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Nutrition and Learning

Inadequate nutrition in infancy may result in permanent impairment of mental function.

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It has long been scientifically acceptable and, in some circles, even fashionable to ascribe many behavioral characteristics of the older child and adult to conditioning experiences received during infancy and perhaps prenatally. More recent data have indicated that some of these conditioning factors, rather than being psychosocial in nature, have a biochemical basis. Alterations of the biological and physical environment produce profound and lasting disturbances of the anatomical, chemical, and thus developmental and behavioral pattern of the organism. This course of events has been aptly termed "biological freudianism" by Dubos *et al.* (*1*).

The best studied aspect of biochemical conditioning is nutrition. In most areas of the world malnutrition in early life is directly or indirectly responsible for more deaths among children than all other causes combined; recent evidence has indicated that deficiencies in nutrition not only affect physical growth but may produce irreversible mental and emotional changes. Many aspects of these long-term effects of malnutrition have been studied in animals (*2*); from these experimental data a series of hypotheses relating to human development has been proposed.

Nutrition and Physical Growth

Numerous observations in animals dating back many years indicate that malnutrition retards physical growth (*3*); if growth is suppressed for a sufficiently long period during a critical phase in the early weeks or days of life, subsequent supplementation of the diet, while initially enhancing the rate of growth, usually does not permit the animal to attain its normal mature size. The same sequence of events has been demonstrated to occur in children who had suffered from severe malnutrition during early life.

To a considerable extent, biochemical development parallels this suppressed physical development in both children and experimental animals. Maturation of a variety of biochemical processes is delayed; thus, malnutrition results in inhibition of the biochemical maturation of the organism, and may, under certain conditions, produce retrogressions to earlier functional patterns. In malnourished children, such widely different measurements as water distribution, fat absorption, concentrations of plasma lipids and cholesterol, and excretion of creatinine approximate corresponding values observed in well-nourished younger children of the same height and weight (*4*). Furthermore, the metabolism of phenylalanine to tyrosine is depressed in malnourished older infants. Such patients show an abnormally high ratio of phenylalanine to tyrosine in the blood plasma and excrete excessive quantities of phenylalanine in the urine;

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this suggests that the enzyme system responsible for the conversion of the one amino acid to the other has either been depressed or has not fully developed. This result strongly parallels the status of the metabolic system in younger infants. In older children, malnutrition affects the ability to metabolize aromatic amino acids; thus these patients show defects closely resembling those associated with certain inborn errors of metabolism (*5*). Of particular interest is the manner in which these defects affect the development and function of the central nervous system.

Nutrition and Neural Growth

Recent investigations (*6*) on the physical and biochemical growth of the central nervous system in animals have provided information helpful to an understanding of the effects of malnutrition on the nervous tissue. Between the 50th day prior to birth and the 40th day postpartum, the brain of the pig grows intensively, gaining an average of 5 to 6 percent of its eventual mature weight every 2 weeks and increasing in weight considerably faster than the spinal cord. In spite of this difference in weight, the biochemical development of the brain is quite similar to that of the spinal cord. During maturation and growth, the amount of water in both organs gradually diminishes, whereas the amount of cholesterol steadily increases. In the pig, the adult concentration of cholesterol is not reached until after the 3rd year, although the cholesterol concentration of DNA-phosphorus, which parallels cell concentration, rises to a peak and begins to fall in the brain and cerebellum prior to birth, while reaching a plateau in the cord prior to birth and then slowly declining. These data have been interpreted as defining two separate phases in the development of the central nervous system. One of these, maturation, consists of a rapid increase in cells, as indicated by the increased concentrations of DNA-phosphorus. The other phase, growth, parallels myelination and is represented by increased amounts of cholesterol. Thus, in the pig, the rate of maturation of the central nervous system peaks prior to birth, whereas the rate of growth of the central nervous system peaks shortly after that time (*6*).

It is therefore not surprising that experiments on various animals have indicated that nutrition inadequate in calories and protein, coinciding with the period in life in which the brain is growing most rapidly, produces a brain which is not only smaller at maturity than in control animals but also one which matures biochemically and functionally at a slower rate (*2*, *7–11*). Even if rats are underfed for only a few weeks after weaning and are then placed on an adequate diet, this same result is produced. From a biochemical standpoint, malnutrition in young rats is associated with decreased synthesis of sulfatide, a lipid which is a component of myelin; thus the time of most active myelin formation is the most vulnerable period for the developing central nervous system (*7*). The brain of the mature rat malnourished during infancy is not only physically smaller but histologically may show degenerative changes of neurons and neuroglial cells. In the adult rat, starvation does not result in significant changes in brain weight or in similar damage to neural tissue.

Results obtained from simple caloric deprivation differ from those based on diets restricted not only in amount but also in quality. For example, simple nutritional deprivation of rats during the weaning period results in lower brain weights as well as in reduction in total brain lipids, phospholipids, and cholesterol (*8*). These three substances are reduced to about the same extent as brain size, with the relative concentrations unchanged. However, the amounts of cerebroside and proteolipid proteins were considerably lower in the brains of undernourished weanlings as compared to normal controls. When the animals were subsequently fed adequate diets, the defects were largely overcome. Similarly, the process of myelination, while being depressed during the period in which the newborn rat was undernourished, proceeded at an increased rate when an adequate diet was fed, so that after several weeks the degree of myelination was the same in the test animals as in the control groups. Thus, in the rat, an insufficient supply of food during the time of most rapid growth results in biochemically immature brains; the rat is capable of recovery if an adequate diet is fed by the 21st day of life.

The interpretation of these results requires some qualification. In the first place, while short-term simple undernutrition during the weaning period of the rat appears to leave few, if any, detectable biochemical traces if the animal is subsequently adequately fed, these studies do not indicate whether the function of the brain is permanently altered. Furthermore, the timing and duration of malnutrition during infancy is probably critical in determining whether anatomic and biochemical damage can subsequently be healed. Another study indicates that in rats neither the deficit in brain size nor the DNA concentration resulting from a restricted diet in the early days of postnatal life could be repaired by subsequent feeding; if, on the other hand, the dietary restriction occurred during a later period of infancy, subsequent adequate feeding would produce a normal-sized brain and normal concentration of DNA (*9*). Thus, early restriction of calories may slow the rate of cell multiplication (maturation) whereas later restriction affects only cell size (growth).

The rat may not represent a suitable model for the study of human development, nor do the experimental conditions resemble those encountered among malnourished infants. In infants there frequently is a long-term deficit in both the quantity of the diet as well as its quality, particularly with respect to protein and perhaps certain vitamins (*12*).

In this regard, observations on human infants have shown that inadequate feeding of pyridoxal phosphate, which serves as a coenzyme for most enzymatic reactions of amino acids, results in a series of changes in the physiological function of the brain and in the appearance of clinical symptoms (*13*). In the newborn baby, the ingestion of a diet deficient in this substance but otherwise adequate results within 6 weeks in hyperirritability, convulsive seizures, abnormalities in development, and behavioral disorders. If this deficit continues for a sufficiently long period, irreversible alterations of cerebral function will occur, resulting in severe mental retardation (*14*). Since pyridoxal phosphate is important in amino acid transport and protein synthesis, it is not surprising that the administration of puromycin, which inhibits protein synthesis, produces degrees of disorientation and loss of memory in mice which parallel the duration of the inhibition of protein synthesis by this antibiotic (*15*). These data suggest that inadequate protein nutrition or, synthesis, or both, during brain development could result in changes in function and that, if the degree of deprivation were sufficiently severe and prolonged, the changes in

function might be permanent. Other experimental observations do in fact indicate that insufficient intake of protein during early neural development affects mentation (*16*).

Nutrition and Mentation

In rats and swine, simple caloric deprivation during the nursing period apparently results in behavioral changes but does not seem to affect the animal's problem-solving ability. On the other hand, protein deprivation in early life not only causes the same behavioral changes but also reduces the capacity of the experimental animal to learn at a later age. Furthermore, rats born of and suckled by malnourished mothers are similarly deficient in their learning capacity (*2*, *10*).

It has been suggested that these deficits do not result entirely from nutritional factors, but that infection and behavioral disturbances produced by the experimental situation itself might be the most important factors. Recent studies with pathogen-free mice and a suitably stabilized environment indicate that these indirect, nonnutritional events have little effect on experimental animals (*17*). In the more complex human case, these environmental factors undoubtedly contribute significantly to the effects of malnutrition on behavior and function.

Protein-calorie malnutrition in the human infant, if severe enough, produces two clinical conditions—infantile marasmus and kwashiorkor (*12*). It seems likely that these two conditions are not separate clinical entities, but that they represent different manifestations of the same basic problem. Infantile marasmus occurs most commonly among babies weaned early without receiving suitable substitutes for human milk (*12*). Since mothers in preindustrialized societies increasingly imitate the cultural practices of more advanced groups, early weaning without the availability of subsequent adequate nutrition has resulted in a rapidly increasing proportion of children with severe protein-calorie deficits (*12*).

The clinical condition called kwashiorkor is most commonly encountered in children who had not been weaned until the 2nd or 3rd year of life and had not been offered adequate food supplements. The diet of the child afflicted with kwashiorkor may be reasonably adequate in calories, but it is grossly deficient in protein (*18*).

The early investigators of protein-calorie malnutrition in infants found that apathy was universally present in these children (*19*). The patients lacked the curiosity and activity found in normal children of similar ages and responded sluggishly, if at all, to a variety of stimuli. Not all of these emotional changes are necessarily the result of malnutrition, since malnourished children often are born to parents who themselves are intellectually and educationally depressed. Furthermore, the degree of apathy shown by malnourished children compares to that observed in healthy children who are abruptly separated from their mothers during the 1st year and placed in institutional situations. Nevertheless, it seems unlikely that apathy in hospitalized malnourished children is entirely due to separation from their mothers, because exactly the same lack of emotional responsiveness is observed among children lovingly cared for at home with an inadequate diet (*19*). Furthermore, one of the early signs of recovery from marasmus and kwashiorkor is the return of responsiveness to the environment (*19*).

There is a parallel between electroencephalographic changes and behavior. The electrical activity of the brain in protein-malnourished children shows consistent abnormalities in the form, frequency, and amplitude of activity. After the child successfully recovers from malnutrition, the wave form tends to conform more closely to that of healthy children of similar age (*20*).

Follow-up studies of children who have been treated for infantile marasmus and kwashiorkor indicate that during recovery they at first grow physically with great rapidity (*19*). However, if observations are continued over sufficiently long periods, the child never completely catches up with his healthy peers; growth stops at the usual chronological age, and the height of the adult is significantly shorter than that of his healthy peers (*19*). Head circumference, a useful but not absolute indicator of brain size, is also smaller, although this measurement is not necessarily related to variations in intellectual capacity. Nevertheless, the intellectual attainments of children who have recovered from a clinically severe episode of protein-calorie malnutrition are consistently lower than those of individuals with adequate nutrition during infancy (*21*, *22*). These findings suggest that less severe but more chronic forms of malnutrition, which do not result in dramatic and life-threatening nutritional diseases, might contribute to the small stature universally observed among the economically poorer families of preindustrialized societies and might be correlated with a decrease in intellectual development.

Nutrition, Growth, Infection, and Environment

Several pioneering studies, on a variety of population groups in whom malnutrition is indigenous, have suggested a relation between short stature and low intellectual achievement (*19*, *21*, *23*). Such investigations are highly complex, since malnutrition does not constitute a single, definable condition and other related factors cannot be adequately controlled. The basic condition, malnutrition, occurs primarily among underprivileged populations and thus is located in a particular physical, social, and biological environment. This environment, and probably malnutrition as well, results in an increased frequency and chronicity of infection, especially diarrhea, among the very young (the so-called "weanling diarrhea"). Repeated respiratory and gastrointestinal infections produce a cycle in which infection increases metabolic demands, decreases food intake, and inhibits the absorption of nutrients, resulting in a further deterioration of the nutritional state (*24*).

The relation between famine and pestilence was recognized in ancient civilizations; conditions associated with acute famine also provide an environment in which infectious diseases can flourish. Thus, the synergism between infectious disease and malnutrition in humans is both direct and indirect.

Infections, such as measles, may result in severe diarrhea and a high incidence of pneumonia in malnourished children (*25*). The reasons for greater severity of disease and increased incidence of complications remain somewhat obscure. Protein deficiency leads to decreased immunologic responses in animals as well as humans; furthermore, some of the normal components of protective serum, such as complement, are reduced. However, it appears unlikely that these changes in blood serology account for the great susceptibility to infection in the malnourished child. Rather, the major defect is probably on a cellular level; not only is it possible that the integrity of the respiratory and gastrointestinal

epithelium is altered, permitting more ready invasion of the body, but normal inflammatory and healing responses may be more or less inhibited (*26*). In kwashiorkor, reduced inflammatory response can be demonstrated clinically: the child enters the hospital without showing signs and symptoms of infection. After the patient has been rehydrated and his nutritional requirements have been replenished, the presence and the physical site of infection become obvious, and signs of inflammation appear, thus illustrating the similarity between the malnourished child and the immature infant (*27*). In the latter, little inflammation around the site of infection may occur, the delayed hypersensitivity response is repressed, and there is little tendency for the invading pathogen to be localized. All of these factors result in increased frequency of infection, increased severity of disease, and disease produced by organisms which under more normal circumstances might not be considered pathogenic (*27*).

Furthermore, certain infections in malnourished children may produce severe and prolonged hypoglycemia, which in itself can cause brain damage (*28*). Furthermore, infection tends to accentuate various biochemical deficits of children with malnutrition; this, in turn, presumably renders the patient more susceptible to further infections. Finally, many infectious diseases or the therapy used in treatment may result in damage to the central nervous system, without this effect necessarily being evident during the acute stage of illness (*28*). Infection and malnutrition thus act synergistically to produce a chronically and recurrently sick child less likely to react to sensory stimuli from his already inadequate social environment. Thus, a third factor, sensory and emotional deprivation related to illness and environment, becomes significant.

Studies among different cultures have demonstrated that one of the more important factors contributing to the intellectual development of a child is the level of maternal education; this influence becomes progressively stronger as the child grows older (*29*). Furthermore, studies of families of severely malnourished children have indicated that the majority of these mothers have low intelligence quotients (*30*). Socioeconomic factors also intervene indirectly; children suffering from severe malnutrition generally come from homes where the immediate economic pressures are such that the parents cannot provide the child with the stimulation necessary for optimum intellectual development (*31*).

Studies of human populations generally have not permitted the investigator to separate the effects of malnutrition from infection and from environmental factors, such as lack of intellectual stimulation and other socioeconomic conditions. Even tissue examination may not be sufficiently sensitive to permit discrimination between these factors; in animals pathological changes quite similar to those accompanying malnutrition can be produced by placing the animal in an environment entirely free of stimulation and by preventing him from exploring it. Furthermore, infections associated with hypoglycemia or severe electrolyte disturbances, as well as recurrent infections (particularly those affecting the central nervous system, the lungs, or the gastrointestinal tract) may act to retard physical growth and may produce tissue lesions similar to those observed in simple malnutrition (*28*).

Thus, it is exceedingly difficult to design field studies which would unequivocally decide whether human malnutrition results in permanent impairment of learning and of adaptive behavior. From a purely pragmatic standpoint, this probably makes little difference. If adequate nutrition in early childhood diminishes the incidence of infection as well as the opportunity for sensory and cultural deprivation, the end result might be much the same. To compound the difficulty, observations would have to be carried on for several decades in order to provide a complete answer, since experimentation with animals suggests that poor nutrition of the infant female may affect the development of her offspring born many years later (*3*).

Research Needs

Progress in this area would be greatly enhanced by comprehensive field and laboratory studies designed to determine the crucial time in development, if any, when malnutrition causes its major effects, as well as the quantitative and qualitative factors involved. No methods exist to identify and quantitate the biochemical abnormalities of mild, moderate, and severe malnutrition. Little is known of the effects of nutrition on the biochemical processes of nervous tissue, nor is there much information on the relation between mentation and the metabolism of these tissues.

Problems of Psychological Testing

Additional studies, based on psychological testing, would also be useful. It is difficult to perform an adequate evaluation of the intellectual capacity of children from preindustrial societies because most generally available tests have been standardized for other groups and cannot be applied cross-culturally. Furthermore, one cannot accept the idea that the motor development at a particular time is an index which will predict the future intellectual development of the child (*16*), since accelerated motor behavior does not necessarily represent a superior intellectual potential. In this instance, intelligence is best defined as the mental adjustment to new circumstances, and it is characterized by increasing complexity in the channels through which the subject acts on objects. Some techniques, such as the Gesell tests, have proved useful, and their reliability on a cross-cultural plane may be high. Thus, examination of the adaptive sphere by the Gesell method, which is based upon the organization of stimuli, the perception of interrelations, and the separation of the whole into its component parts with subsequent resynthesis, can perhaps serve as an analog to later intelligence (*23*).

The determination of the Gesell development quotient for a group of chronically undernourished children indicated that infants recovering from severe protein-calorie malnutrition persisted in low performance scores in tests of adaptive behavior during rehabilitation (*23*). Similarly, a measurement of visual, haptic, and kinesthetic integration, which appears to be unaffected by cultural factors, shows that children subjected to chronic but moderate degrees of malnutrition, as reflected by their heights, exhibit major functional lags in the development of this capacity (*19*). The ability to integrate visual with haptic, haptic with kinesthetic, and visual with kinesthetic stimuli is undoubtedly involved in most learning experiences which depend on the ability to integrate patterned information.

Should studies (*32*) indicate that the backwardness of many preindustrial societies is related to the inhibitory effects of malnutrition on physical, mental, and emotional development, one would still have to determine how this defect can best be corrected. Simply providing food is not the answer to the problem, since tradition has convinced the people of many cultures that foods we consider important to young chil-

dren are harmful to them. Thus, nutritional supplements may be sold or traded for other substances thought to be more useful or of greater importance to the adult. Hence, where tradition rather than education determines food utilization, the forces behind the tradition must be understood before positive approaches toward reeducation in food utilization can be undertaken.

Political and Social Considerations

In any discussion of the relation between malnutrition and intellectual achievement and behavior, the enormous political and socioeconomic consequences of such a finding also need be considered (*33*). In preindustrial societies, the socially and politically dominant classes can utilize malnutrition as a means of maintaining their control over vast numbers of economically deprived groups. If chronic malnutrition leads to decreased mental function and apathy, it represents a powerful tool of the oppressor over the oppressed. Thus, it would be to the advantage of the ruling group to maintain the majority of the population under conditions favoring widespread malnutrition.

If the socially deprived groups had access to increased amounts of food, then agitation for social, cultural, and political reforms would increase, and should political oppression continue, revolutionary movements and violence would probably ensue. Thus, it seems likely that improvements in nutrition may have the paradoxical effect of causing revolts, although classic political-economic theory would indicate the opposite. Recognition of this fact might therefore handicap any major attempt to reduce the high incidence of malnutrition in many areas of the world.

Summary

Observations on animals and human infants suggest that malnutrition during a critical period of early life results in short stature and may, in addition, permanently and profoundly affect the future intellectual and emotional development of the individual. In humans, it is not known whether these results may be caused by malnutrition alone or whether such intimately related factors as infection and an inadequate social and emotional environment contribute significantly to the problem. Field studies to test these hypotheses are, at best, difficult to design and to carry out; it seems likely that it will prove impossible to separate clearly the individual effects of malnutrition, infection, and social environment. While progress has been made in understanding the biochemical development of nervous tissue, little is known of the effects of nutrition on the physiological processes of these organs, nor is there adequate information on the relation between mentation and cellular metabolism.

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