Kwashiorkor and Intellectual Development*

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SUMMARY

Forty Cape Coloured children who had been hospitalized for kwashiorkor in infancy were compared with their siblings on an intelligence test battery at the 10th year of follow-up. No significant differences in intelligence test performance were noted. A significant discrepancy between the intelligence test score and the drawing score in late-onset cases may be due to affective factors. The groups were similar in terms of height, weight and head circumference. The differences between well nourished and poorly nourished groups found by previous investigators may be accounted for by the independent operation of non-nutritive variables in the social and emotional environment. The use of intrafamilial controls in the present study minimized these influences, as well as possible genetic factors in intellectual development.

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Kwashiorkor is a protein-calorie nutritional disease which occurs typically in children under the age of 2 years. The disease was recognized in Africa and Asia in the early 1930s, but only later was the nutritional aetiology realized.[70] The World Health Organization report by Brock and Autret[9] gave a clear exposition of the clinical picture and geographical distribution of the syndrome and made the scientific world conscious of the magnitude and significance of kwashiorkor as one of the most severe forms of malnutrition in children. Today the concept of kwashiorkor is that of a well-defined syndrome representing one pole of the broad clinical spectrum of nutritional disease referred to as protein-calorie malnutrition (PCM).[36,37] In contrast to marasmus, which represents the opposite end of the continuum, the calorie deficiency in kwashiorkor is not as severe as is the protein deficiency. The onset of kwashiorkor usually follows weaning, and the diet is grossly deficient of milk or other high protein foods. The calorie intake is provided by refined carbohydrate foodstuffs. Marasmus, being the childhood equivalent of starvation, is characterized by an onset often in the first year of life when breast feeding provides a quantitatively insufficient calorie intake and where supplementary feeding is not provided. However, the majority of cases of PCM do not show either of the pure syndromes of kwashiorkor or marasmus, but present a mixed picture and occupy an intermediate position on the PCM spectrum.[37]

The idea that kwashiorkor may have an effect on the intellectual development of the child is suggested by the stress laid on symptoms of CNS dysfunction during the acute stage of the disease. These are apparent in the earliest reports.[70]

Only recently, however, has this idea been taken up and explored further, possibly stimulated by the comment of Brock and Autret[9] that 'although the mental apathy of kwashiorkor is well known, it has apparently been so much taken for granted that it has been left out of most descriptions'.

LITERATURE REVIEW

For a long period interest has been focused mainly on the physical sequelae of PCM. The major concern of workers has been survival. Over the past 15 years a better understanding of the biochemical pathology of malnutrition has resulted in more effective treatments and a consequent reduction of the mortality rate (from 50% to ± 10%) in recent years. In spite of the frequent stress laid on symptoms of CNS disturbance in the acute phase, and reports concerning persistent EEG disturbance following an episode of kwashiorkor,[27,54,55] attention has turned only recently to the effects on subsequent intellectual development. The awareness of a growing population of rehabilitees who would probably have succumbed a decade previously has indicated the importance of systematic study in this area. Combined with this has been a steady and pressing flow of reports of experimental work on animals, confirming that defective nutrition has a permanent effect on both physical and CNS development in various species. Learning ability, memory, emotionality and other aspects of behaviour have been implicated and the effects have been found cumulative over several generations.[5,36,37]

While hypotheses concerning the actual mechanisms whereby nutritional deprivation alters the optimal development of the brain and interferes with its cognitive functions continue to be formulated and tested in the laboratory, a few field studies have been conducted which attempted to test the proposition by direct study of the individuals involved. Some of these have investigated marasmic children; only 2 have studied chilren specifically presenting with the syndrome of kwashiorkor.

Kugelmass and Others

In 1944 Kugelmass *et al.* formulated the relationship between malnutrition and intellectual function as follows:

'Mental energy is a product of two factors—capacity and intensity; the one is determined by heritage and maintained by essential nutrients, especially proteins, lipids, water and anions, while the other factor depends on immediate availability of dextrose, oxygen, vitamins and cations. Metabolic disorders affecting the capacity factor or brain structure tend to produce irreversible anatomic lesions, while nutritional disorders affecting cerebral function tend to produce reversible

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biochemical lesions. The role of some essential nutrients has been evaluated in the mental activity of experimental animals, but the applicability of this knowledge to children is a moot question. Since multiple nutritional deficiency predominates, the pertinent problem is to determine the effect of malnutrition on retarding mental function."[45]

In a preliminary study, these authors analysed the effects of nutritional improvement on psychological test performance in 182 children, aged 2 - 9 years. One half of the sample were institutionalized and the sample was divided into 2 groups each consisting of 50 normal and 41 mentally retarded children. One group was malnourished at the first testing but well nourished at the time of the second testing; the other group was well nourished at initial and final testing. The groups were equated for chronological age, IQ, and interval between Kühlman-Binet or Stanford-Binet tests.

An average improvement of 10 points for retarded children and 18 points for normal-IQ children was noted in the previously malnourished group, while no change was found in the initially well nourished group. A correlation was found between age at first testing and IQ rise: the younger the malnourished child when treatment was instituted the greater the chance of improvement. A sharp decline in IQ rise was found when treatment began after the age of 4 years, suggesting the occurrence of irreparable damage. The flexibility of IQ change before this age and the relative constancy of IQ change in the older children denotes irreversibility in mental development following prolonged malnutrition.

First Cape Town Study

The first controlled field study was semi-longitudinal and begun by Stoch and Smythe in 1955.[67,68] The authors selected 20 of the most grossly undernourished (marasmic) Cape Coloured children that could be found. Birth weights were said to have been normal apart from 3 children, who were below 2·5 kg. The subjects were matched for age and sex with 20 children whose early nutrition has been supervised in a creche. The groups were comparable in respect of parental intelligence, but there was a very marked disparity in their living conditions—'alcoholism, illegitimacy and broken homes were the rule in the undernourished group, whereas the control group lived under more stable home conditions. Only 6 parents of the undernourished group were gainfully employed'.[68] Intelligence, head circumference, height and weight were recorded approximately every 2 years. Significant differences on all these variables were found consistently, and the means at the 11th year of follow-up in 1967 were as follows:

TABLE I. DIFFERENCE BETWEEN MEANS FOR MARASMIC AND CONTROL SUBJECTS[68]

	Subjects	Controls	Difference
Intelligence score	**61·2**	**76·7**	**15·5**
Weight (kg)	**24·38**	**29·45**	**5·07**
Height (cm)	**125·73**	**133·68**	**7·95**
Head circumference (cm)	**49·58**	**52·04**	**2·46**

The authors regard the reduced head circumference together with defects of visuomotor and pattern perception on the non-verbal subtests as evidence that lower intelligence scores of the undernourished group may be due to organic brain damage resulting from gross undernutrition in early infancy.

Cravioto and Robles

Some confirmation for these findings derives from a study reported by Cravioto and Robles in 1965.[20] The Gesell method was used to study the psychological test performance of 20 infants and pre-school children during rehabilitation from kwashiorkor. Testing was begun as soon as acute infections and electrolyte disturbances had been corrected, and continued at intervals of 2 weeks for up to 6½ months.

All children showed lower scores than expected for their chronological age and ethnic group. As recovery progressed, however, the difference between the chronological age and the developmental age in the fields of adaptive, motor, language and personal-social behaviour tended to decrease except in the group of children whose chronological age on admission to hospital was less than 6 months.

In these children the initial deficit remained constant during the entire period of observation. On the basis that the adaptive behaviour of the infant may be analogous to the later intelligence of the adult, the authors conclude that the possibility is high that at least the children severely malnourished during the first 6 months of life might retain a permanent mental deficit. The authors discuss their findings as supporting those of Geber and Dean in Uganda,[30,31] Barrera-Moncada in Venezuela and Robles in Mexico, all of whom reported that undernourished children tested with the Gesell scales showed a marked retardation in all four areas of behaviour sampled by the technique. They quote another study by Barrera-Moncada who found that intelligence tests given 2 years after discharge to 20 rehabilitated cases who were all older than 2 years 10 months at the time of admission showed normal IQ.

Cabak and Najdanvic

In 1965, Cabak and Najdanvic reported a follow-up study in Yugoslavia.[12] The children had been admitted for marasmus between the ages of 4 and 24 months during the years 1951 - 1957. Chronic diseases of the CNS and tuberculosis were excluded and no child was more than 73% of expected weight on admission. One-third of the group had parents who were army officers or in the professions; the rest were skilled or unskilled workers, in an urban area.

Thirty-six children aged 7 - 14 years were tested on an adapted Binet-Simon scale. Fifty per cent of the group scored within the 'normal' limits of 91 - 110. One-third scored in the 'stupid' range of 71 - 90, and the remaining 6 children had IQ scores of 70 or below. Thus half the group were below the limit of normal intelligence and the difference between normal and subnormal intelligence was significant. No local standards for the dispersion of IQ

were available so the results were compared with those for Serbian children, of whom 21% were below normal intelligence as against 50% of the undernourished group; and 32% of Serbian children were above the range of the undernourished group.

The mean IQ of the undernourished group was 88, compared with a mean of 93 for children from families of 'non-qualified' workers.

The undernourished group did not differ significantly in height or weight from healthy local school children. No correlation was found between the age of illness and subsequent IQ, but there was a correlation between the deficit in expected weight for age on original admission and subsequent test performance.

Cravioto and Others

In 1966 Cravioto *et al.*[19] published the results of a study in Mexico which related height to intersensory organization. A cross-sectional study was carried out on all primary school children (age range 6 - 11 years) living in a rural village of Guatemala.

Malnutrition was defined retrospectively on the basis of height for age: a child who showed significant diminution of stature relative to his age-mates in the total village population was assumed to have an increased likelihood of having earlier been at risk of malnutrition. In this way, an experimental group was identified representing the lowest 25% of the height distribution and was compared with a group consisting of all those children in the tallest quartile for age. Information on the stature of parents of both groups was obtained to control for familial factors. A second control sample drawn from an upper-class urban population was selected consisting of children of the same ages who exhibited equivalent differences in height but who had little or no likelihood of ever having been at nutritional risk. Broad details on the social, economic and educational state of all families was collected. For the rural children a difference in height was accompanied by a difference in sensory integrative ability. This relationship was not found in the upper-class urban sample. The authors discuss the findings in terms of two possible schemes, viz. (*i*) that both poor intersensory development and malnutrition arise out of social impoverishment where poor stature is an incidental sequel to the malnutrition, or (*ii*) that both poor intersensory development and low stature are sequelae of malnutrition, itself arising out of poor social conditions. On the basis that poor intersensory function and low stature were not significantly associated with adverse social conditions the authors favour the second scheme, thus relating reduced intersensory ability directly to the possibility of early malnutrition as gauged by reduced height for age.

Champakam and Others

Using the same method, together with a suitably constructed intelligence test battery, Champakam *et al.* (1968)[14] studied Indian children who had been treated successfully for kwashiorkor in infancy. Nineteen children between the ages of 18 - 36 months admitted during the period 1959 - 1962, were tested between the ages of 8 - 11 years. For every 1 experimental child, 3 matched control children were selected taking account of age, sex, religion, caste, socio-economic status and educational background. In addition, the intelligence test was standardized on the group of 50 children of the same age range and derived from the same socio-economic group and geographical area as the experimental group. A significant difference in performance on the intelligence battery was found between the experimental and control groups. This difference was particularly marked in the younger age group (8 - 9 years) and tended to diminish in the older group (10 - 11 years). Intersensory organization was poorer in the experimental subjects—markedly so in the younger age group, with a tendency to improve in the older age group. The deficits were particularly marked with regard to perceptual and abstract abilities.

Heights, weights and head circumferences of the experimental children were generally similar to those observed in the matched controls, though the weights tended to be somewhat lower in the experimental group. Intelligence score, head circumference and height were correlated in the control subjects aged 8 - 9 years, but no other significant correlations were found. Although the findings are clear-cut, the authors are extremely cautious in their interpretation and question whether they are directly attributable to the earlier episode of PCM. Further factors which they invoke are:

1. Whether the prolonged immobilization before and after hospitalization resulted in a loss of 'learning time', together with the emotional stress and anxiety incidental to the hospitalization.
2. Whether the poor performance of the experimental group is merely a reflection of the low level of intelligence, motivation and resourcefulness of their parents—factors which determined the development of full-fledged kwashiorkor in the children.

Mönckeberg

Mönckeberg (1968)[22] is much more certain in his conclusion that permanent brain damage results from early malnutrition. Fourteen children (Chilean) admitted to hospital between the ages of 3 - 11 months were followed after treatment, correction of the undernutrition being attempted by an adequate free supply of milk to the families. The children were tested by Binet and Gesell methods when the age range of the group was 3 - 6 years. The average Binet IQ was found to be 62 and in no case above 76. This was significantly less than the average of Chilean pre-school children of low socio-economic level. On the Gesell test, only 1 child attained the 42nd month in all 4 areas. The best development was usually in the personal-social area; the most retardation was seen in language. Head circumferences were definitely below normal; heights were all below average (3rd percentile) whereas weights were all found to be above average (3rd percentile). The relation of weight to height was above normal; in some cases so much so as to give the impression of obesity.

The author attributes the low test scores of the group to brain damage directly resulting from a disturbance of protein synthesis during brain growth, and likens the effect of malnutrition in the first month of life to that of hypothyroidism, galactosaemia and phenylketonuria. The irreversibility of the brain damage is seen in the lowness of the scores despite improved nutrition as indicated by the above-average body weights.

Mönckeberg[52] derived further evidence from a study of the relative influence of social class and malnutrition on psychological deficit. He tested 153 pre-school children within three social groups. Group A included middle-class children; Group B and C were lower class with the same average income *per capita* and similar educational levels of parents. Group B was from a population with no malnutrition, due to free distribution of milk and medical assistance over the previous 10 years. The proportion of children with normal intelligence was essentially similar in Groups A and B, whereas in Group C only 50% were normal. The author recognizes that a supplemental feeding programme affects the environment, maternal motivation and nutritional state, so that the differences in intelligence level cannot be ascribed entirely to the nutritional factor.

In 1954, Trowell *et al.*[71] pointed out that 'Nothing is known about the completeness of recovery from kwashiorkor'. With regard to the psychological features of the clinical syndrome, this is probably still true today. While an improvement in the mental state has long been regarded as a sure, favourable prognostic sign during treatment of the acute phase, the long-term consequences in terms of psychological performance are still uncertain.

Investigators have become well aware of the multiplicity of factors which have an adverse effect on intellectual development and which inevitably co-exist with under- and malnutrition. The most recent review of the subject in *Nutrition Reviews*[56] concludes that 'If we are to know whether dietary deficiences *per se* are a cause of subsequent poor mental performance, then studies will have to be conducted which will separate the nutritional variable from genetic factors and from many environmental variables. High priority should be given to research of this kind because the results have great practical importance for underprivileged people everywhere' (p. 49).

BACKGROUND OF THE STUDY

Hypotheses considering malnutrition as a cause of permanent intellectual deficit are readily acceptable—partly due to the powerful emotional appeal in the socio-political connotations and partly because they sound so plausible. This applies particularly to those hypotheses which postulate the effects of malnutrition in terms of quantitative inhibition of brain growth.

Brain Size, Malnutrition and Intelligence

It has been demonstrated experimentally in many species that if an animal is deprived of dietary essentials for growth during critical stages of postnatal development, it will remain physically retarded, notwithstanding later correction of the dietary deficiency.[72,73] A logical extension would be that dietary deficiency in infancy will impede brain growth quantitatively and cause mental retardation, the extent of which is related both to the age of onset and the duration of the nutritional insult. The period of maximum human brain growth starts in the 5th foetal month: at birth the brain weighs about 40% of its adult weight. Seventy per cent of adult brain weight is achieved by the end of the first year.[10] The period of maximum vulnerability would seem to be largely in the prenatal period and in the first few postnatal months.

However, there are two important assumptions underlying these formulations which are not valid: viz. that intelligence is related to gross brain size, and that head circumference is an index of gross brain size. Anatomists and social anthropologists have found large normal variations in brain size within all mamalian species[46] and, looking back, have found some of the greatest intellects of the past to have resided in remarkably low cranial capacities. Quantitatively, the equivalent of modern man's brain was achieved by Neanderthal man more than 100 000 years ago.[51] The men of our own species who replaced the Neanderthalers also had brains of full modern size.[33]

Although a relationship between brain size and intelligence has been entertained in the past, the evidence is overwhelming that the two can only be correlated in definite anomalous extremes such as anencephaly and microcephaly.

Nor does the correlation of brain size with head circumference stand scrutiny. Fielden (quoted by Dodgson)[24] showed that in micro-encephalic calves the external skull dimensions were normal although the brain weight was only 1/6th of normal.

Furthermore, in malnutrition there is thinning of skull bones and loss of temporal musculature making for reduced external skull circumference. Also, Illingworth and Lutz[40] have pointed out that head measurements only become meaningful when taken as a ratio of total body size. Dean[21] found head size the least affected of various body measurements in malnutrition; it was always larger in relation to body size than in normal children.

An important consideration in regard to the effect of malnutrition on gross brain size is the relative metabolic stability of the brain, and the protective mechanisms whereby the brain is afforded nutrient priority over other developing organs. Donaldson in 1908 (quoted by Dobbing)[22] recognized that however much growth is retarded, it is difficult at any age to induce the brain:body ratio to depart from the normal value for body weight. Jackson pointed out in 1909[41] that in atrophic infants the brain continues to grow, so that emaciated infants can have normal brain weights. Waterlow *et al.*[72] showed experimentally that in protein-depleted animals there is a concentration of protein synthesis in the internal organs at the expense of muscle and skin. An investigation of brain size in children at postmortem by Brown[10] in Uganda showed that although the brains of malnourished children weighed absolutely less than those of non-malnourished children, when the brain weight:body weight ratio was calculated the malnourished group had higher ratios. 'Small-for-dates' babies have a brain:body weight ratio

elevated to a value higher than would be consistent with the body weight; and in underfed rats the brain weight deficit is consistently relatively less than the body weight deficit.[23]

Thus, although reduced head circumferences have been noted in malnourished children by both Stoch and Smythe[67,65] and Mönckeberg[52] it must be recognized that these cannot be uncritically accepted as evidence for reduced brain size or related to reduced intellectual 'capacity' or performance.

Structural CNS Changes, Malnutrition and Intelligence

To look for gross anatomical changes in the brain as a consequence of malnutrition and to use external head measurements as an index is likely to be fruitless. Investigators have thus turned their attention to consideration of more subtle effects of malnutrition on the biochemical structure of the growing brain on the one hand, and to functional interrelationships as an index on the other hand. The nature of the relationship, if any, between these two aspects is still obscure.

Normal functioning of the nervous system depends upon an entire chain of biochemical events. In any biochemical system, interference with specific aspects of the metabolic events produces a 'biochemical lesion'. The interference can be direct when the integrity of the system is disturbed by the absence of an enzyme essential to the sequence of metabolic events. Or the interference may be indirect when the velocity of intermediary metabolism is disturbed by alteration of the enzyme action or the substrate upon which it acts.[61] Phenylketonuria remains the paradigm of such biochemical lesions on a genetic basis, as proposed originally by Garrod in 1923 as 'inborn errors of metabolism'. A possible association between biochemical lesions, errors of metabolism and nutritional deficiency, was expressed by Kugelmass, Poull and Samuel[45] in their initial formulation.

Several reviewers[35,26,32,75] have referred to the delayed maturation of a variety of biochemical processes in malnutrition, i.e. the measurements of biochemical functions approximate the values observed in well-nourished younger children of corresponding height and weight. These observations, together with the specific finding of depressed metabolism of phenylalanine to tyrosine in patients with kwashiorkor, have led to speculations that enzyme activity can be inhibited by malnutrition, causing abnormalities in intermediary metabolic sequences and blood amino acid patterns *per se*, as well as the formation of degradation products. Amino acid transport across the cell membrane could thus be interfered with, resulting in reduced availability of amino acids to the neurone.

However, in contrast to earlier theories that protein synthesis cannot take place at the synapse, Gordon and Deanin[28] have recently shown that, *in vitro* at least, this is possible. All the requirements for the operation of a transport mechanism for protein destined to be the source of amino acids for new protein at the synaptic ending are present. Potentially a mechanism is provided whereby neuronal structures are protected against at least short-term variation in the supply of essential amino acids to the whole organism.

Additional evidence of the unique protein metabolism of the brain is provided by the investigations of Ogata *et al.*[57] in Japan. Using radio-active leucine, the authors found that the protein synthetic activity of the adult rat brain is not affected by a protein-deficient diet fed for 7 days, in contrast to the protein synthetic activity of the liver under the same conditions. The authors suggest that brain protein may be metabolized independently of other tissues because of the presence of the blood-brain barrier, although its metabolic activity is high and comparable to that of liver.

Severe and prolonged deprivation may ultimately have its effect in spite of these protective mechanisms. Gordon and Deanin[28] quote investigations which showed that undernourished rats, in contrast to malnourished ones, showed no measurable deficits in the number of brain enzymes or inability to learn. Both groups were well below the *ad-libitum* fed controls in body weight gain.

Conceivably, protein deprivation during early development of the brain may affect its later protein metabolism on the basis that protein requirements may be relatively increased in the developing brain as opposed to the relatively stable requirements of the fully developed system for the maintenance of the cell membrane and neuronal function. Unfortunately, no data are available for differential amino acid requirements, quantitative or qualitative, at various stages of maturation of the human brain.

In the instance of phenylketonuria the effect of the 'lesion' on CNS function is clearly indirect; the action of toxic metabolites being responsible for impaired CNS function. However, a 'biochemical lesion' within the metabolic system of the brain itself has been postulated by Rosenzweig *et al.*[60] whereby the hydrolysis of acetylcholine is reduced by the absence of adequate amounts of cholinesterase. Impulse transmission at the synapse is thus paralysed by excessive concentrations of unsynthesized acetycholine. Since all behaviour depends on neural processes, it is reasonable to expect that such alterations in biochemical events will be reflected in behavioural changes, including cognitive functions. Thus Rosenzweig *et al.*[60] related problem solving and adaptive behaviour in rats to differences in the distribution of cholinesterase in the rat brain; and a genetic factor was postulated in the determination of 'maze dullness' or 'maize brightness' in rats, in that it was possible by selective breeding to produce 'maze bright' and 'maze dull' rats; the former have a higher concentration of brain cholinesterase.

More recently the nutritional quality of the rats' early environment has been implicated as a determining factor.[44] Difficulties arise in attempting to place biochemical events and behavioural patterns in a direct causal relationship. For example, when the experiment was reversed the maze learning ability was studied in rats which had been specially selected for high or low cholinesterase; the rats with more cholinesterase were duller. Therefore the bright rats in the earlier study may have had increased cholinesterase because of increased 'neural activity' as reflected in more competent maze performance or more successful maze learning.[1]

Brain growth in mammals has been demonstrated by Dobbing[22] to comprise 2 component growth spurts: the first consists of glial proliferation of which tissue DNA-phosphorus content is an index, and peaks in man in the weeks before birth; the second, consisting of myelinization by deposition of lipids, is estimated by tissue cholesterol content and takes place primarily in the first weeks after birth.

The 'growth spurts' represented by the peaks of each of these stages could represent periods of vulnerability during brain development. Marked variations between species of the spurts in relation to birth were noted by Dobbing[22] indicating that a nutritional insult could have different effects at different stages in different species. This calls for the utmost caution in extrapolating from work on infra-human species to man.

Brain growth in the rat, for example, takes place almost entirely in the postnatal period, which causes the rat brain to be theoretically far more vulnerable to environment insult than the human brain. Dobbing also stresses that although some of the results of early nutritional deprivation in animals may be interpreted as interference with myelinization of the CNS, the question of whether the physical deficits have any more than a co-incidental relationship with the behavioural deficits still remains unanswered.[23]

This applies also to the work of Winick,[74] who has used analysis of DNA content as an index of rate of cell division in the developing brain, and found a markedly reduced DNA content in the brains of children who died of malnutrition during the first year of life.

Short-term Malnutrition and Intelligence

The immediate effects of calorie restriction (acute starvation and semi-starvation) in adults have been reviewed by Brozek[11] and by Sourkes.[65] Reduced performance on intelligence batteries could be attributed to consistent changes in mental state, viz. poor concentration and attention, apathy, fatigue, irritability and depression. With refeeding, these symptoms are reversed and test performance returns to previous levels. The relative contribution of various essential amino acids and vitamins (notably glutamic acid, uric acid, thiamine and riboflavine) has been investigated by selective refeeding. However, Keys *et al.* (quoted by Sourkes),[65] in studies of the effects of starvation entailing reduced protein intake, found that the single most important nutritional factor in successful rehabilitation was caloric intake.

Stewart and Platt[66] produced marked cellular changes in the nervous system and neurological signs in pigs and dogs by feeding an unlimited low-protein diet from weaning, and during pregnancy and lactation. The pigs developed a physical state resembling kwashiorkor and were grossly deficient in physical size compared with normal animals of the same age. EEG changes were also observed. Most of the changes, however, were found to be reversible with rehabilitation. No tract degeneration or necrosis occurred, although the significance of permanent loss of cells due to neuronophagia during the initial stages of recovery is not known.

These findings invite the hypothesis that children who have suffered an early nutritional illness may lag in intellectual performance behind those who have not, for a period following the initiation of refeeding but, all things being equal, should eventually catch up. The basis for such a hypothesis would be that the period of apathy represents a period of reduced opportunity for practice of skills combined with reduced sensory stimulation. A more pessimistic viewpoint refers to the so-called 'critical periods' in behavioural development, disruption of which may result in a permanent deficit in that particular area of behavioural skill.[62]

Non-nutritive Factors, Malnutrition and Intelligence

The word 'kwashiorkor' is said to mean 'displaced child': it was given as a name for the syndrome by Cicely Williams in 1935 on the basis of the observation that the disease usually followed on the disruption of breast-feeding by the arrival of another sibling.[70]

The term 'kwashiorkor' thus characterizes the high degree of maternal deprivation which all workers recognize as inevitably co-existing with the nutritional deprivation.

It has been well demonstrated[2,47,48,49] that stimulation in the form of handling and gentling of the newborn rat resulted in acceleration of physiological development of gross morphological, functional and structural characteristics of the organism to earlier maturity. Body hair appeared earlier, eyes opened sooner and CNS myelination occurred sooner in handled animals. Differences in response to external stress were related to differences in ACTH levels and response. The work of Dennis[22] provides convincing evidence of the retarding effect of understimulation and maternal deprivation on psychomotor, intellectual and physical development in children.

Bakwin[3] found the evidence conclusive for emotional and stimulus deprivation as causes of the infants' failure to thrive. In a review of the effects of stimulus deprivation, Senn[64] states that: 'Almost all studies of the past 30 years on the institutional care have one postulate in common: that the absence of individual, personalized nurture of the infant has been the effect of a disease or environmental defect'. Jones and Thomas[42] on the basis of work by Le Gros Clark and other neuro-anatomists demonstrated in rats that the normal dendritic structural organization of neurones is dependent on the integrity of their afferent input: a clear example of the fact that functional and structural CNS changes can be brought about by disuse. Recently, Powell, *et al.*[55] described growth retardation in 13 children closely simulating idiopathic hypopituitarism as a consequence of emotional and social deprivation. The children were grossly undersized for age, and nutrition did not appear to play any significant role; serum proteins were normal. IQs were below average range. Growth spurts occurred with removal of the children to an enriched environment, and ceased when they returned to the home environment.

These considerations introduce a complication in the interpretation of psycho-developmental studies on malnourished children. While most authors have been well

aware of the influence of non-nutritive factors, no one has succeeded in excluding them. Both malnutrition and maternal deprivation can give rise to apathy and depression in the child: this in turn may cause a reduction in the quality and frequency of infant cues on which normal mothering behaviour is partly dependent.

Further difficulties arise when the effect of parental intellectual and educational level on the test performance of the child is considered. The extent to which genetic factors are responsible is not clear, because intelligence is not inherited as a single unitary trait.[70] A positive correlation between maternal educational level and infant development is clearly demonstrated by Knoblock and Pasamanick[48] who give the following table:

TABLE II. DEVELOPMENTAL QUOTIENT BY AGE IN FULL-TERM INFANTS ACCORDING TO RACE AND EDUCATION OF MOTHER

Education of mother	40 weeks		3 years	
	White	Negro	White	Negro
<9th grade	103	100	109	90
9th - 11th grade	104	104	108	102
High school +	102	104	115	105

Further evidence for the maternal effect on intellectual development is derived by Knoblock and Pasamanick[48] from the following table:

TABLE III. DEVELOPMENTAL QUOTIENT BY AGE AND GRADE OF MATERNAL CARE IN MATURE CONTROL INFANTS

Maternal care	2 years	3 years	4 years	5 years
Best	107	108	110	118
Middle	103	103	103	106
Poorest	98	97	98	95

Further studies in Aberdeen, reviewed by Richardson,[50] provided clear evidence of a relationship between socio-economic level and mild to moderate mental subnormality, as opposed to severe subnormality which was evenly distributed over 5 social classes, and associated with a raised incidence of CNS damage. Studies of the maternal social background showed the women with an upper-class upbringing have children with higher intelligence and reading skills than women from a lower-class background, even though the social class was the same for both groups after marriage.

Malnutrition in children is usually associated with low maternal intelligence and education (Martinez, De La Fuente and Ramos-Galvan, quoted by Cravioto)[18] and this may indeed contribute to the development of malnutrition in the child. Family size and position in sibship can also have an effect on intelligence level.[7,33]

Limitations of Animal Experiments in the Study of Malnutrition and Intelligence

Animal studies, while contributing some useful data with regard to causal relationships between isolated variables, fail to account adequately for the complexity of variables in what is a distinctly human problem. One reviewer comments thus: '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' (p. 645).[26]

Animals may be experimentally deprived of nutrients and calories in various combinations to produce varying degrees of undernutrition without necessarily developing the disease syndrome of kwashiorkor with its pathognomic features. The internal metabolic state of the undernourished animal does therefore not reduplicate that of the malnourished child.

Hansen and co-workers have stressed the invariable existence of a synergistic relationship between malnutrition and infection in human populations.[38,76] The lack of infection in animal studies is a factor of unaccounted-for significance.

The infinitely complex and variable influences to which developing animals and humans are exposed in the form of varying physical and biological environment, and the process whereby lasting changes in physiological and hence behavioural patterns are produced, has been termed 'biological Freudianism'.[25] In the mouse colonies studied by Dubos,[25] these influences included: the effect of indigenous microflora on food utilization; the effect of maternal diet on growth of the young; the effect of early sub-clinical infections on physical growth; and the effect of nutritional status on resistance to infection. Early subclinical infection produced a similar depression of growth and ultimate size as did suckling from underfed mothers.

Added to factors in this category are those of the psychosocial environment, which may be relatively more influential in humans than in animals; but the assumption that these factors are more readily controlled in animal studies is not always borne out. For example, Franková,[29] in a series of sophisticated rat experiments of multivariate design, attempted to study the simultaneous interaction of nutritional deprivation, litter size and handling. However, the design failed to account for the effect of litter size on tactile stimulation (both by the rats in a relatively reduced space and by more frequent entry into the cage of the hand of the handler) on exploratory behaviour and on competitive behaviour.

This series of experiments also raises the difficulties in the evaluation and interpretation of behaviour as the dependent variable in animals. Thus Franková[29] interpreted increased exploratory activity of the rats on low-protein diets as reflecting a higher level of excitability in the CNS. This was regarded as beneficial in that it represented an intensified response to the environment. Collier,[20] however, in commenting on these results suggests that activity involving substantial expenditure of energy can affect growth and survival and is part of a regulatory mechanism for

body weight and composition. In this case, increased activity may be regarded as a physiological response to an imbalance produced by the diet, rather than a beneficial effect resulting from the diet.[62]

Barnes[5,6] quotes studies in which the water-maze was used in order to avoid the confusion of a food reinforcement being used with animals which have an altered drive for food as a consequence of earlier nutritional deprivation. No significant differences were found in water-maze performance between rats fed high- and low-protein diets. Similarly, defaecation cannot be accepted as a valid index of differences in 'emotionality' in the presence of markedly different dietary regimens.

THE PRESENT STUDY

General Features

The general aim of the present study was to investigate the effect of severe protein-calorie malnutrition during infancy on subsequent intellectual development. Many indications for the form and direction emerged from the studies described in the literature review.

Several weaknesses in previous field studies are apparent. None of the investigations were done blindly. All used extra-familial controls which meant that the experimental and control subjects had been exposed to different environments. The differences found could thus be accounted for by the differences in stimulus quality and quantity of the childrens' environments. Furthermore, it could be postulated that the experimental children became severely undernourished because poor adaptive and motor behaviour placed them at a disadvantage in a competitive family group. Thus the studies possibly contained a built-in selection for primary mental subnormality. This hypothesis could be applied particularly to the finding of Cravioto and Robles[20] that those children who became acutely ill before 6 months of age showed the least improvement in test performance during rehabilitation. This hypothesis could be tested, and the non-nutritive environmental factors adequately controlled, only by pairing intra-familial subjects and controls.

The most important feature of the present study is the use of siblings as controls, in an attempt to control the many non-nutritive factors which play a part in the determination of intelligence level. It is not assumed that siblings are exposed to the same early environment: however, this is likely to be mode constant and similar within one family over a period of a few years than between different families over a period of a few months.

No previous study has compared malnourished children with their siblings in terms of intelligence. The probable reason for this is that the siblings of children who present with an acute episode of PCM are often also below the optimum in nutritional status. Thus Stoch and Smythe[67] believed that only by comparing the extreme cases on a nutritional spectrum could any significant differences be demonstrated. But the effective non-nutritive factors coincide with the nutritive factors, making control extremely difficult. For example, Stoch and Smythe's control group had the benefit of nursery school experience—a factor which can appreciably affect the child's performance on an intelligence test.[35]

A unique opportunity was provided in Cape Town by the existence of a large group of kwashiorkor rehabilitees whose social and medical status has been followed for more than a decade. The psychological test evaluation of these children seemed valuable as representing a contribution to the meagre information concerning the relationship between early nutritional deficiency and intellectual development.

The weakness seen in the previous studies of children malnourished before the age of 2 years was that the hypotheses on which they were based were not capable of being disproved in actual practice. This arises from the nature of the control groups (where these were in fact included) in which a number of variables were operating independently, possibly accounting for the variations between the experimental and control groups. The design of the present study was such that the hypothesis on which it was based could be disproved, viz. that infants deprived of dietary protein during brain growth are significantly less intelligent than those who had not been deprived in this way. A correlation of 0·5 - 0·6 is normally found between the intelligence quotients of siblings. The null-hypothesis was thus formulated that there is no significant difference between the intelligence test scores of children who suffered kwashiorkor in infancy, and their siblings.

The Sample

Experimental group: The experimental group consisted of 40 Cape Coloured children between the ages of 9 and 14 years. The primary criterion for selection was that the child had been hospitalized at least once during infancy for treatment of full-blown kwashiorkor as defined by Hansen.[36] A secondary criterion for selection related to the control group, viz. the availability of a like-sexed healthy sibling whose date of birth was within 2 years of the subject and who had never shown clinical evidence of severe PCM. An attempt was made to select children in whom the initial episode of kwashiorkor had occurred early in life (within the first year) or late in life (after 18 months of age). The age on admission to hospital served as an index of the age of onset of kwashiorkor.

Control group: The control group thus comprised 40 Cape Coloured children aged 8 - 15 years, each being the nearest in age and of the same sex as the experimental subject, but without any past history of kwashiorkor. Children were not included in this study if there was any doubt about the paternal and maternal parentage of both subject and sibling.

In all cases both subject and sibling had lived together under the same social conditions for their whole lives to date. Children in foster-parent care or adopted children were included only if both the subject and his/her sibling

had been placed with the same foster parents or adoptive parents at the same time.

The experimental and the control groups thus resembled one another in terms of parental factors, age, sex, social, economic and emotional environment. The independent variable was PCM to the degree of fulminating kwashiorkor.

The Test Battery

The battery of tests was selected to give a picture of the children's present over-all intellectual performance. Because no standardized test exists for Coloured children in this age group, it was decided to apply the New South African Individual Scale, a battery recently standardized on White children in South African urban and rural areas.* This had the additional advantage of making the results comparable with those of Stoch and Smythe.[68] In addition the Goodenough-Harris 'Draw-A-Man' test[39] was given, partly because of its value as an introductory technique in the establishment of rapport.

New South African Individual Scale:[69] This scale is similar in construction to the Wechsler Intelligence Scale for Children (WISC). The battery comprises 9 subtests (5 verbal, 4 non-verbal) as follows:

Vocabulary: a picture-type test using a total of 30 vocally presented stimulus words; the test thus requires the perception and integration of an auditory stimulus with a visual stimulus.
Comprehension: 10 questions relating to everyday life situations and customs. Responses are scored on 3 levels of qualitative differentiation, and are thought to indicate 'judgement' or 'common sense' performance in which both emotional and intellectual functions play a part.
Verbal reasoning: a similarities test, the first two items of which are in analogical form. Responses are scored according to Rappaport's levels of reasoning, i.e. abstract, functional, concrete. Performance on the test depends on the ability to distinguish between essential and non-essential similarities, to generalize and think abstractly.
Problems: 15 verbally presented arithmetical problems, considered mainly as a test of concentration ability. Successful performance is dependent on training and the score therefore reflects level of school achievement.
Memory: a test of recall of meaningful verbal material vocally presented.
Pattern completion: performance requires free response in the completion of 16 partially completed designs; time may be taken into account in scoring. Visual orientation as well as ability to concentrate is involved in performance.
Block design: a Koh's type test which requires analytico-synthetic ability and especially the ability to solve problems in spatial relationships. Scoring may include a time factor.
Absurdities: similar to Wechsler's Picture Completion subtest but containing incongruities as well as omissions.
Form board: an adaptation of the Leake-Smith Form Board and consisting of 6 figures: three of 3, and three of 4 loose coloured pieces. Scoring is based on time taken to complete each figure. The test is regarded as an indication of qualitative aspects of intelligence and of temperament factors in the solution of concrete problems.

The battery uses point scales, so that the same test item can be applied, all the way through, to all age groups, and the standard deviation—IQ method replaces the mental-age method. Performance is indicated in terms of standard scores or normalized scaled scores. In the present investigation, 'power-plus-time' scores were used throughout.

Because this test has not yet been standardized for the Cape Coloured population, the terms 'verbal quotient', 'non-verbal quotient' and 'full scale quotient' were replaced by the terms 'verbal score', 'non-verbal score' and 'full scale intelligence score'. These 'scores' thus represent the child's performance in terms of the White standardization sample. The only significance which is attributable to the scores is thus the difference between scores obtained by the experimental and control groups. The scores cannot be interpreted in any way as 'IQ' with reference to the population.

Despite the absence of normative data for the population sampled in this study, the application of the NSAIS was justified on the basis that our sample comprised exclusively urbanized children, many of whom are attending urban schools at present, or had done so in the past. This would serve to minimize the cultural differences, which approach significant proportions only in the Vocabulary and Comprehension subtests and, to a lesser extent, in the Memory and Absurdities subtests. Cultural factors are further minimized in that, for our purpose, we were interested in differences in performance between 2 siblings, both of whom had been exposed to the same sociocultural influences. Differences in performance would then be significant in that they would reflect the extent to which there had been differential integration of the same environmental stimuli by siblings. This would have significance in terms of the child's cognitive functions, especially for his 'conceptual maturity' as formulated by Harris.

A further justification for the use of the NSAIS scale was seen in the fact that a start has been made towards the standardization of the test on the Coloured schoolchild population, and ultimately it may be possible to convert the raw scores obtained by the present sample to appropriate normalized scores, gaining further valuable data retrospectively.

Harris-Goodenough Drawing Test: As a departure from the outdated notion of unitary intelligence, Harris[39] revised the well-known Goodenough 'Draw-A-Man' test to evaluate 'intellectual maturity'. By this is meant the ability to form concepts of an increasingly abstract nature. Three functions comprise the process of concept formation, viz.:

(i) the ability to perceive, i.e. to discriminate likenesses and differences;

(ii) the ability to abstract, i.e. to classify objects according to perceived likenesses and differences; and

(iii) the ability to generalize, i.e. to assign a newly experienced object to a correct class, according to the discriminations made. A child's drawing of any object will reveal the discriminations he has made about that object as belonging to a class, i.e. the level of his conceptual maturity, and his concept of such a frequently and universally experienced object as a human being provides an index of the growing complexity of his concepts generally, par-

*Special permission for the application of this scale to the sample was granted by the Director, National Bureau of Educational and Social Research, Pretoria.

ticularly as it requires integration of affective and cognitive elements.

The drawings required are the child's free responses to the requests 'Make the very best picture you can' of (1) 'a man', (2) 'a woman', and (3) 'yourself'. Emphasis is placed on the whole 'man', 'woman' or 'self'.

The formal and structural elements of the drawings are scored basically on 3 levels, viz. presence, dimensions, and proportion. Raw scores are converted to standard scores for the age group 3 - 15 years; standard scores on the man and woman drawing are averaged and can be converted to percentile ranks.

The test is particularly useful in that it is non-threatening to children, administration and scoring is rapid, reliability and validity is adequate.

A verification of this test has been carried out in South Africa on a population of White school-children by Strumpfer and Mienie[69] using the NSAIS. They found reliability co-efficients of 0·88 for the 'man' scale and 0·92 for the 'woman' scale, by the split halves method. Low, but statistically significant, correlations were found between the Goodenough-Harris scores and NSAIS subtests; the highest co-efficient of 0·61 was obtained between the 'man' scale and the non-verbal IQ on the NSAIS. Generally, correlations were lower for the 'woman' scale than the 'man' scale which confirms Harris' statement that: 'Possibly the point scale method for scoring the woman figure is not quite as revealing of changes in psychological maturity as is the man figure'.[39] In the present study, only the 'man' scale was finally used, as time did not always permit the completion of 3 drawings by the children.

The drawings were also subjectively assessed according to the conflict indicators of Machover,[50] viz. omissions, excessive erasures, marked shading and sexual symbolism. The assessment was done blindly: the drawings in which there were marked indications of emotional disturbance were selected and identified later.

Procedure

Testing of the children was begun in March 1968 and continued through May 1969.

Conditions in the test situation were kept as constant as possible. Sessions were all held in the afternoon, in the Psychiatric Clinic of the Red Cross War Memorial Children's Hospital. The children were tested individually by the same examiner. A subject and his sibling were tested on the same day; the order in which they were tested was determined by flipping a coin. The battery of tests was divided into two roughly equal parts, so that each child had a rest period of at least 60 minutes between parts: when the first part had been completed by both children they joined each other for a 15-minute break during which they were given fruit cordial and biscuits.

All testing and scoring were done blindly—the test score sheets were coded and shuffled before scoring, and the group assignment of the children was not revealed to the examiner by the collaborator until after the quotients had been calculated. Social and scholastic data were also revealed only after the final quotients had been calculated.

Standing height, weight, and head circumference were measured on each child at the end of the testing session. The Boston growth charts were used as reference standards for height and weight. Children at or above the 3rd percentile (equivalent to ± 80% of expected height or weight for age) were regarded as having attained normal growth.

Social data were obtained by a trained social worker who had been in constant touch with the families over the past 10 years. The social conditions under which the family lived were rated on a 3-point scale, the intervals being described as 'fairly poor' (1), 'poor' (2) and 'very poor' (3). Scholastic data were obtained from the child's school principal by means of a questionnaire. Eighteen children had EEGs done as part of an earlier investigation; the alpha index was used as a measure of maturity of cortical rhythm.[28] Electronic data processing was performed on an ICT 1301 computer. Multiple t-tests and correlation coefficients were computed.

RESULTS

The means and standard deviations for the experimental (kwashiorkor) and control (sibling) groups are summarized in the following table:

TABLE IV. RESULTS OF TESTS ON EXPERIMENTAL AND CONTROL GROUPS

	Kwashiorkor		Sibling			
Variable	Mean	SD	Mean	SD	t	P
Age (years)	**11·10**	**1·04**	**10·99**	**1·87**	**0·32**	**NS**
Intelligence score	**77·37**	**15·22**	**77·67**	**14·85**	**0·16**	**NS**
Verbal score	**81·57**	**17·22**	**81·42**	**16·39**	**0·07**	**NS**
Non-verbal score	**77·55**	**11·92**	**77·55**	**12·33**	**0**	**NS**
Harris score	**75·52**	**17·82**	**79·62**	**18·03**	**2·52**	**<0·02**
Weight (% normal)	**73·65**	**10·78**	**74·34**	**11·12**	**0·35**	**NS**
Height (% normal)	**89·92**	**5·57**	**90·24**	**6·04**	**0·29**	**NS**
Head circumference (inches)	**20·26**	**0·60**	**20·17**	**0·45**	**0·98**	**NS**
Position in sibship	**4·92**	**3·35**	**4·67**	**3·54**	**0·97**	**NS**
Weight on discharge (% normal)	**67·85**	**12·03**	—	—		

The difference between the groups in mean age at the time of testing was not significant.

New South African Individual Scale

No significant differences were found between experimental subjects and controls on full scale intelligence score, verbal score or non-verbal score of the NSAIS. There was a positive correlation of 0·62 between subjects and siblings on full scale score.

No significant differences between the groups were found on the subtest scores. The correlation between intelligence score and degree of social pathology was −0·43 in the experimental group and −0·37 in the control group. Low negative correlations were found between intelligence score and family size in both groups.

Harris-Goodenough Drawing Test

A significant difference was found between subjects and controls on the Harris Drawing Test score ($P < 0·02$). The correlation between subjects and siblings was 0·84. A correlation of 0·62 between Harris score and full scale intelligence score was found in the control group and 0·67 in the experimental group. Similar correlations were found in both groups for all subtests of the NSAIS except for the Form Board in the experimental group, where the correlation was lower (0·33).

Of the 14 drawings selected as indicating marked emotional disturbance by Machover's[50] criteria, 9 were from the experimental group and 5 from the control group.

Height

Twenty-two children in the experimental group and 21 control children were below the 3rd percentile for height on the Boston growth charts. The mean intelligence score achieved by these children did not differ significantly from the mean score obtained by those children who had attained the 3rd percentile in either of the groups ($t = 0·3$ in the experimental group; $t = 1·01$ in the control group).

Nor was there any significant difference between the two groups for the mean intelligence scores obtained by children above and children below the 3rd percentile in height. The mean percentage expected height was 89·9% in the experimental group and 90·2% in the control group. The difference was not significant ($t = 0·03$).

Weight

Sixteen of the experimental subjects and 15 control children were below the 3rd percentile in weight for age at the time of testing on the Boston growth charts. There was no significant difference in either of the groups between the mean intelligence score of those children above and those children below the 3rd percentile in weight ($t = 0·24$ in the experimental group; $t = 1·57$ in the control group). The difference in intelligence score was not significant when experimental subjects who were below the 3rd percentile were compared with control children who were below the 3rd percentile ($t = 0·68$). No significant difference in intelligence score was found when experimental subjects and control children who were above the 3rd percentile were compared ($t = 0·68$).

The mean percentage of expected weight was 73·6% in the experimental group and 74·3% in the control group. The difference was not significant ($t = 0·3$). No correlation was found between the percentage of expected weight at the time of discharge from hospital and verbal, non-verbal or full scale intelligence scores in the experimental group. The mean percentage of expected weight on discharge from hospital for the experimental group was 67·85%. No correlation was found between intelligence score and percentage of expected weight at the time of testing in either of the groups. A low negative correlation (−0·29) was found between percentage weight on discharge from hospital, and the degree of social pathology.

Head Circumference

No significant differences were found between experimental subjects and control children in head circumference ($t = 0·98$; $P > 0·05$). The correlation between head circumference and full scale intelligence score was 0·24 in the experimental group and 0·11 in the control group.

Alpha Index of the EEG

The alpha index (percentage time that alpha rhythm is present) did not correlate with intelligence score in the 9 paired experimental subjects and controls. There was no significant difference between the subjects and controls in alpha index ($t = 0·9$).

Age of Onset of Kwashiorkor

A negative correlation of −0·38 occurred between the age of the child on admission to hospital and the full scale intelligence score in the experimental group. The mean age at first admission was 19·6 months (SD 9·6). (One child was admitted twice—aged 15 months and 26 months).

The sample was then divided into 2 subsamples on the basis of age of admission to hospital. Subsample I consisted of 19 subjects who had been admitted between the ages 10 - 15 months, and their controls. Subsample II consisted of 21 subjects admitted between the ages 16 - 48 months and their controls. Mean full scale intelligence scores for the subsamples are shown in Table V.

The difference between the experimental and control groups in either of the 2 subsamples was not significant. However, significant differences in full scale intelligence scores between the 2 subsamples were found in both the experimental and the control groups. The data were sub-

TABLE V. MEAN FULL SCALE INTELLIGENCE SCORES

	Age on admission		Intelligence score			
	Kwashiorkor	Sibling	Kwashiorkor	Sibling	t	P
Subsample I:						
N = 19 pairs	**10 - 15 months**	**—**	**84·7**	**82·6**	**0·76**	**NS**
Subsample II:						
N = 21 pairs	**16 - 48 months**	**—**	**70·7**	**73·2**	**1·4**	**NS**
			t = 3·24	**t = 2·07**		
			P<0·01	**P<0·5**		

jected to further analysis in an attempt to elucidate this finding.

No significant differences between the 2 subsamples in either of the groups were found in percentage of expected height, weight or in head circumference, family size or position in sibship.

In both the experimental and control groups, significant differences between the two subsamples occurred in full scale intelligence score, verbal and non-verbal scores, Harris-Goodenough score and all NSAIS subtest scores except Memory, Blocks, and Form Board. Because the subsamples were not paired or matched, comparisons are not valid. Intergroup differences in test scores were therefore looked for within the two subsamples. The results are shown in Table VI.

The difference between the early-onset and late-onset groups were thus eliminated by the controls, but a significant difference between experimental subjects and controls on the Harris-Goodenough test and the Problems subtest emerged in the late-onset subsample.

Scholastic Data

Data concerning performance in school was available for 30 of the experimental subjects and 27 of the control children. Three children (2 from the experimental group and 1 from the control group, were in special classes for children of subnormal intelligence). Fourteen experimental subjects (46·6%) and 9 of the control children (33·3%) were above the average age of their classes. Ten experimental group children (33·3%) and 11 control children (40·7%) were younger than the average age for their classes. Four children (13·3%) in the experimental group and 6 control children (22·2%) were average in age for their classes.

Scholastic achievement was strikingly lower in the experimental subjects of the late-onset subsample when compared with the control group. In the early-onset subsample, experimental subjects and control children were equivalent in level of school performance.

Social Data

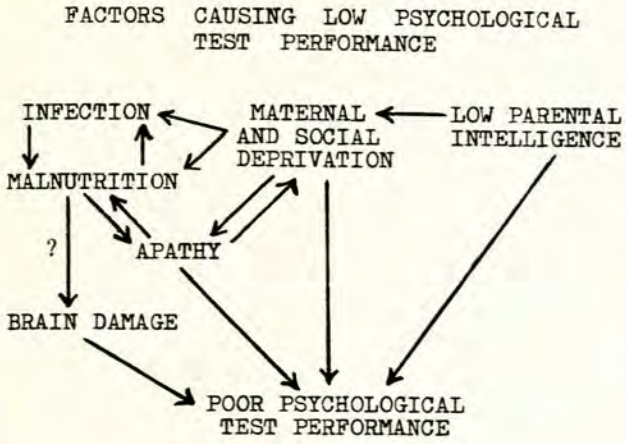
The mean rating of social pathology on the whole sample was '2', i.e. 'poor' social conditions. The mean number of siblings in the families sampled was 8·4; the range was from 2 - 17 siblings per family. The mean social pathology rating in the early-onset subsample was 1·8; and 2·3 in the late-onset subsample. The difference was significant (t = 2·19; P <0·05).

TABLE VI. MEAN TEST SCORE FOR EXPERIMENTAL AND CONTROL GROUP ACCORDING TO AGE OF ONSET (ADMISSION TO HOSPITAL)

	Subsample I			Subsample II		
Group	Kwash.	Sib.	Diff.	Kwash.	Sib.	Diff.
Verbal score	**89·6**	**87·5**	**NS**	**74·3**	**71·0**	**NS**
Non-verbal score	**82·8**	**80·4**	**NS**	**72·8**	**74·4**	**NS**
Full scale score	**84·7**	**82·6**	**NS**	**70·7**	**73·2**	**NS**
Harris score	**82·3**	**84·8**	**NS**	**69·4**	**75·9**	**t = 5·9; P = <0·001**
Vocabulary score	**9·9**	**10·2**	**NS**	**7·5**	**8·3**	**NS**
Comprehension	**9·6**	**8·5**	**NS**	**6·9**	**7·2**	**NS**
Verbal reasoning	**10·3**	**9·6**	**NS**	**8·4**	**8·0**	**NS**
Problems	**7·4**	**7·0**	**NS**	**5·2**	**6·1**	**t = 3·0; P = <0·01**
Memory	**6·7**	**6·7**	**NS**	**5·2**	**5·0**	**NS**
Patterns	**7·4**	**6·9**	**NS**	**5·6**	**5·6**	**NS**
Blocks	**7·9**	**7·3**	**NS**	**6·9**	**7·2**	**NS**
Absurdities	**8·0**	**8·1**	**NS**	**6·8**	**6·4**	**NS**
Form board	**7·2**	**7·0**	**NS**	**6·2**	**7·1**	**NS**

DISCUSSION AND CONCLUSION

Discussion of the results of this study is facilitated by the following diagrammatic representation of the variables:



In the previous studies reviewed, brain damage resulting from PCM was postulated as the cause of poor psychological test performance in groups of children rehabilitated after marasmus and/or kwashiorkor. Brain damage, however, is only one of several variables which contributed to poor test performance, others being the apathy of the acutely ill or sub-optimally nourished child; an impoverished and non-stimulating social and emotional environment; and low parental intelligence level. These factors also contribute to the incidence of PCM. In the present study, the groups differed only in that the PCM in the experimental group had been of sufficient severity to cause an episode of fulminating kwashiorkor requiring in-patient hospital treatment. A consistent significant difference in the psychological test performance between the groups could thus be attributed directly to the effects of this severe form of PCM on the central nervous system.

The results of this study showed no significant differences in intelligence score between the groups of rehabilitated kwashiorkor subjects and their siblings. Nor were there any significant physical differences between the two groups. This indicates that the episode of kwashiorkor itself had no significant effect on the intelligence test level or the physical parameters used in this study.

The finding of a negative correlation between the age of onset and the intelligence score appears to be contrary to the expectation of Stoch and Smythe[97] that the earlier the insult, the more significant would be the impairment of brain development and function. However, as the age at time of hospitalization was used as the index of onset, this finding may indicate a relationship between prolonged, chronic PCM during infancy and later intellectual performance. Conversely, earlier treatment and the initiation of long-term medical and social supervision may have alleviated prolonged, chronic PCM in the family, and contributed to improved social conditions generally. Thus both subjects and siblings of the early-onset subsample had significantly higher intelligence scores than the subjects and siblings in the late onset subsample. Social conditions under which the late-onset subsample lived were also significantly worse than those of the early-onset subsample, as indicated by the significantly higher social pathology rating in the former subsample. This factor could also account for the differences in intelligence scores: severity of social pathology and intelligence score were negatively correlated. The significantly lower verbal scores which lowered the full scale scores for both subjects and siblings in the late-onset subsample may also reflect the significantly greater degree of social deprivation found in this subsample as compared with the early-onset subsample. For example, Birch[8] found in a Latin American community that the mothers whose children tended to grow poorly spoke most frequently to their children in a local dialect rather than in the European language of the larger community; from the first days of life onward, poorly nourished children tended to be exposed to a cultural and linguistic environment which differed from that of children who were growing well.

The findings which possibly can be attributed to the effect of kwashiorkor are the significantly lower scores on the Harris Drawing Test and Problems subtest achieved by the kwashiorkor subjects in the late-onset subsample. The lower Problems score may be a reflection of the lower scholastic achievement in this group, or may indicate reduced ability to concentrate. The significant difference between kwashiorkor subjects and their siblings on the Harris Drawing Test in the absence of significant intelligence score differences suggests the interference of emotional or affective factors with the children's cognitive functioning. Harris[39] quotes studies which associated a discrepancy between Goodenough score and Binet IQ with maladjustment and delinquency; positive affective states induced experimentally in children were shown to raise the Goodenough score. In a more recent study, Levine and Gross[47] showed that Harris-Goodenough scores were significantly lower than WISC and Binet scores in a population of children referred for psychiatric treatment.

The finding of greater numbers of drawings with signs of emotional conflict among the late-onset kwashiorkor subjects lends support to this postulate. Eight of the 14 drawings selected as showing evidence of relatively marked emotional disturbance were responses of subjects in the late-onset kwashiorkor subsample. Only 3 were identified as siblings of late-onset subjects: 1 was from the early-onset kwashiorkor group, and 2 from siblings of this subsample. The poor scholastic performance of the late-onset kwashiorkor group could also be indicative of poor social and emotional adjustment.

The mean intelligence scores found in the present study approximate closely to the mean intelligence score in Stoch and Smythe's control group, on the same test battery.[98] Low intelligence test scores in their marasmic group were associated in 8 cases with a reduced EEG alpha index, due to a dominance of theta activity.[4] In another investigation, no significant difference was found in the mean alpha index between a large group of kwashior-

kor rehabilitees and their siblings.[28] These EEG findings corroborate the intelligence test findings in both the present study and the study of Stoch and Smythe.[68] However, the differences between the groups in the latter study cannot be ascribed with confidence to PCM *per se*, due to the important non-nutritive, social differences which existed between the marasmic and control groups.

The postulate in some of the previous studies that primary mental subnormality may have contributed toward the occurrence of kwashiorkor, is not borne out by the findings of the present study. Again, however, the possibility is maintained that the results of those studies may be due to the influence of uncontrolled non-nutritive factors.

CONCLUSION

The results of this study indicate that there are no significant differences in intellectual development between children who suffered from kwashiorkor early in infancy (under 15 months of age) and their siblings who had had no such acute nutritional illness. However, a deficit in intellectual maturity was found when the acute episode of kwashiorkor had occurred later in life (after the age of 16 months) which could have been caused by interference of affective factors in the children's cognitive processes.

The possibility is not excluded that children who have suffered very severe and prolonged nutritional deprivation may show intellectual retardation when compared with children who have lived under similar social circumstances but have not been nutritionally deprived. The major obstacle in investigating this possibility lies in locating such a group. One possble way of further testing this hypothesis would be to compare children who are nutritionally deprived by virtue of an intestinal malabsorption syndrome with their siblings, making due allowances for the effect of differential parental attitudes to their 'sick' and 'well' children. No such systematic studies have been done, but the clinical evidence so far is that children with cystic fibrosis, coeliac disease, etc. are not generally intellectually impaired.[34]

This work was done in the MRC Clinical Nutrition Research Unit of the University of Cape Town and the Red Cross War Memorial Children's Hospital, Rondebosch. The children studied were made available from a larger group which has been kept continously under observation by Miss A. D. Moodie for the possible long-term effects of protein-calorie malnutrition. Anthropological and other findings are reported in the next article in this issue. We wish to thank Professor W. P. Radloff for providing encouragement, helpful advice and stimulating ideas, Dr M. V. Buhrmann for the use of playrooms at the hospital, Mr W. B. de V. Smit and Mrs Ensor of the University of Cape Town Computer Centre for assistance with the data analysis.

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