorghum, green leafy vegetables, and beans. These foods were either negatively associated with growth or their consumption reflected the inability of poor households to afford animal products. Intakes of fiber and phytate were negatively related to height at 30 months. For school-aged children, the associations between dietary pattern and size or growth rate were strongest in the case of Mexico, where the higher-quality diet pattern predicted greater weight, height, and weight gain. In Kenya, it predicted only height gain, while in Egypt, height gain was more rapid with higher meat intake.

Morbidity explained some growth failure. When toddlers were ill, they consumed less food; in Egypt, average intake fell from 1150 to 1077 kcal/day ($p < 0.07$), in Kenya, from 862 to 730 kcal/day ($p < 0.0001$), and in Mexico, from 1116 to 884 kcal/day ($p < 0.08$). After adjusting for energy intake, severe diarrhea was negatively related to linear growth of Kenyan preschoolers and their weight at 30 months. Similarly, attained length of Egyptian preschoolers was lower in children who had suffered more severe diarrhea. Interestingly, low weight-for-age or weight-for-height at 18 months predicted an on-going risk of severe illness, although it is also clear that Egyptian preschoolers suffered from the most illness despite adequate energy intake.

Analyses of data for preschool-aged children revealed two interesting findings.[15] First, the rate of weight gain was positively associated with the rate of length gain only in those children whose diets were of reasonable quality. If dietary quality (intake of animal products) was poor, weight and length gain were *inversely* correlated, suggesting that these different aspects of growth can take place simultaneously only if micronutrient intake is adequate to support it. This means that using one of these indicators as a proxy for nutritional status rather than the other will classify different children as malnourished. The second observation was that the size of a mother is positively associated with the size of her preschooler only if the child is eating a high-quality diet; if the diet is poor, the child's genetic potential is not realized at that age.

In summary, by 18 months of age the toddler is already stunted and soon after grows closer to the NCHS reference rate. Energy intake in Kenya, and better dietary quality in all three locations, was associated with more growth between 18 and 30 months. Severe diarrhea adversely affected growth in Egypt and Kenya. The household environment is

Table 2. Factors Associated with Weight and Growth of Preschoolers and School-Aged Children[a]

	Egypt				Kenya	
	Preschool		School		Preschool	
Factor	Weight	Growth	Weight	Growth	Weight	Growth
Socioeconomic status	0	0	—	0	+	+
Sanitation	+	0	0	0	+	+[b]
Morbidity[c]	—[b]	0	0	0	—[b]	—[b]
Maternal BMI	+	0	0	0	+	0
Energy intake	0	0	—	0	+	+
Dietary quality	0	0	0	+[d]	+	+

[a] Adapted from Ref. 7; symbols same as in Table 1. NR = not reported.
[b] Significant for length only.
[c] For preschoolers, when added in regression models, including socioeconomic status, sex, sanitation, maternal height, and child's energy intake.
[d] Meat intake.

also an important predictor, with the smallest children at this age clearly coming from larger households with lower socioeconomic status, literacy, and sanitation; these factors are also associated with the quality (and in the case of Kenya, the quantity) of the children's diet.

Cognitive and Behavioral Outcomes

The findings suggest that, overall, growth-stunted children of all ages tended to perform less well on cognitive tests than their heavier or taller peers.

Infants

From the description of pregnancy outcomes, maternal size and diet during pregnancy appeared to affect infant neurobehavioral performance at birth. Mother's size and diet also predicted infant behavior during the first six months of life, although growth-stunting also played a role.

In all three countries, smaller infants smiled less and were more drowsy at three and six months. Mexican and Egyptian[16] infants who smiled more often had mothers who consumed more animal products and a better quality diet. The importance of maternal micronutrient status is also demonstrated by the positive associations between Mexican women's iron and vitamin B_{12} status in pregnancy and lactation and their infants' performance on the Bayley Motor and Mental scales at three and six months. Egyptian mothers who were anemic spent substantially less time taking care of their infants.

Maternal dietary quality was strongly associated with Egyptian infants' motor performance at six months; infant gastrointestinal disorders had a negative impact. Mental and motor performances were better in Mexican infants who were heavier and taller at three months. This association between size and performance was less clear at six months, when the best predictors of mental and motor performance were higher birth weight and the mother's diet quality during pregnancy and lactation. Analyses have not yet been performed to determine the predictors of mental performance in Egyptian infants or the relationship between the diets of Kenyan women and infant cognition and motor ability.

Preschool-Aged Children

In all three countries, smaller preschoolers tended to perform less well on cognitive tests. Energy intake per kilogram of body weight was not related to cognitive performance, but dietary quality was a consistent positive predictor. The association between stunting and cognitive ability, however, generally remained significant even after controlling for environmental and parenteral factors and food intake (quality and quantity).[17] Thus, dietary quality may affect the size of preschoolers and possibly their play, behavior, and verbalization. The quality of child care, including the amount of social and verbal interaction, also made a difference in all three locations and appeared to be more important than socioeconomic status per se.

It is difficult to say whether current diet plays an important role in current performance or simply represents a continuation of the type of diet that was associated with growth-stunting earlier in life. Three observations suggest that previous growth-stunting is more important than current diet. Children who were stunted at 18 months tended to perform less well at 30 months, emphasizing the importance of early growth deficit for later performance. In Mexico, analyses revealed that relationships between cognitive function at 30 months and current diet quality disappeared when length at 18 months was controlled statistically. A follow-up study performed three years later in Kenyan chil-

		Mexico			
School		Preschool		School	
Weight	Growth	Weight	Growth	Weight	Growth
+	+	+	0	+	0
+	+	+	0	+	0
NR	NR	0	0	0	0
+	+	+	0	+	0
+	0	0	0	+	0
0	+[b]	+	+	+	+[b]

dren produced the impressive finding that between 18 and 30 months energy intake and especially the intake of animal products were positively associated with cognitive skills at five years of age.[18] The best set of predictors of five-year performance were animal product intake between 18 and 30 months, the Bayley mental score at 30 months, and household socioeconomic status. The dietary and environmental resources of households affected the five-year cognitive score independently.

Intensive observations of Mexican preschoolers revealed that more growth-stunted preschoolers (who had poorer quality diets) had adverse behavioral changes. Specifically, these children were more apathetic, spent considerable time doing absolutely nothing, more often followed an adult passively, had less affect, cried more, and had fewer positive interactions with others.[19] Both Egyptian and Kenyan children who were fed more animal products played and verbalized more, using symbolic play, which is considered an early marker for later advanced cognitive development.

These results illustrate that marginal malnutrition not only affects children's growth and mental function, but has adverse effects on their emotions and behavior, quality of life, and ability to function in society. Such behavior changes are likely to affect children's interactions with their environment, leading to further developmental delays. The extent to which these might be reversible by nutritional interventions is unclear.

School-Aged Children

School-aged children who were heavier and taller in Kenya and Mexico had higher scores on tests of verbal understanding and Raven's Progressive Matrices (a fairly good measure of overall intellectual ability). Virtually all the anthropometric and dietary measures were positively associated with cognitive scores in Kenya.[20] In Mexico, size was also a good predictor of cognitive performance, but measures of fatness were not.[21] Equivalent Egyptian analyses have not been reported.

Better nutrition (diet quality but not energy intake) also improved the attentiveness of Kenyan school-aged children to their class work. In this group, duration of schooling, intake of animal products, weight-for-age, and socioeconomic status accounted for 54% of the variance in cognitive scores. Virtually the same predictors were found in Mexico.

Playground behaviors in Kenya were more positively related to concurrent food intake than to size or dietary quality; the Kenyan children often ate little before school and brought little or no food with them. Mexican boys who consumed poor-quality diets were more likely to be rated by their teachers as withdrawn, while girls were not. This may reflect sex stereotypes on the part of the teachers. In addition, cognitive and behavioral performance of Mexican girls was quite strongly related to socioeconomic status of their home, whereas for boys it was not, suggesting less restriction of boys by the home environment. In general, Mexican children with higher cognitive scores were more socially competent and less introverted.

Marginal iodine deficiency in Kenya was associated with poor performance by school-aged children. Iodized salt was used by only about one-third the households, and failure to use it had adverse effects on school examination performance and scores on Raven's Progressive Matrices, Verbal Meaning, Picture Drawing, and Block Design tests. Thyroid hormone levels (T_3) were positively related to school examination scores and verbal ability, attentiveness in class, and activity on the playground.

Specific Micronutrient Deficiencies

Given the importance of dietary quality as a predictor of adverse functional outcomes, some effort was made to confirm the probability of specific micronutrient deficiencies from dietary intake data and to substantiate these with available biochemical and hematologic information. Murphy et al.[7,22,23] used the probability approach to estimate the risk of inadequate mineral and vitamin intakes. This task was made feasible by creating an "international minilist" of food composition data. For minerals, factors that affected bioavailability were calculated and considered in the estimates of probable risk. These included phytate, fiber, ascorbic acid, meat factor, heme iron, and tea. Table 3 shows the predicted prevalence of inadequate intakes of the major nutrients for preschool- and school-aged children. The pattern of low intakes was similar for adults because members of the same household usually ate the same foods.

In all locations, the total dietary intake of minerals was reasonably adequate, although mineral bioavailability was a potential problem. For iron, the estimated amount of absorbable iron eaten by preschool-aged children, for example, was only 0.4–0.7 mg/day, compared to the requirement of 1 mg/day. The potentially poor absorption was due to the high phytate and fiber content of maize and legumes (in Kenya and Mexico), the low intake of iron from meat, fish, or poultry (in Kenya and Mexico), and low dietary vitamin C (in Mexico). These estimates of low iron bioavailability were supported by the high prevalence of anemia in all countries.[21] For example, 60–70% of the preschool-aged children across projects had anemia, 35–39% had low ferritin, and about 27% had both. A similar prevalence of iron deficiency was found in school-aged children, and approximately 20–50% of adult women were anemic. Anemia was rare in men in Egypt and Kenya but not in Mexico. Low ferritin was uncommon in men in all three locations and suggests that the anemia in Mexican men was due to a deficiency of vitamin B_{12} rather than of iron (unpublished).

The quantity of zinc consumed by Kenyans was low, and because of the high dietary phytate and fiber, its bioavailability was very low in Kenya and Mexico and poor in Egypt. Few Kenyan children and only about half the Mexicans met their normative zinc requirement (the amount needed to maintain stores). The higher calcium intake of Mexicans was from the lime added during the preparation of tortillas. Interestingly, the predicted risk of zinc inadequacy was lowest in Egypt, although zinc deficiency at a population level was first identified there several decades ago. Copper intakes were unlikely to be a problem in any of the locations, at least for healthy children.

Compared to normative requirements, intakes of thiamin, riboflavin, and vitamins A, B_{12}, D, and E were most often inadequate across all three projects. Surprisingly, given the lower amount of food and animal products available to Kenyans, they ranked lowest only in retinol (but not total vitamin

Table 3. Predicted Percent Prevalence of Inadequate Micronutrient Intakes in Children[a,b]

	Toddlers			School-Aged Children		
Nutrient	Egypt (N = 96)	Kenya (N = 100)	Mexico (N = 59)	Egypt (N = 63)	Kenya (N = 138)	Mexico (N = 84)
Iron, basal	65	36	88	70	31	87
Iron, prevent anemia	36	13	43	43	8	41
Zinc, normative	36	90	68	24	79	43
Zinc, basal	10	57	25	3	29	9
Copper, normative	0	0	0	0	0	0
Copper, basal	0	0	0	0	0	0
Calcium	90	88	2	69	91	0
Phosphorus	2	6	0	0	0	0
Magnesium	0	0	0	0	0	0
Thiamin	1	0	6	0	0	7
Riboflavin	20	2	52	16	2	83
Niacin	0	0	0	0	0	0
Folate	0	0	0	0	0	0
Vitamin B_{12}	3	44	8	24	87	38
Vitamin B_6	0	0	0	0	0	0
Vitamin C	3	1	63	2	0	35
Vitamin A, normative	32	12	68	34	6	61
Vitamin A, basal	2	0	19	9	1	24
Vitamin D	100	100	100	100	100	100
Vitamin E	21	85	92	4	43	86

[a] The basal requirement is the amount needed to prevent clinical signs of functional impairment. The normative requirement is that needed to maintain desirable tissue stores.
[b] Adapted from Ref. 7.

A), and vitamins B_{12}, D, and E—most of which are found mainly in animal products. From plasma and milk analyses in Kenya and Mexico (unpublished), vitamin B_{12} deficiency was found to be common. Only one of 59 Mexican preschoolers met the recommended intake of 0.4 mg α-tocopherol equivalents per gram of polyunsaturated fatty acid; a more recent study of preschoolers in the same region showed that most had low plasma levels of vitamin E, with about one-third having low levels of retinol as well (E. Muñoz et al., unpublished data). Poor ascorbic acid intakes were common for Mexican children and could adversely affect iron absorption.

In summary, based on nutrient intake data, a high risk of multiple micronutrient deficiencies was observed in all three populations. This observation is supported for iron deficiency by the common occurrence of anemia and low plasma ferritin. Although other biochemical analyses were project-specific, for every nutrient examined (except folate in Mexico), substantial numbers of persons showed evidence of deficiency.

Conclusions and Policy Implications

In these communities, as is typical in developing countries, growth-faltering starts almost immediately after birth. The Nutrition CRSP demonstrated that stunting during this period is responsible for small size later in childhood and most likely throughout life. The significance of this early growth failure is that it is accompanied by measurable deficits in behavior and cognitive performance that are still manifest during the school-age years. This finding was also confirmed in the recently completed INCAP follow-up study, which examined the relationship of early stunting and nutritional supplementation to later size and function. Work performance and mental function in late adolescence were better in those who had been nutritionally supplemented in early childhood.[24]

It is imperative that we make more effort to understand the reasons for this early growth-faltering, which is most rapid from about three months after birth, when the infant depends primarily on nutrients stored during fetal development and consumed during lactation. This finding raises the potential importance of maternal nutritional status as a determinant of infant growth. In the Nutrition CRSP, birth weight predicted infant size at six months, as did maternal weight and especially fatness. This indicates intergenerational effects of growth-stunting by unknown mechanisms that might include, for example, differences in placental size. Certainly, the growth failure cannot be ascribed to "genetic" differences because Mexican-American children who move to the United States at an early age grow to the same size as those on whom the reference is based.

What role does nutrition play in growth-stunting? The Nutrition CRSP was designed to test the hypothesis that marginal *energy* deficit, caused by lack of food, adversely affected human functions. This seemed most probable given the current realization that protein was unlikely to be the limiting nutrient in most populations. One of the more surprising findings of the Nutrition CRSP was that energy intake was not inadequate, and therefore was not associated with growth-stunting or poor performance in the Egyptian or Mexican groups. In addition, inadequate protein or amino acid intake did not appear to be a serious problem in any of the three countries.

In retrospect, it is obvious that energy deficiency is likely to be present when there are frank shortages of food or incomes are very low; to avoid energy deficiency, households will resort to various strategies in an attempt to procure enough energy from staple foods, but the quality of the diet will be inadequate. These relationships are illustrated clearly in Figure 2, produced by Backstrand from the Mexican data,[6] showing that as the total household energy needs increase (a function of more persons in the household and their age, sex, and size), the quantity of energy consumed from maize increases linearly and keeps pace with needs, while the intake of nonmaize foods falls off rapidly. It follows that where energy/food shortage exists, dietary quality will be a problem as well.

These results suggest that marginal energy deficiency in a community would be most readily de-

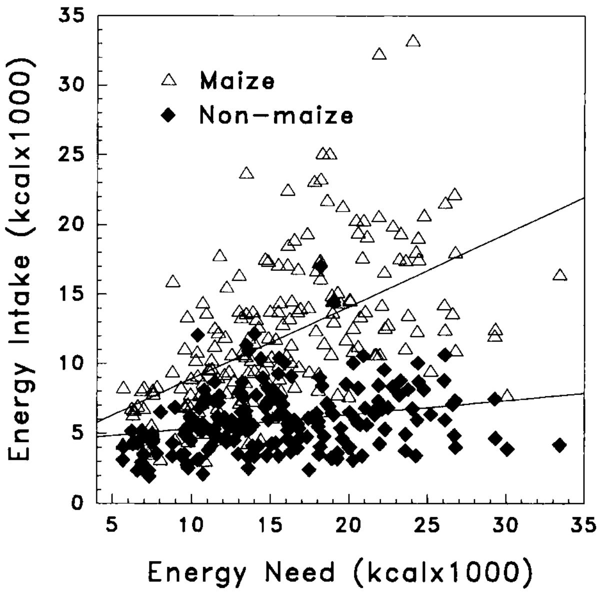

Figure 2. A scatterplot of household dietary energy from maize and nonmaize sources with respect to household energy needs.

tected by monitoring food security/food shortages, while inadequate diet quality would be revealed by measuring the frequency of consumption of animal products or other nutrient-rich foods that can be included in the diet when resources are less scarce. Both of these are qualitative approaches and might replace difficult, expensive, and time-consuming quantitative food intake methods.

The term "poor quality" describes a diet that is low in vitamins and absorbable minerals. Persons could be classified in terms of where they ranked in their community's dietary continuum, ranging from a poor-quality diet in which most energy and other nutrients come from cereals and legumes to a better-quality diet that contains more animal products, fruits, and vegetables. Children in all three countries who consumed better quality diets grew faster, performed better on cognitive tests and in school, and behaved in a more interactive, less apathetic manner. Even as early as birth and the first six months of life, infants had better neurobehavioral development if their mothers had better-quality diets during pregnancy and lactation.

The specific micronutrients limiting growth and behavioral development have yet to be identified. Using the diets of preschoolers and school-aged children as examples, the probability was high that intakes of iron, zinc, calcium (except Mexico), riboflavin (except Kenya), vitamin B_{12}, vitamin C (Mexico only), and vitamins A, D, and E would be inadequate. The high fiber and phytate content of maize-based diets in Kenya and Mexico impairs the absorption of minerals such as iron and zinc.[25] Anemia related to iron deficiency was highly prevalent in persons of all ages and was probably related to poor vitamin B_{12} status in Kenya and Mexico. Vitamin B_{12} deficiency has been assumed to be rare in developing countries, but its high prevalence in the two countries in which deficiency was examined means that this situation should be reexamined using more accurate modern assessment techniques. Few analyses were performed on breast milk samples, but the low concentrations of vitamin B_6 in Egypt and vitamin B_{12} in Kenya and Mexico suggest that the nutritional adequacy of breast milk should be reexamined in developing countries. Morbidity, especially that involving malabsorption and parasitic infections, would be expected to contribute to multiple micronutrient deficiencies in persons of all ages.

From the results of the Nutrition CRSP, we can arrive at several indisputable conclusions that have obvious policy implications. First, there is a need to develop and test interventions that will improve the micronutrient status of marginally malnourished populations. Second, pregnant and lactating women, infants, and probably preschoolers are the most urgent candidates for these interventions. Interventions for the mother may improve infant outcomes at birth and reduce early growth-stunting. During lactation, breast milk quality (especially vitamin content) and subsequent infant development are likely to benefit from interventions to improve micronutrient status; such efforts may also help to protect the mother and fetus from depleted stores in the next pregnancy. Without such interventions, the promotion of exclusive breast-feeding, which is important for other reasons, may fail to provide the infant with adequate amounts of nutrients. Third, micronutrient interventions or improvements in dietary quality may improve the growth of school-aged children as well as their cognitive, behavioral, and school performance. Finally, we now know that marginal malnutrition, with associated poor quality diets, may be even more prevalent than formerly recognized. It is particularly clear that growth-stunting is accompanied by deficits in human development and function that should not be ignored.

How do we improve the availability of micronutrients to persons in communities such as these? This is currently a "hot topic" within and among organizations concerned with improving the nutritional status of persons in developing countries. Much has been written about the relative situational merits of strategies such as providing supplements, fortifying and enriching foods, preserving foods that are rich sources of carotenoids, and improving weaning foods. The Nutrition CRSP showed that multiple micronutrient deficiencies undoubtedly exist simultaneously, which underscores the need to improve on "magic bullet" approaches that provide only one or a few micronutrients. (Iodine is the exception here in that deficiency can occur in otherwise well-nourished individuals.)

In part, the current resurgence of concern about micronutrient status may be ascribed to the proven impact of intervention programs. For example, the observation that vitamin A interventions reduce child mortality, as well as prevent onset of permanent clinical deficiency symptoms, has been a powerful and effective argument in support of putting more resources into vitamin A interventions. In addition, we now realize that it may actually be possible to prevent some of the consequences of marginal malnutrition by economically and logistically feasible micronutrient intervention strategies. This is different from the scenario only a few years ago when it was assumed that only radical changes in economic, health, and resource status could treat the problem of chronic malnutrition in developing countries. While such changes are undeniably still desirable, the nutrition community now feels empowered to try food- and nutrient-based approaches to alleviate the problem. Much remains to be learned about which of these are most effective and in what situations, but at least major efforts are underway at last.[26]

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26. For example, the Agency for International Development, which funded the Nutrition CRSP, is launching a massive effort (OMNI, the Opportunities for Micronutrient Interventions project), to provide technical assistance for combating micronutrient deficiencies in developing countries.