At the present time, more children survive acute protein malnutrition than those who die of it; however, a number of studies indicate that these children show retardation of growth, physiological disorders, and retardment in some aspects of their biochemical maturation.

Scope of the Problem of Malnutrition in Preschool Children

Almost fifty years have elapsed since Correa in Yucatán, Mexico, described under the name culebrilla a pathological condition present mainly in toddlers and associated with a deficient intake of foodstuffs of animal origin. Reports from South America, India, Africa south of the Sahara, the Balkans, China, Southeast Asia, the Philippines, and Central America between 1908 and 1952 showed the widespread occurrence of the disease (1, 2). The prevalence surveys of Brock and Autret (3) in Africa, Autret and Béhar (4) in Central America, and Waterlow and Vergara (5) in Brazil made apparent the great magnitude of the problem, confirming previous reports on the frequency of cases admitted to general and pediatric hospitals.

Since 1955, protein-calorie malnutrition has been recognized as a disease of world-wide incidence; though it may vary in cause, it has basically the same characteristics of clinical and biochemical pathology in all countries and with regional variations of only secondary importance (6).

A number of reviews of protein-calorie malnutrition have appeared during the past fifteen years. Particularly detailed have been those of Waterlow (7) in the West Indies, Meneghello (8) in Chile, Brock and Autret (3) in Africa, Oomen (9) in Indonesia, Gopalan and Ramalingaswami (10) in India, Gómez et al. (11) in Mexico, Trowell, Davies, and Dean (12), Béhar et al. (13), Ramos Galván and Cravioto (14), Waterlow, Cravioto, and Stephen (2), and Viteri et al. (15).

Prevalence and Incidence

There are no reliable statistics on the incidence of protein-calorie malnutrition. Hospital statistics are of little value for the purpose. In some regions 50 per cent of all children admitted to the pediatric wards are said to be suffering from malnutrition of one degree or another. Hospital figures, however, can only show whether a disease is rare, common, or very common, since without knowing the size and composition of the population served by the hospital it is impossible to relate these figures to the population at risk.
Few field surveys have been done on a large enough scale to provide valid data. An exception was the survey of Rao et al. (16) in India, in which more than four thousand children under five were examined in their homes. The prevalence of severe protein-calorie malnutrition accompanied by clinical edema was just under 1 per cent. Since the subjects were examined only once, and since it is reasonable to assume that in a month's time a child with severe protein malnutrition either recovers or dies or is removed to a hospital for treatment, it is reasonable to estimate—if there is no seasonal variation—that some 10 per cent of the preschool children would develop severe protein deficiency in the course of the year.

**Mortality**

When the age-specific mortality rates for preschool children in the U.S.A. are compared to those in areas where protein-calorie malnutrition is prevalent—for example, the rural areas of Guatemala—it is readily apparent that starting with figures almost equal for deaths occurring during the first day of life, the U.S. rates decline rapidly in contrast to the Guatemalan figures. This phenomenon is even more striking when the comparison is expressed as a ratio (see Table 1, Figure 1) (17).

In the United States the rate decreases rapidly after birth, as soon as perinatal causes cease to be the main determinants; after the first month of life, and more so after the first year, the chances of a preschool death are rather small. In rural Guatemala, on the other hand, as in most preindustrial countries, survivors of the perinatal period are still quite likely to die during the first year of their lives and continue at great risk for another two or three years.

An investigation of causes of death after the perinatal period shows that respiratory and gastrointestinal disorders, together with intestinal parasites, are those reported most frequently in the official records. Very seldom are deaths registered as due to any form of malnutrition. Evidence indicates that this is largely an artifact of registration practice. Béhar (17), through an investigation of each death occurring over a period of two years in four rural Guatemalan villages where the mortality rates are similar to those for the country as a whole, found that out of 109 deaths occurring in children under five, 38 were typical cases of severe protein-calorie malnutrition accompanied by edema (kwa-
shiorkor), and 2 were of severe malnutrition without edema. In other words, approximately 33 per cent of all deaths in this age group were undoubtedly related to malnutrition. If to this figure are added all the other cases in which malnutrition was an important contributory factor although not the immediate cause of death, it can easily be concluded that malnutrition played a major role in no less than 50 per cent of the total number of deaths in preschool children (18).

At present it is an accepted fact that deaths due to malnutrition are customarily listed under other causes and that official statistics fail to reveal protein malnutrition as a main contributor to the high rates of preschool mortality. The reason is that in the vast majority of regions where malnutrition is prevalent there is little or no medical certification of death and only rarely can the layman in charge of the civil register make a diagnosis of malnutrition. Moreover, since a large number of malnourished children die of acute electrolyte disturbances due to diarrhea (19) or of respiratory infections, many deaths from malnutrition are officially entered, even in places with medical certification, as caused by infectious diarrhea and/or bronchopneumonia.

Because of inadequate sanitary conditions, children living in preindustrial regions tend to suffer more from enteric infections and other communicable diseases, but it is also important to consider that the severity of the consequences has been shown to be due in part to the almost universal presence of malnutrition of various degrees. Thus, Gordon et al. (20) have reported that in a rural area of Guatemala between February 1961 and June 1962, the percentage of cases of severe diarrhea came to 22.9 among well-nourished children but 40 among third-degree-malnourished subjects. Similarly, Vega et al. (21), studying a measles epidemic, found that the frequency and severity of bacterial complications increased in proportion to the intensity of malnutrition in children below the age of five.

Separately or in combination, infection and malnutrition as important causes of death have been disappearing in highly industrialized countries, but in the preindustrial areas of the world they continue to be responsible for the largest proportion of total deaths (22).

**Morbidity**

It is important to recognize that at present more children survive severe protein malnutrition than die of it. Better knowledge of the biochemical characteristics of malnourished children, together with better means for rapid diagnosis and assessment of the effect of treatment of electrolyte disturbances and infections, has played a major role in this reduction. The increasing number of survivors is reflected in the fact that whereas in 1952 approximately 30 per cent of children with third-degree malnutrition died, fewer than 5 per cent died during 1962-1964. Thus, at present the great majority of children with protein-calorie malnutrition do not die, but yield a pool of survivors who may be handicapped in a variety of ways and for varying periods of time, transiently or permanently.

When malnourished children start to recover they do so with great rapidity at first. They very often grow at twice or three times the normal rate for their chronological age. However, if observations are continued for a longer period it becomes apparent that the initial rate is not excessive but is equal to that seen in a normal younger child of the same size as the malnourished subject; later on the rate shows the periodic accelerations and decelerations of normal growth but with a time lag in comparison with the child who has not suffered early malnutrition. Therefore, the weight gain is size-dependent and not age-based.

Pediatricians and nutritionists have often been misled by the high rates of growth at the beginning of the rehabilitation period. They have speculated that it will continue
Until the child catches up to normal children. Unfortunately, the few studies available indicate that puberty appears and growth ceases at the usual chronological age, with the net result being an undersized adult. At adolescence children from areas where infantile malnutrition is prevalent are shorter than children from the same age and ethnic group in more developed areas (23–28).

Dean’s studies on body weight and measure of rehabilitated cases show that after the child has recovered his length remains shorter and his skeletal development retarded in comparison to those of normal individuals of the same age and ethnic group (29). Similar findings have been reported by Barrera Moncada (30), who has followed Venezuelan children recovered from malnutrition for periods up to ten years.

The effect of previous malnutrition on the ultimate proportions of body segments is illustrated by the data of Leitch (31) whose analysis of the Carnegie United Kingdom Dietary and Clinical Survey showed that leg length was better than body height as an indicator of expenditure on food, an indirect way of assessing nutritional status. Ramos Galván (32) has reported that ratios of body proportions in school children living in conditions that produced chronic malnutrition in early infancy might be a better way of assessing adequacy of intake than total height or weight.

Numerous examples of physiological and biochemical alterations in malnourished children show that malnutrition not only arrests certain aspects of biochemical maturation but also seems capable of producing a reversion to an earlier stage of development. Thus, for example, when water content and distribution in malnourished children are recalculated on the basis of the age indicated by the actual weight or height, it is apparent that both content and distribution are “normal” for a child who would have the same height or weight as the pathological patient (33). Similar conclusions can be reached when the data for fat absorption, plasma lipid concentrations, changes in proportions of alpha and beta lipoproteins, modifications of cholesterol concentrations in blood, and urinary excretions of creatinine are plotted against the age for height and/or the age for weight (34).

Immunologically, too, it is of interest that when challenged antigenically children recovering from malnutrition give responses similar in magnitude to those obtained in normal infants very much younger (35).

Kumate et al. (36) found in 118 malnourished children a diminution of about 20 per cent in the levels of hemolytic complement. The decreases were similar for all four components determined: C-1, C-2, C-3, and C-4. The correlation between the degree of malnutrition, estimated as the percentage of difference between the theoretical and the actual body weight, although low, was statistically significant. Similar results were obtained by Ramunni and Moretti (37) and by Vasile (38).

Unpublished observations of Kumate at the Children’s Hospital of Mexico have shown that 7-S gamma-globulin is reduced in severe malnutrition, with average values of about 400 mg per cent as against about 1,000 mg per cent in well-nourished controls.

Free amino acid concentrations in blood plasma of children affected with either marasmus or kwashiorkor generally show an abnormally high ratio of phenylalanine to tyrosine (39). A similar finding in urine previously reported by Cheung et al. (40) suggests the possibility of a defect in the enzyme system that metabolizes phenylalanine into tyrosine.

The extent to which normal biochemical maturation can be altered in humans by malnutrition is perhaps best illustrated by Dean (41), who has been able to reproduce in preschool malnourished children the main biochemical lesions characteristic of the absence or a marked reduction of certain enzymes participating in the metabolism of the aromatic amino acids histidine, tyrosine.
and phenylalanine—a phenomenon normally present only in the newborn infant.

Studies on morbidity thus show that previously malnourished children are stunted in growth, exhibit physiological derangement, and are delayed in some aspects of their biochemical maturation.

Psychobiological Development

In spite of these impressive advances made in the knowledge of the clinical and biochemical aspects of nutrition deprivation during the past seventeen years, scientists have only recently become concerned about the potential delay in the psychobiological development of infants suffering from protein-calorie malnutrition.

The little attention given to this subject matter is quite surprising in view of the fact that from the very first descriptions of protein-calorie malnutrition in children it was clearly stated that disturbed behavior was among the earliest symptoms, that it prevailed throughout the duration of the disease, and that a return to normal behavior could be considered one of the best guides for prognosis. The accounts given by several authors showed that apathy was probably the single most common finding; the severely ill patients seemed to have lost all the normal curiosity and desire for exploration so characteristic of the normal child. Renewal of interest is still considered one of the most reliable signs of improvement (11, 42-44).

Following Wilson’s attempt to distinguish different categories of apathy—primarily physiological, “apathy” at the community level, and “apathy” as a characteristic of a regional culture (45)—the apathy of the protein-calorie-deficient child would possibly be a mixed type: deprivation itself could cause it, as is the case in experimental animals fed on low-protein, high-carbohydrate diets (46), and on the other hand it could also be elicited as a sequela to the emotional deprivation and loss produced by the separation that accompanies hospitalization.

It has been repeatedly stated that in most communities where malnutrition is highly prevalent the mother-child relationship prior to weaning is a very close one, to the point that the mother takes the nursling with her everywhere she goes. In conjunction with the observations of Geber and Dean (47) that recovery is more rapid among infants whose mothers show the greatest interest and solicitude, this fact has been interpreted as suggesting that separation anxiety may play an important role in the behavioral disturbance. In addition, the psychological behavior of malnourished infants is markedly similar to that of healthy children fifteen to thirty months old who have been separated from their mothers by hospitalization, as described by Bowlby (48). Deprivation of an effective and continuing mother-surrogate—for example, by repeated, random changes in responsibility for the child’s care—may also play a part in some communities, where this is a common practice starting when the mother’s next pregnancy becomes evident (Cravioto, in preparation). However, it is important to remember that, as Meneghello (8) has pointed out, the psychological changes in malnutrition are not simply a response to hospitalization, since they are already present.

No matter what the cause of the apathy, it is clear that as chronic malnutrition develops from mild-moderate to severe, failure to respond appropriately to changing stimuli is reflected in progressive behavioral regression.

Since behavioral changes, though less dramatic than physical wasting, may have a greater importance and in the long run be more important because of their possible interference with cognitive development, research from areas in which protein-calorie malnutrition in children is widespread has tried first of all to answer the practical question of whether the resulting biochemical and growth lags are associated with slowness in mental development. Investigators from these areas have also wished to know
whether such lags, when found, are permanent or merely transient.

Three strategies have been used to assess the potential relationship between nutritional deprivation and the functioning of the central nervous system: electroencephalography, psychological test behavior, and evaluation of development of brain functioning.

Electroencephalographic Studies

Electroencephalography as a method for studying neural functions in malnourished infants has been employed by Sarrouy (49), Engel (50), Valenzuela (44), and Nelson and Dean (51). The EEG recordings have consistently shown changes in the form, frequency, and amplitude of the waves, even in mild-moderate cases. On admission all the patients exhibit either polyrhythmic or monorhythmic and sinusoidal waves. The frequency is considerably diminished; the amplitude, also markedly reduced, attains values of only 30 to 50 microvolts instead of the 150 to 200 characteristic of waves of such a low frequency. Using chloral hydrate sedation, Valenzuela found an absence of the rapid rhythm normally shown by healthy infants under sedation. With successful treatment the EEG tends more and more to conform to that of healthy children of similar age. First the frequency and amplitude of the waves increases, although bouts of slow monorhythmic waves appear from time to time. Finally, when the child is well on the way to recovery, the abnormalities disappear; the total rehabilitation takes from forty to sixty days.

In 5 out of 47 patients studied, Nelson and Dean found focal disturbances in the temporal areas of the brain. These have been interpreted as indicative of a local reaction to the generalized state of intracellular overhydration that is a very common feature of severe chronic infantile malnutrition (52). Their usual origin in the temporal lobe may be only a reflection of the lobe's tendency to react more easily than other brain regions.

Psychological Test Behavior

1. Mild-Moderate Forms of Malnutrition

Kugelmass, Poull, and Samuel (53) studied the effects of nutritional improvement on mental performance in children matched for chronological age and IQ but differing in nutritional status. Two matched groups each containing 50 children ranging in age from two to nine years were established. One was identified as normal well-nourished, the other as normal malnourished. After a period varying from one to three and a half years, during which the nutritional status of the normal malnourished group was improved, the psychological testing was repeated. Whereas the average IQ of the initially well-nourished group remained markedly stable, that of the initially malnourished group rose an average of 18 points following improvement in nutritional status.

Stoch and Smythe (54) in South Africa have followed semilongitudinally two groups each composed of 18 Negro children ten months to two years old and 3 between two and three years. At the beginning of the study none of the children showed evidence of organic disease apart from gastroenteritis that responded rapidly to treatment. The essential difference between the two groups was in their state of nutrition, as judged by anthropometric measurements.

The group considered better-nourished included children attending an all-day nursery, where they received adequate meals and vitamin supplements, while both parents worked. The undernourished children were seen for the first time at the age of about one year and were subsequently examined at six- to twelve-month intervals. Although the families of the better-nourished group tended to be larger and to have higher incomes, less unemployment, and slightly better educations, both groups were considered to belong to the lowest economic stratum of unskilled labor. The intelligence quotients of the parents in both groups were very low. The raw scores on the Raven Test...
of Intelligence were not significantly different.

The children were tested by means of the Gesell Infant Scales of Mental Development up to the age of two years; with the Merrill-Palmer test, adapted to African children, from two to six; and thereafter with the Individual Scale of the National Bureau of Educational Research of South Africa, which is based on the 1916 Stanford-Binet Scale. Anthropometric measurements were also taken every time the children were examined.

The results showed that at all ages not only were the figures for height, weight, and head circumference lower for the undernourished group, but the mean intelligence quotient was also well below that of the better-nourished group. The disparity remained relatively constant throughout the observation period. A difference of 22.62 points found on the final testing was statistically significant at the 1 per cent level.

Cross-sectional studies of behavioral development conducted in Africa (55), Mexico (56), and Guatemala (57), using the Gesell technique and the André-Thomas method, show that in these preindustrial countries newborn infants generally score higher, and never lower, on psychomotor and adaptive development than North American or European children. The Gesell tests, usually considered suitable only for children over four weeks of age, can be used with younger African, Mexican, and Guatemalan children because their motor development at two or three weeks is similar to that of Western European infants twice or three times as old. Interestingly enough, Nelson and Dean (51) have reported that electroencephalograms of newborn African infants are suggestive of greater maturity than is usually found in the newborn European child. Soon after birth, however, children from these preindustrial areas show deceleration, so that by the time they are eighteen to twenty-four months old their performance is below that shown by their European counterparts.

Following Dean's idea of expressing the Gesell Developmental Quotients (Y) for a given age (x) on the basis of a scale on which 100 represents the performance of the “normal” North American or European child of the same age as the children being tested, the relationship between quotients and chronological age could be described by a curve of the type \( Y = ax - b \) for the total span of 0 to 42 months; a satisfactory approximation of this curve would be obtained by fitting a series of straight lines over subsets of smaller age intervals (Tables 2 and 3).

Even children who later develop kwashiorkor usually grow well during the first months of life. Later on, when the mother's milk no longer meets the infant's needs and

<table>
<thead>
<tr>
<th>Field of behavior</th>
<th>Age group (months)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-12</td>
<td>13-24</td>
<td>25-36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a</td>
<td>b</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Motor</td>
<td>155.03</td>
<td>-5.22</td>
<td>128.18</td>
<td>-1.53</td>
</tr>
<tr>
<td>Adaptive</td>
<td>122.69</td>
<td>-1.76</td>
<td>110.07</td>
<td>-0.53</td>
</tr>
<tr>
<td>Language</td>
<td>131.51</td>
<td>-2.84</td>
<td>90.62</td>
<td>-0.07</td>
</tr>
<tr>
<td>Personal-social</td>
<td>110.68</td>
<td>-0.73</td>
<td>111.49</td>
<td>-0.06</td>
</tr>
</tbody>
</table>
TABLE 3 — Calculated Values of a and b for Relation between Percentage of Theoretical Behavior Determined by Gesell Test (Y) and Chronological Age in Months (x), Derived from Results in Groups of Pre-School-Age Groups in Rural Mexican Village (Empirical Equation of the Type Y=a−bx).

<table>
<thead>
<tr>
<th>Age group (months)</th>
<th>Field of behavior</th>
<th>0-12</th>
<th>13-24</th>
<th>25-36</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a</td>
<td>b</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Motor</td>
<td>137</td>
<td>-2.61</td>
<td>124</td>
<td>1.36</td>
</tr>
<tr>
<td>Adaptive</td>
<td>143</td>
<td>-3.77</td>
<td>116</td>
<td>-1.21</td>
</tr>
<tr>
<td>Language</td>
<td>139</td>
<td>-3.29</td>
<td>116</td>
<td>-1.44</td>
</tr>
<tr>
<td>Personal-social</td>
<td>128</td>
<td>-2.09</td>
<td>114</td>
<td>-1.15</td>
</tr>
</tbody>
</table>

Suitable supplements are not added, weight and height increments begin to diminish. By the time the child is completely weaned, which in most areas of Latin America is usually around the eighteenth to the twenty-fourth month, height is practically stationary and weight may even show a slight decrease.

In six different communities—two of typical mestizos, one of Zapotec Indians, one of Nahua Indians in Mexico, and two of Cakchiquel Indians in Guatemala—high correlations were found between deficits in height and weight and motor and adaptive developmental scores (Table 4). No statistically significant association could be demonstrated between mental scores and cash income, crop income, parental education, parental hygiene, or type of housing (58-61).

Ramos Galván (62), through a series of cross-sectional and longitudinal studies, has constructed provisional weight and height tables for age of normal Mexican children. When the actual weights and heights of rural Mexican children with mild-moderate protein-calorie malnutrition, expressed as a percentage of the provisional standard, were compared with performance scores on the Terman-Merrill test adapted to local conditions, a positive correlation was found. Better scores were associated with the smallest differences between theoretical and actual weight and height. Further, when “age for height”—that is, the age of a normal child of the same height as the malnourished subject—was related to mental performance, a positive and highly significant correlation was found, suggesting a concurrent deceleration of somatic and mental growth (63).

2. Severe Protein-Calorie Malnutrition

Barrera Moncada has explored the psychological test behavior of severely malnourished children by means of the Gesell technique. Performance in all the fields of behavior tested gave lower developmental
scores than the standard calculated for children of similar age and ethnic group. The better scores were in general motor development and the greatest retardation was in language. As a rule, older patients exhibited more marked deficits. Similar findings have been described for Africa (64) and Mexico (65).

Studies on the somatic growth of infants in Latin American communities with a high prevalence of malnutrition and infectious diseases have indicated that the weight curves during the first five years of life can be described in three well-defined phases. The first comprises a period of four to six months after birth. It is characterized by weight gains similar to those of normal children born in highly industrialized countries—a phenomenon most apparent when the gains are expressed as percentages of birth weight. The second phase extends from the sixth to approximately the thirtieth month. During this period weight gains are progressively lower, reaching their minimum between the eighteenth and the twenty-fourth month, after which they tend to rise steadily. The third phase marks an apparent return to values normal for the chronological age (24).

In view of all this, and considering that it is during the period of maximal growth that malnutrition might most strongly influence the ultimate size and performance of the mature individual, Cravioto and Robles (66) sought to assess the psychological test performance of severely malnourished children during at least three different age periods: below six months, between six and thirty months, and after thirty months.

From among the children admitted to the Nutrition Ward of the Children’s Hospital of Mexico, all who were classed as suffering from third-degree protein-calorie malnutrition were considered suitable for the study. The definition of “third-degree” followed the criteria of Gómez et al. (19) and the suggestion of José María Bengoa (personal communication), who includes in this group all malnourished children with pitting edema, regardless of their weight.

Immediately after any infectious and/or electrolyte disturbances had been corrected the psychological test behavior of the children was explored by the Gesell method. The tests were repeated every two weeks during the entire time the children were in the hospital.

At the end of one year of study it was possible to analyze serial information obtained in 6 infants below six months of age, 9 children between fifteen and twenty-nine months, and 5 children between thirty-seven and forty-two months.

The results of the first test session confirmed once more the previous reports of lower scores in all fields of behavior. As the patients recovered from malnutrition, their developmental quotients increased in most cases and the gap between the theoretically normal and the actual performance progressively diminished, except in the group whose age on admission was below six months. These infants increased their mental age only by a figure equal to the number of months they remained in the hospital. In older children not all the fields of behavior explored with the Gesell technique recovered at the same speed. Language, which was in general the most affected, returned toward normal at the lowest rate.

When serial data for each child were plotted against days of hospitalization, the rate of recovery from the initial deficit was seen to vary in direct relation to chronological age at admission. The older the group, the steeper the slope (Table 5). The slopes are steep enough and progress in the first two weeks of treatment great enough that the difference between early and final test results are unlikely to be due solely to the extra care and attention that the children received in the hospital.

Of the factors that contribute to a child’s intellectual development, among the most influential are considered to be the educa-
TABLE 5 — Regression Equations for Relation between Psychological Test Behavior (Y) and Days of Successful Treatment (x) in Three Groups of Children Recovering from Severe Protein-Calorie Malnutrition.

<table>
<thead>
<tr>
<th>Field of behavior (developmental quotient in months)</th>
<th>Age group (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-6</td>
</tr>
<tr>
<td>Motor</td>
<td>2.18 + 0.03x</td>
</tr>
<tr>
<td>Adaptive</td>
<td>2.30 + 0.03x</td>
</tr>
<tr>
<td>Language</td>
<td>2.0 + 0.03x</td>
</tr>
<tr>
<td>Personal-social</td>
<td>2.11 + 0.03x</td>
</tr>
</tbody>
</table>

...
Taking into account all the previous considerations, the persistence of low performance scores during rehabilitation among the infants who suffered protein-calorie malnutrition before the age of six months seems to indicate a probable loss in intellectual potential. In older groups, it is possible that the initial deficit will completely disappear if other relevant factors do not interfere.

These proposals seem to be supported by the findings of Barrera Moncada (30), who has reported normal IQ's in 20 rehabilitated cases all of whom were over two years and ten months of age at the time of admission to the study, when tested two years after their discharge from the hospital. Similarly, Kugelmass, Poull, and Samuel found, as has been said, that improvement in the diet of undernourished children over two years of age was followed by an improvement of 18 points in the IQ. The results obtained in adult volunteers by Keys et al. (71) point in the same direction. As age advances the effects of nutritional deprivation on the central nervous system tend to disappear more rapidly.

Evaluation of Development of Brain Functioning

To explore further the hypothesis that serious malnutrition of either primary or secondary causation during the preschool years interferes with the development of the central nervous system and lowers the adaptive capacity, Cravioto, Licardie, and Birch (72) carried out a cross-sectional study of the total primary-school population of a rural Guatemalan village in which prior information indicated the presence of a significant amount of acute or prolonged malnutrition in preschool children. Malnutrition was defined retrospectively in the children ranging from six to eleven years.

The primary basis for such identification was significantly shorter stature than the rest of the children. With this procedure, two groups of the same ethnic background were identified, representing the upper and lower quartiles of the age groups studied. In order to account for inherited differences in height, anthropometric information was obtained on the fathers and mothers. Further, since no psychological capacity is immune to environmental influences, comparative information was obtained on the socioeconomic and educational status of the children's families.

In addition, the rural study was replicated on an upper-class urban sample of schoolchildren whose variations in height would be most unlikely to be related to nutritional deprivation.

The behavioral function chosen for study was the development of intersensory organization, because its course is clearly defined and because this is a primary mechanism underlying more complex adaptive capacity. The specific method employed was that elaborated by Birch and Leford (73). These authors have shown that when studied by the technique of intersensory equivalence, the interrelations among three sense systems—touch, vision, and kinesthesia—improve with age as a function of growth.

Intersensory equivalence was evaluated in three sensory systems: vision, kinesthesia, and haptic touch. A haptic stimulus is one that is mediated through touch and active exploratory movement of the hand. The children were asked to judge whether two simultaneously presented stimuli were the same or different in shape: a form presented to one sensory system (standard) was compared with forms presented in another sensory system (variable). Thus, a visually presented standard was compared with a series of forms presented either haptically or kinesthetically. Similarly, a haptically presented standard was compared with a kinesthetically presented series. From such examination was determined the existence of cross-modality equivalences and nonequivalences between the visual and the kinesthetic, the visual and the haptic, and the haptic and kinesthetic sensory systems.
Eight blocks, selected from the Seguin Form Board, were used as the test stimuli for the visual and haptic modalities. As a visual stimulus, the block was placed on the table directly in front of the child. For haptic stimulation, the child actively explored with his hand a Seguin block placed behind an opaque screen, where he could not see it. Kinesthetic information was provided by the examiner’s guiding the child’s hand, again behind a screen out of his sight, through a path describing the geometric form. The patterns—the same in size and shape as the blocks used for visual and haptic stimulation—were cut one-eighth of an inch deep in four-by-six-inch linoleum blocks. The forms used are shown in Figure 2.

The results showed that each of the pairs of intersensory relations improved with age in both the rural and the upper-class urban groups. The error curves are almost identical in shape (see Figure 3), the only difference being that the urban children were significantly more advanced.

When the intersensory performances of children in the upper height quartile were contrasted with those in the lower quartile, it was only in the rural group that significant differences were manifested. This difference is illustrated by Figures 4 and 5, in which haptic-kinesthetic performances by age of the two height extremes are plotted.
The anthropometric information collected for the parents revealed that the height difference between the upper and the lower quartiles of the urban sample was mainly a reflection of family differences in stature. In the rural population, on the other hand, there was no significant association between the statures of parents and of children.

The lack of association between height and performance in the urban group has been interpreted as an indication that such a correlation exists only when the height difference reflects a different nutritional background—which could derive either from failure to have received appropriate amounts and kinds of food (primary malnutrition) or from repeated infectious episodes that have interfered with the child’s nutritional status (secondary malnutrition). This interference could occur directly, through an increase in tissue protein catabolism without a concomitant increase of protein intake (74), or indirectly, through anorexia and through the social custom of reduced feeding, particularly for preschool children, during illness and convalescence (75).

A question arises whether the inadequacy in intersensory functioning found in the short children of the rural group is part of the picture of malnutrition or whether both intersensory inadequacy and poor growth are associated with underlying subcultural differences that may have contributed to each of them independently. In one case, that is, the immediately underlying process is viewed as malnutrition; in the other, social conditions lead directly to poor intersensory functioning. The two alternatives can most readily be analyzed if they are considered diagrammatically.

In Scheme I, malnutrition and intersensory inadequacy both derive from a background of social impoverishment. They bear no direct relation to each other but are indirectly associated by virtue of a common origin. In Scheme II, social conditions result in malnutrition, which in turn leads to low stature and poor intersensory development.

Although it is impossible, on the basis of the available information, to accept or reject either hypothesis, certain inferences attaching to each can be explored. The main thrust of Scheme I is that social deprivation, including inadequate opportunities for learning, independently contributes to poor intersensory development. If this were correct both low stature and poor intersensory performance would be expected to show a significant association with a variety of social conditions that have been implicated as contributing to poor psychological growth. Of great importance, therefore, is the fact that the family data collected for the rural children revealed no association with financial status, with housing facilities, with proportion of total income spent on food, or with personal hygiene, and a reverse correlation with the father’s education. The only social background factor found to have a strong association was the mother’s educational level. This suggests the possibility that the better-educated mother relies less on traditional feeding practices, which are the commonest direct cause of reduced nutrient
intake during healthy early infancy and during later illness and convalescence.

Although these findings do not make it possible to reject outright the alternative depicted in Scheme I, they strongly suggest that it is not the social background as such that is interfering with the child's growth and function. If taken together with the large body of evidence that implicates nutritional deprivation in growth failure and with the data on more global behavioral disturbances following malnutrition, they make it seem likely that protein-calorie malnutrition is the intervening variable between social conditions, growth, and intersensory adequacy. Obviously, a definite answer can only be obtained through an anteropositive-oriented longitudinal study, in which it would be possible to take environmental circumstances and inadequate nutrition into account without being dependent on a later outcome measurement such as height. Such a study, which over the next decade will provide a more direct test of the hypothesis, is at present the major endeavor of our research group.

If for all these reasons there is a strong possibility that malnutrition interferes with intersensory organization, a few words about the possible mechanisms of action may be relevant. Theoretically, malnutrition could act either directly, by interfering with the development of the central nervous system, or indirectly.

**Indirect Mechanisms**

To examine the second possibility first, three mechanisms are readily apparent:

1. **Loss of learning time.** During the periods of malnutrition the child is less responsive to his environment and consequently has less opportunity to learn; at the very least he loses a certain number of months and would therefore be expected to show some long-term developmental lag.

2. **Interference during critical periods of learning.** Experimental evidence has been advanced suggesting that each new function of the brain is sequentially acquired and integrated into the total pattern of performance and experience. Timing is of the utmost importance, since each new function makes its appearance chronologically and is apparently optimal in operation at that particular point. In other words, learning cannot be considered as simply additive. Evidence exists that interference with the learning process at specific times during its development may result in disturbances that are not a simple function of the length of time the organism is deprived of opportunities for learning; rather, what appears to be important is correlation of the experiential opportunity with a given stage of development. These stages are what is known as "critical periods of learning" (76-78).

Alterations so produced may be clinically evident immediately, but more often they do not show up until a later age.

The critical periods in human learning have not been definitively established, but some useful information can be derived from an examination of the consequences of interference at different ages. So far as malnutrition is concerned, the previously cited findings of Cravioto and Robles may be relevant: the mental age of infants under six months of age, as calculated from their psychological test behavior, did not improve, whereas with the older patients the rate of recovery from the initial deficit varied in direct relation to chronological age at admission. Similarly, the findings of Barrera Moncada in Venezuelan children and those of Keys et al. in adults point to a marked association between the persistence of later effects on mental performance and the period of onset and the duration of malnutrition.

3. **Motivation and personality changes.** It is a recognized fact that to a considerable extent the infant's reactions determine the mother's response (79). The diminished responsiveness to stimulation and the emergence of apathy that are one of the first
effects of malnutrition may in turn reduce the child's value as a stimulus and thus adult responsiveness to him. Apathy can provoke apathy and contribute to a cumulative pattern of reduced adult-child interaction. This situation has consequences for stimulation, for learning, for maturation, for interpersonal relations, and so on—the end result being a significant risk of backwardness in more complex learning.

Direct Mechanisms

The possibility that malnutrition directly affects intersensory organization could stem from its ability to modify the growth and biochemical maturation of the brain. It should be remembered that increase of cell cytoplasm, with extension of axons and dendrites—one of the two main processes morphologically associated with the growth of the human brain at birth—is largely a process of protein synthesis. From microspectrographic investigation of the regenerating nerve fibers, it has been estimated that protein substance multiplies by more than 2,000 as the apolar neuroblast matures into the anterior young horn cell. Perhaps an easier way to grasp the magnitude of this process may be simply to recall that at the time of birth the human brain is gaining weight at a rate of 1 to 2 milligrams per minute. Moreover, as has been said, changes in the structure of the central nervous systems of animals due to grossly inadequate diets have been documented by Barness (Lowry et al., 80) and Platt (46). Widdowson, Dickerson, and McCance (81) have shown gross alterations in the content of water and of several electrolytes in the brain substance, and Flexner and associates (82) have advanced evidence that interference with protein synthesis in the brain produces loss of memory in mice.

Ambrosius (83) has reported that in severely malnourished children the normal relation between brain weight and total body weight is distorted. He and his associates have interpreted their findings as an indication of arrested growth of the central nervous system.

It may well be that so-called critical periodicity in behavior represents the responsiveness of the nervous system at a given stage of biochemical organization. If so, nutritional inadequacy may interfere with the staging and timing of the development of both brain and behavior.

Characteristics of Learning

Considering that, independently of the mechanism involved, the children who showed poor growth also showed delayed development in intersensory functioning, it seems important to discuss the possible significance of the developmental lag to more complex behavioral functioning. Two significant features of learning will be considered: conditioned-reflex formation and the acquisition of academic skills.

In most conditioning situations, what is demanded is the integration of two stimuli each belonging to a different sensory modality. For example, in classical salivary conditioning or in conditioning of leg withdrawal, a taste or a touch stimulus is being linked to an auditory or a visual one. The establishment of equivalences between them is thus required. If interrelations among the sensory modalities are inadequate, conditioning may be either delayed or ineffective. Therefore, if intersensory integration fails to occur at normal age-specific points, a risk of inadequate primary learning at each level can be created.

Alekseeva and Kaplanska-Raiskaya (quoted by Brózek, 84) have found that protein deficiency often alters conditioned responses in young children. The capacity to elaborate new conditioned reflexes is said to be affected first, but even previously well-established reflex responses may be depressed or abolished. Andriasov and Makarychev (also quoted by Brózek) have reported on animal experiments that confirm the observa-
tions made in children. It has been reported that visual-motor control in design copying is dependent on visual-kinesthetic intersensory adequacy (73). If it is recognized that, as Baldwin has pointed out, such visual-motor control is essential for learning to write, it becomes apparent that inadequacy in intersensory organization can interfere with this primary educational skill. Moreover, Birch and Belmont, in their studies of reading disability in British and U.S. schoolchildren, have shown that backwardness in reading is far more strongly associated with inadequate auditory-visual integration than with such characteristics as laterality or right-left awareness. A lag in the development of certain varieties of intersensory integrations thus appears to have a high correlation with lag in the acquisition of still another primary educational skill.

So the evidence available indicates that inadequacies in intersensory development place the child at risk of failing in his preschool years to establish a normal background of conditionings and of failing in his school years to profit from his exposure to education.

Children with these probable drawbacks are, it is not difficult to realize, more at the mercy of their environment than normal children. Eisenberg (85) has aptly said that “for the adequately endowed child a variety of environments suffice to permit adequate if not optimal development. For the handicapped child limited in his adaptive capacity there is a considerable restriction in the number of environments within which effective development is possible.” Considering the kinds of environment available to malnourished children, what we see in many older children and adults living in areas with a high prevalence of infantile malnutrition must be a combination of the probable effect of malnutrition per se with the effects of cultural deprivation.

The net result of nutritional deprivation and social impoverishment is what in an ecological sense could be called a circular effect. A low level of adaptive capacity or ignorance or social custom results in malnutrition and produces a large number of people whose functioning is suboptimal and who are themselves more ready to be the victims of ignorance and less effective in social adaptations than would otherwise be the case. In turn, they may rear children under conditions and in a fashion that will produce a new generation of malnourished persons.

Summary

Numerous surveys indicate that protein-calorie malnutrition exists throughout the world, and that there is a high probability that it is accompanied by abnormal psychobiological development in the child. Behavioral changes, especially a gradual regression characterized by apathy, are initial symptoms which persist throughout the disorder. Conversely, any show of renewed interest in the outer world by the child is a sign of improvement.

Three methods have been used in assessing the potential relationship between nutritional deprivation and the functioning of the central nervous system: (1) Electroencephalography has shown changes in the form, frequency, and amplitude of brain waves, even in mild-moderate cases of malnutrition; focal disturbances in the temporal areas of the brain have been recorded in some severe cases. (2) Psychological test behavior, studied in all cases of malnutrition, whether slight, moderate, or severe, has shown the presence of low test scores. When malnutrition occurs prior to age 6 months, there is apparently a loss of intellectual potential. (3) Evaluation of development of brain functioning, according to the results of a study made in a Guatemalan village among schoolchildren who apparently had suffered from malnutrition in the preschool period, indicates that there is a strong possibility that malnutrition interferes with intersensory organization.
It is noted that malnutrition is capable of acting either directly, by interfering with the development of the central nervous system, or indirectly. The indirect mechanisms are:
(1) loss of learning time; (2) interference during critical periods of learning; and (3) motivation and personality changes. Direct mechanisms point to the possibility that malnutrition modifies the growth and biochemical maturation of the brain, and thus affects later intellectual development.

In studying the possible significance of retarded development, two important learning characteristics are considered: formation of conditioned reflexes, and acquisition of knowledge at school. Intersensory development deficiencies may be the reason why the child is unable to establish a normal basis of adjustment, or to take full advantage of his school years. Observations made in malnourished children indicate that the condition is usually the result of a combination of the probable effects of malnutrition itself, plus the effects of cultural deprivation.

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