Kwashiorkor : A Prospective Ten-Year Follow-up Study*

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SUMMARY

The physical status of 123 cases of kwashiorkor, followed up longitudinally for 10 years, was analysed. Their status was compared with that of 97 control siblings who had never suffered from kwashiorkor, but who had grown up under the same environmental conditions as the ex-patients.

It was found that 10 years after the episode of kwashiorkor about half of the children had reached international growth standards in weight and height, thus demonstrating the capacity for complete physical recovery.

No significant anthropometric or biochemical differences were found between ex-patients and control siblings at the 10-year follow-up examination. This is adequate proof that the episode of kwashiorkor per se cannot be held responsible for the growth retardation that occurred in some of the children.

The children who were most severely retarded in weight and height on admission tended to remain the most severely retarded in growth after 10 years. The children who were the oldest on admission were more retarded in weight after 10 years than the children who were admitted at a younger age. Although these facts may imply that the severity and possibly the duration of the malnutrition episode adversely affected subsequent physical growth, a high current incidence of hypoalbuminaemia was found in both ex-patients and control siblings, indicating continuing malnutrition, the effects of which cannot be separated from possible deleterious effects of the original malnutrition episode. Linear growth also correlated significantly with midparental height and a complex of adverse social circumstances.

Failure to attain international growth standards in some of the children was therefore apparently due to a combination of factors and at present it is impossible to distinguish any single one of these as being more important than the others.

Since about half of the children did reach adequate growth standards despite their poor living conditions, it is clearly worth while to treat every case of malnutrition. At the same time public health supervision and preventative social measures should be greatly increased to protect the child population throughout the growing period.

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'An enhanced interest has recently been shown in consideration of the young child recovering from protein-calorie malnutrition. This is long overdue, because for many years emphasis was placed on the clinical, biochemical and pathological features of kwashiorkor and nutritional marasmus. This change is clearly indicated by the interest being shown by nutritionists and behavioral scientists in the intellectual development of children following protein-calorie malnutrition, and a resurgence of research in the area of physical growth following malnutrition.'[63]

The extent of the problem is further underlined by a recent estimate that 60% of the total pre-school population of the world (i.e. 300 million children) suffer from mild to moderate protein-calorie malnutrition.[7] The most frequent manifestation of protein-calorie malnutrition is retarded growth.[20] From both an individual and public health point of view, it is of paramount importance to determine whether such children still have the potential to grow and develop normally, or whether irreversible physical or mental damage has been inflicted by the malnutrition episode.

The longterm effects of severe protein-calorie malnutrition in childhood are still largely unknown. There is evidence that growth and adult size of some animal species may be permanently affected by nutritional deprivation at critical periods. For example, if rats are made to grow slowly during the first 3 weeks of their lives by being suckled in large groups, they do not catch up in growth in spite of unlimited food supply after weaning and they become small adults.[43,87,88] Winick and Noble found that malnutrition in neonatal rats resulted in permanent reduction in the cell number of several organs and a resultant permanent growth failure.[89]

Undernutrition of similar severity and for the same length of time after, rather than before weaning, interferes much less with the prospect of successful rehabilitation in rats. It is only by prolonged and severe undernutrition after weaning that the attainment of adult size can be hindered to the same extent as it can by a temporary nutritional setback earlier in life.[54] On the other hand, pigs may reach near normal growth in spite of prolonged periods of undernutrition[85] and, in Rhesus monkeys that are fed diets deficient in nitrogen between the first and seventh month of life, the potential for recovery from malnutrition is markedly efficient on resumption of an adequate diet.[44]

Thus, in addition to species differences, the timing, severity and duration of the malnutrition are additional factors affecting growth potential in animals.[54]

In man, the results of the different longterm follow-up studies on infantile malnutrition are difficult to com-

pare, because of variation in the case material, age of subjects at the time of nutritional stress, duration of follow-up and the difficulty of finding adequate controls. It is therefore not surprising that the findings obtained in some of the studies are contradictory. They vary from failure to demonstrate any catch-up in growth at all[45] to normal[13] or even slightly superior physical growth[30] after infantile malnutrition.

In addition, growth is bound to be affected by subsequent diet and social circumstances. Unless these factors are taken into account, the effects of one or more episodes of infantile malnutrition are impossible to evaluate.

In Cape Town, a prospective follow-up study on kwashiorkor was commenced in 1958. Contact was maintained with children discharged from hospital after an episode of kwashiorkor. Three, five and ten years after discharge from hospital, the children were examined by a paediatrician. The results of the 3- and 5-year follow-up study of some of these children have already been reported,[11,60,90,92] and their social background has been described.[59]

In the present report, the physical status and environmental background of 123 children, 10 years after an episode of kwashiorkor, are analysed in detail. As controls, 97 siblings who had never suffered from kwashiorkor were used. The 10-year follow-up results are also compared with the results obtained at the 5-year follow-up examination and on admission to hospital 10 years earlier.

A detailed report on the intellectual assessment of some of these children is available,[24] and the results are also reported in this issue.[25]

CASE MATERIAL

Ex-patients

The study commenced with 221 cases of severe kwashiorkor admitted serially to the hospital, provided that they lived within a 12-mile radius from the hospital. Their ages ranged from 5 months to 4 years and 4 months. About half of the children were admitted to a metabolic research ward, where male cases were given preference of admission, accounting for the preponderance of males in this study.

Of the 221 cases, 57 (26%) died in hospital, leaving 164 cases discharged alive for follow-up. Contact with the ex-patients was maintained by means of home-visits approximately thrice-yearly in the first 5 years and twice-yearly thereafter by one of us (A.M.). This frequency was considered suitable for ensuring that the families were not lost, while minimizing the influence of the investigation on the course of events. Advice on child care was not withheld but the mothers were free to follow it or not as they chose. Only in rare cases, if the child appeared to be in danger at the time of a visit, were more active steps taken. Medical treatment at hospital and preventive care at Welfare Centres remained available for these as for other children in the community. The children's subsequent fate is shown in Table I.

TABLE I. CASE MATERIAL: EX-PATIENTS

Cases originally admitted to hospital	221
Deaths in hospital	57
Discharged alive	164
Lost in the series after discharge:	
Died of relapsed kwashiorkor	15
Died in car accident	1
Died of pneumonia	1
Died of postoperative complications	1
In sanatorium with tuberculosis	1
Left Cape Town	22
Total available for study after 10 years	123

Excluding the child in the sanatorium, the sample studied at the 10-year follow-up examination therefore represents a 100% follow-up of those children still living in Cape Town. At the 5-year follow-up examination one

TABLE II. CASE MATERIAL: EX-PATIENTS AND CONTROL SIBLINGS: AGES AND NUMBERS OF CASES ON ADMISSION, AFTER 5 YEARS AND AFTER 10 YEARS

		Ex-patients		Siblings	
		Mean age in months ± 1 SD	Number of cases	Mean age in months ± 1 SD	Number of cases
Admission	M* + F†	18·8 ± 8·4	123	26·8 ± 15·7	62
	M	18·8 ± 7·6	78	26·5 ± 16·2	38
	F	18·8 ± 9·7	45	27·3 ± 15·2	24
5-year follow-up	M + F	81·6 ± 8·8	122	64·5 ± 21·8	81
	M	81·1 ± 8·8	77	65·5 ± 22·6	46
	F	82·4 ± 10·0	45	63·6 ± 21·3	35
10-year follow-up	M + F	137·4 ± 9·7	123	129·1 ± 27·2	97
	M	137·3 ± 8·8	78	127·3 ± 25·7	54
	F	137·4 ± 11·3	45	131·4 ± 29·2	43

* M = males; † F = females. Applies to all the tables.

of these 123 children was temporarily absent from Cape Town. There were 105 Cape Coloured children and 18 Bantu children in the sample.

The mean ages and sex distribution of the ex-patients are shown in Table II.

Controls

At the 10-year follow-up examination the sibling nearest in age to the ex-patient was studied (Table II). In 26 instances no such sibling was available because the sibling nearest in age was also known to have suffered from kwashiorkor, or because the patient had been adopted by foster parents or was an only child. The available 97 siblings therefore had never suffered from an overt episode of kwashiorkor, but had otherwise grown up under the same circumstances as the ex-patient.

In the previously reported 3- and 5-year follow-up studies from our group,[11,59,60,90,92] the sibling sample was selected differently, i.e. several siblings (even 6) of some of the patients were used, no attempt being made to examine one sibling for each individual case. In retrospect, this was considered an error in method. Accordingly, in the current report, the 5-year follow-up sibling sample only includes those cases who were also studied at 10 years. This has caused a reduction to 81 in the number of siblings for whom data were available for the 5-year follow-up.

The 'admission sibling' sample consisted of 62 of the 81 cases studied at the 5-year follow-up examination. These children were examined 0 - 2 years after their brothers or sisters suffering from kwashiorkor had been discharged from hospital, and such siblings were usually older than the ex-patient. This accounts for the higher mean age of the admission sibling sample as compared with the ex-patients. At the 5- and 10-year follow-up examination siblings younger than the ex-patient also became available, thus reducing the discrepancy in the mean ages of the two samples.

METHODS

For the 10-year follow-up examination, the following data were obtained from the 123 ex-patients and their 97 control siblings:

1. A clinical history and physical examination.
2. Anthropometric measurements.
   (*a*) Body weight, standing height and head circumference using accepted international techniques.[16,41,67]
   (*b*) Triceps and subscapular skinfolds using a Harpenden skinfold caliper[23,37,78] by the method previously described.[42]
   (*c*) The mid-upper arm circumference (MUAC) was measured on the left side with a 1 cm wide non-stretchable tape, at a point midway between the tip of the acromial process of the scapula and the olecranon process of the ulna.
   (*d*) The mid-upper arm muscle circumference (MUAMC) was calculated from the formula MUAC = MUAC $- \pi \times$ Triceps skinfold.[41]

All the anthropometric values thus obtained were then expressed as a percentage of a standard or expected value for the particular age and sex of the child. The standard values for these calculations were the following: For weight and height, the 50th percentile values of the Boston standards;[62] for head circumference, the values of Watson and Lowrey;[84] for triceps and subscapular skinfolds the 50th percentile values of Tanner and Whitehouse[80] and for MUAC and MUAMC the standard values of Jelliffe.[41]

3. An X-ray of the hands and wrists. Bone age was estimated by comparing the children's X-rays with the plates in the atlas of Greulich and Pyle.[35] Each X-ray was interpreted individually by two radiologists and the mean of the two readings was used in the calculations. The radiologists were not supplied with the ages of the children.

4. (*a*) Serum albumin and serum globulin by the Biuret method.[19,56]
   (*b*) Blood haemoglobin, packed-cell volume and mean corpuscular haemoglobin concentration, by the methods described previously.[90]

5. The standing heights of both parents of 55 ex-patients were obtained in the homes of the children by one of us (A.M.).

6. Twenty pairs of ex-patients and control siblings were subsequently admitted to hospital for more detailed examination. These 20 pairs of children consisted of 4 groups, each group comprising 5 pairs of children, selected randomly from the total sample:

Group A: Ex-patients and control siblings under the 3rd Boston percentile in weight.

Group B: Ex-patients under the 3rd percentile in weight, siblings over the 3rd percentile in weight.

Group C: Ex-patients over the 3rd percentile in weight, siblings under the 3rd percentile in weight.

Group D: Ex-patients and siblings both over the 3rd percentile in weight.

The following investigations were done on these children:

   (*a*) Oral lactose tolerance tests. Lactose was given as a 10% solution after an overnight fast in a dose of 2g/kg body weight with a maximum of 50 g. Fasting, 30-, 60-, 90- and 120-minute capillary blood sugar levels were estimated by the Somogyi-Nelson method.[61,74]
   (*b*) Microscopy and culture of warm stools.
   (*c*) Chemical and microscopic examination of urine.
   (*d*) Serum urea[83] and cholesterol[82] after an overnight fast.

7. Social circumstances.

For approximately 19 months between 1958 and 1960 notification was received from two hospitals of the admission of any child suffering from kwashiorkor. The series was then closed. The method of medical-social interview and follow-up has been described elsewhere.[59] For the first 5 years a check was kept on growth by weighing and measuring the children at home and social data were continuously added to the original record. At the end of this period the children were brought to

hospital for full clinical examinaiton and at this time there was also a review of medical-social data.[60] During the second 5 years weighing and measuring were not done at home but social details and especially progress at school were recorded. At the time of the 10-year clinical examination social circumstances were reviewed under the following headings and a percentage score was calculated for each:

(*a*) *Housing space.* Adequacy of housing space was derived from the Occupation Density[4] of each household.

(*b*) *Economic status.* Mean economic status was calculated from three assessments made in relation to the Poverty Datum Line,[5] i.e. on admission, after 5 years and after 10 years.

(*c*) *Diet.* Dietary adequacy was estimated according to the frequency of intake of key protein foods during a typical week.

(*d*) *Stability.* Family stability was scored in relation to the following sets of adverse factors: incomplete or impermanent parental background; problems associated with alcohol; failure of the father in the role of bread-winner; separation from the mother; delinquency within the family.

For each child the percentage score obtained from the above 4 factors was then meaned to give a 'Multiple Social Index' (MSI).

8. A record was kept of the children's progress at school and the number of times that they failed to pass their grades. In the 95 cases in which both ex-patient and sibling were attending school their progress was compared.

Statistical analysis was done by means of a Wang Model 370 computer, using the formulae in Documenta Geigy.[18]

All the anthropometric and clinical data, except the skinfolds and arm circumference values, had also been obtained at the 5-year follow-up examination in all the ex-patients as well as some of the control siblings.

All admission weights of the ex-patients at the start of the study were known. For 54 children daily weights during their hospital stay were available and in these children the lowest weights recorded immediately after loss of oedema were used in all the calculations instead of the admission weights when the children were still oedematous. Most of these children were boys admitted to a metabolic ward. Apart from metabolic ward cases, heights on admission were not available.

The weights and heights of the admission sibling sample were obtained in the children's homes. A portable spring-balance scale was used for weighing. Heights of children who were big enough to stand were obtained by standing them against a wall but smaller children's heights were not taken.

RESULTS

General

Most of the children appeared well proportioned and happy. The majority admitted to *Ascaris lumbricoidis* infestation, 5 ex-patients and 1 sibling complained of chronic diarrhoea and 2 ex-patients and 1 sibling were under ambulatory treatment for tuberculosis. Scabies was extremely common and often complicated by superficial skin infection. More than two decayed teeth were present in about 50% of the children. Bilateral parotid enlargement was noted in 19 ex-patients (15·4%) and 14 siblings (14·4%). The liver size and consistency appeared normal in all children except in one ex-patient suffering from liver cirrhosis probably caused by infective hepatitis.

Breast development had commenced in 11 ex-patients and 13 siblings. One of the ex-patients (2·8%) and 6 of the siblings (13·9%) had started to menstruate.

Weight

Mean percentage of expected weight (Table III): (*i*) *The ex-patients*: On admission to hospital 10 years before, the mean percentage of expected weight was 62·5%. The superior weight of the girls at that time may have been due to the fact that most girls were assessed before loss of oedema (see under Methods).

TABLE III. WEIGHT: EX-PATIENTS AND SIBLINGS: MEAN PERCENTAGE OF EXPECTED WEIGHT (% EW)

		Ex-patients		Siblings		
		Mean % EW ± 1 SD	Number of cases	Mean % EW ± 1 SD	Number of cases	Significance
Admission	**M + F**	**62·5 ± 13·0**	**123**	**80·1 ± 15·3**	**62**	**$p<0·001$**
	M	**60·2 ± 11·4**	**78**	**79·5 ± 14·0**	**38**	**$p<0·001$**
	F	**66·5 ± 14·7**	**45**	**82·3 ± 16·9**	**24**	**$p<0·001$**
5-year follow-up	**M + F**	**76·3 ± 10·9**	**122**	**78·2 ± 12·8**	**81**	**NS***
	M	**75·5 ± 10·6**	**77**	**76·1 ± 12·2**	**46**	**NS**
	F	**77·4 ± 11·2**	**45**	**80·7 ± 13·6**	**35**	**NS**
10-year follow-up	**M + F**	**76·4 ± 11·2**	**123**	**76·9 ± 10·2**	**97**	**NS**
	M	**75·3 ± 11·6**	**78**	**74·9 ± 9·7**	**54**	**NS**
	F	**78·3 ± 10·5**	**45**	**79·4 ± 10·3**	**43**	**NS**

* NS = not significant. Applies to all the tables.

At 5 years the mean percentage of expected weight had increased significantly to 76·3% ($p<0·001$) but at 10 years there was no further improvement.

(*ii*) *The siblings*: On admission the mean percentage of expected weight was significantly more than that of the ex-patients but at 5 and 10 years the two groups were comparable.

Both the ex-patient and sibling females when compared with boys had higher mean values for percentage expected weight on admission and at the 5- and 10-year follow-up examination. This sex difference was statistically significant at 10 years in the siblings ($p<0·05$).

The frequency distribution of percentage of expected weights: The frequency distribution of percentage of expected weight in the ex-patients at the 5- and 10-year follow-up is shown in Fig. 1A. A proportion of children had improved in percentage of expected weight (area X) but on the other hand a proportion of children had deteriorated (area Y). This held true for boys as well as for girls (Figs. 1B and 1C).

In Fig. 1D the frequency distribution of percentage of expected weight of ex-patients is compared with that of the siblings at the 5-year follow-up examination. Fig. 1E shows the same comparison at the 10 year follow-up examination. The differences shown at 5 years were no longer evident at 10 years, when the distribution had become nearly exactly superimposable.

Weight in relation to the 3rd Boston percentile: Mean percentage of expected weight fails to indicate how many children have reached adequate weight standards. Frequency distribution of percentage of expected weight gives a better indication of adequate attainment of weight. This method is, however, subject to wrong interpretation when comparing children of different ages, eg. ± 80% of expected weight in young children coincides with the 3rd percentile, but in a child of 15 years, 76% of expected weight may still be above the 3rd percentile. The children were therefore divided into those who had reached the 3rd percentile of weight and those who had not (Table IV). The results are illustrated in Figs. 2A and 2B (ex-patients) and Figs. 3A and 3B (siblings).

During the episode of kwashiorkor very few of the children were above the 3rd percentile. At 5 years 42% of children reached the 3rd percentile, and at 10 years 53%. The improvement from the 5 to 10 years was mainly due to an improved status in the girls (Table IV).

TABLE IV. WEIGHT: EX-PATIENTS AND SIBLINGS: PERCENTAGE OF CHILDREN ABOVE THE 3RD BOSTON PERCENTILE

		Percentage of children above third percentile	
		Ex-patients	Siblings
Admission	**M + F**	**10**	**52**
	M	**5**	**50**
	F	**16**	**54**
5-year follow-up	**M + F**	**42**	**49**
	M	**42**	**46**
	F	**42**	**54**
10-year follow-up	**M + F**	**53**	**52**
	M	**44**	**41**
	F	**69**	**65**

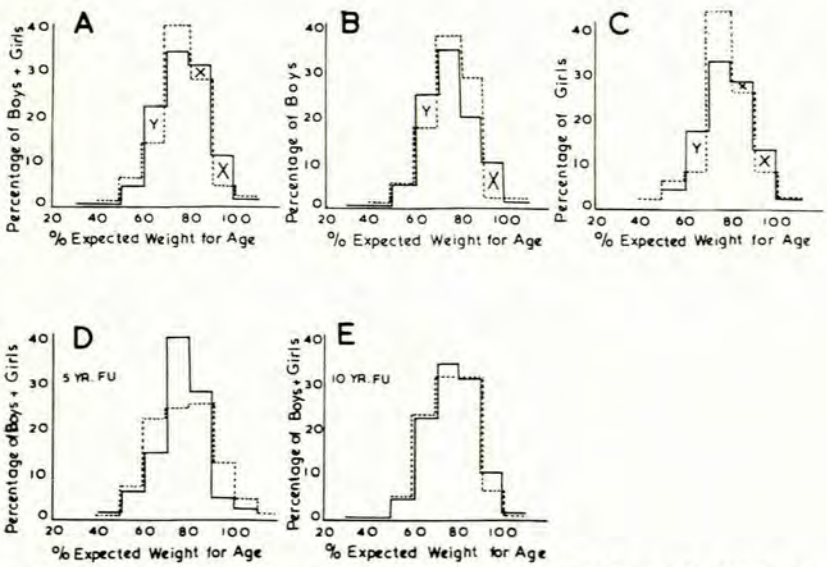
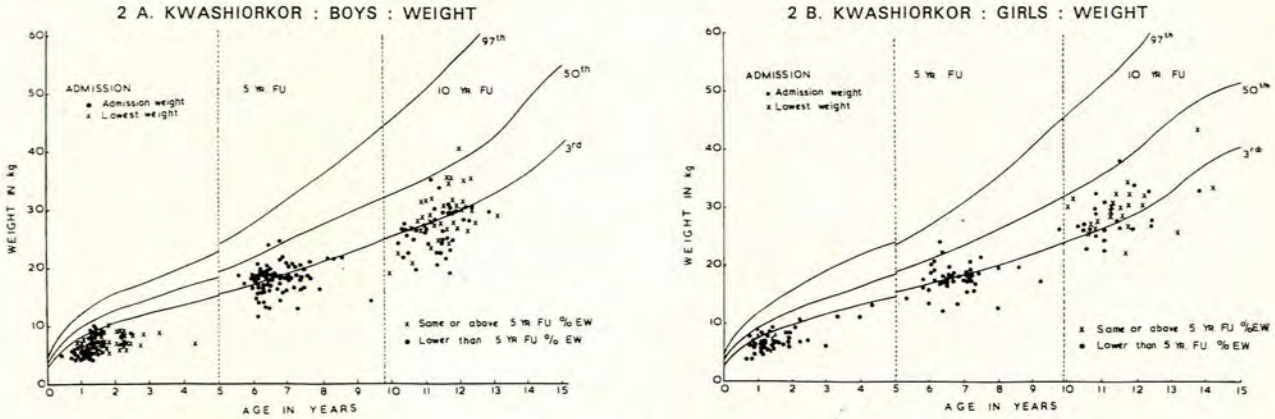


Fig. 1A. Frequency distribution of percentage of expected weight of the ex-patients at the 5-year follow-up examination (dotted line) and at the 10-year follow-up examination (solid line).
B and C. The same distribution curve for ex-patient boys and girls separately.
D and E. The frequency distribution of percentage of expected weight at the 5-year and 10-year follow-up examinations respectively in ex-patients (solid line) and siblings (dotted line).



Figs. 2 A and B. Weights of ex-patient boys (A) and girls (B) in relation to the 3rd Boston percentile on admission, at 5 years and at 10 years.

At 5 years the siblings still showed a slight superiority over the ex-patients but at 10 years there were only minor differences. As with the ex-patients more sibling girls than boys had reached the 3rd percentile in weight at the 5- and 10-year follow-up.

Individual ex-patients showing improvement in percentage of expected weight: Figures 2A and 2B also indicate the ex-patients who improved in percentage of expected weight from the 5- to the 10-year follow-up, i.e. 38 of 78 boys (49%) and 23 of 45 girls (51%). This increase in expected weight, however, does not necessarily imply that the children had reached the 3rd percentile since many of them still remained far below it.

Height

Mean percentage of expected height. (Table V): (*i*) *The ex-patients*: The mean percentage of expected height on admission was 86·6% in the boys. Only one height for girls was recorded on admission and this was 85% of expected height.

At 5 years the mean percentage of expected height was 88% (boys 87·4%, girls 89·1%) and at 10 years this had increased significantly to 90·5% ($p<0·001$) (boys 90·1%, girls 91·0%).

(*ii*) *The siblings*: The mean percentage of expected height on admission was 88·1%, at 5 years it was 88·3% and at 10 years the mean percentage of expected height had increased significantly to 90·8% ($p<0·005$).

At 5 years there were no statistically significant differences between heights of the ex-patients and the siblings but at 10 years sibling girls had a statistically significant better mean percentage of expected height than the ex-patient girls ($p<0·05$).

As with weight, in both the ex-patients and siblings, girls had a higher mean percentage of expected height than boys at both the 5- and 10-year follow-up examination. These differences between boys and girls were statistically significant at 5 and 10 years in the siblings only ($p<0·05$).

TABLE V. HEIGHT: EX-PATIENTS AND SIBLINGS: MEAN PERCENTAGE OF EXPECTED HEIGHT (% EH)

		Ex-patients		Siblings		
		Mean % EH ± 1 SD	Number of cases	Mean % EH ± 1 SD	Number of cases	Significance
Admission						
	M + F	—	—	**88·1 ± 5·3**	**42**	—
	M	**86·6 ± 6·9**	**35**	**87·9 ± 5·5**	**25**	**NS**
	F	—	—	**89·0 ± 5·3**	**17**	—
5-year follow-up						
	M + F	**88·0 ± 5·5**	**122**	**88·3 ± 6·4**	**122**	**NS**
	M	**87·4 ± 5·2**	**77**	**86·8 ± 6·1**	**46**	**NS**
	F	**89·1 ± 5·7**	**45**	**90·3 ± 6·5**	**35**	**NS**
10-year follow-up						
	M + F	**90·5 ± 4·9**	**123**	**90·8 ± 5·3**	**97**	**NS**
	M	**90·1 ± 5·0**	**78**	**89·1 ± 5·0**	**54**	**NS**
	F	**91·0 ± 4·9**	**45**	**93·1 ± 4·5**	**43**	**$p<0·05$**

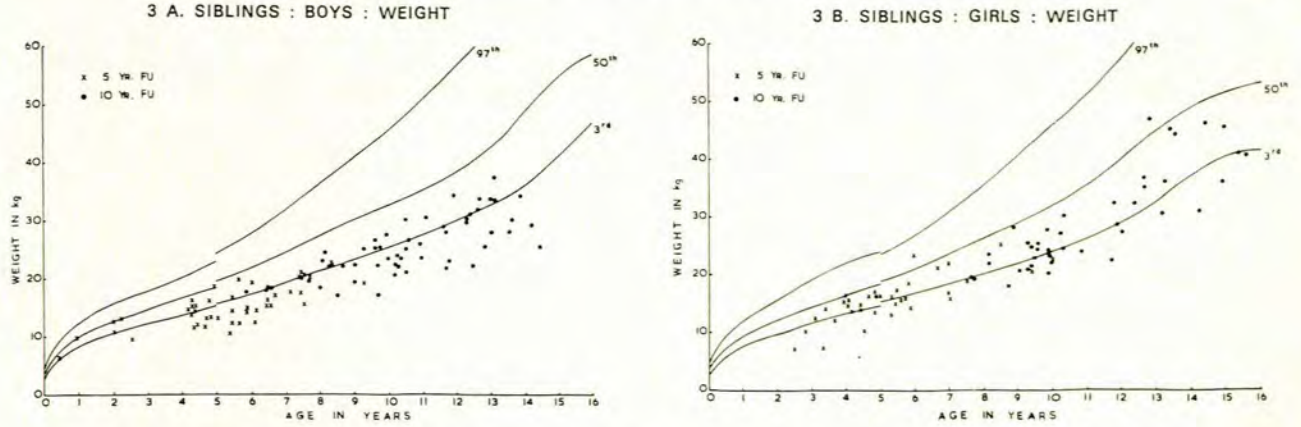


Fig. 3 A and B. Weights of sibling boys (A) and girls (B) in relation to the 3rd Boston percentile at 5 and 10 years.

The frequency distribution of percentage of expected height: The frequency distribution of percentage of expected height in the ex-patients at the 5- and 10-year follow-up is shown in Fig. 4A. There was a considerable improvement from 5 to 10 years in the proportion of children showing an improvement in percentage of expected height (areas X). In contrast to weight, there had been no deterioration. This held true for boys as well as for girls (Figs. 4B and 4C).

In Figs. 4D and 4E the frequency distribution of percentage of expected height of ex-patients is compared with that of the siblings at the 5- and 10-year follow-up examinations respectively. At the 10-year follow-up the distribution curve of the siblings is to the right of that of the ex-patients, probably due to the superior length of the girl siblings.

Height in relation to the 3rd Boston percentile: Table VI shows the division of the children into those who had

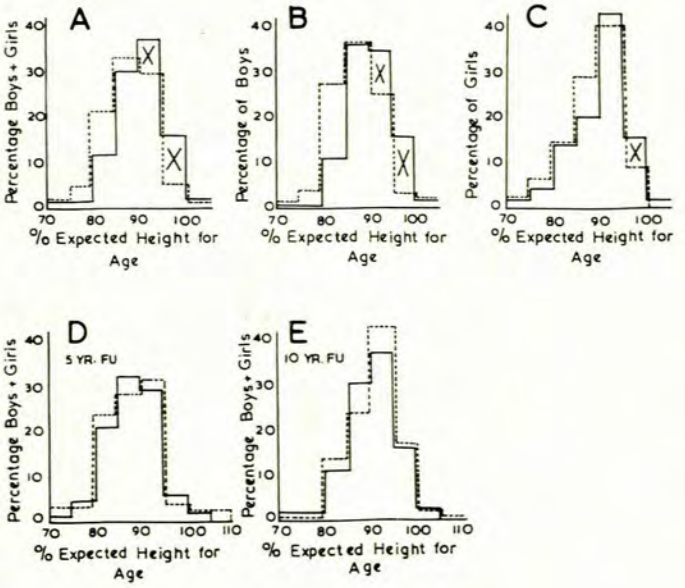


Fig. 4A: Frequency distribution of percentage of expected height of the ex-patients at the 5-year follow-up examination (dotted line) and at the 10-year follow-up examination (solid line).
B and C: The same distribution curve for ex-patient boys and girls separately.
D and E: The frequency distribution of percentage of expected height at the 5- and 10-year follow-up examinations respectively in ex-patients (solid line) and siblings (dotted line).

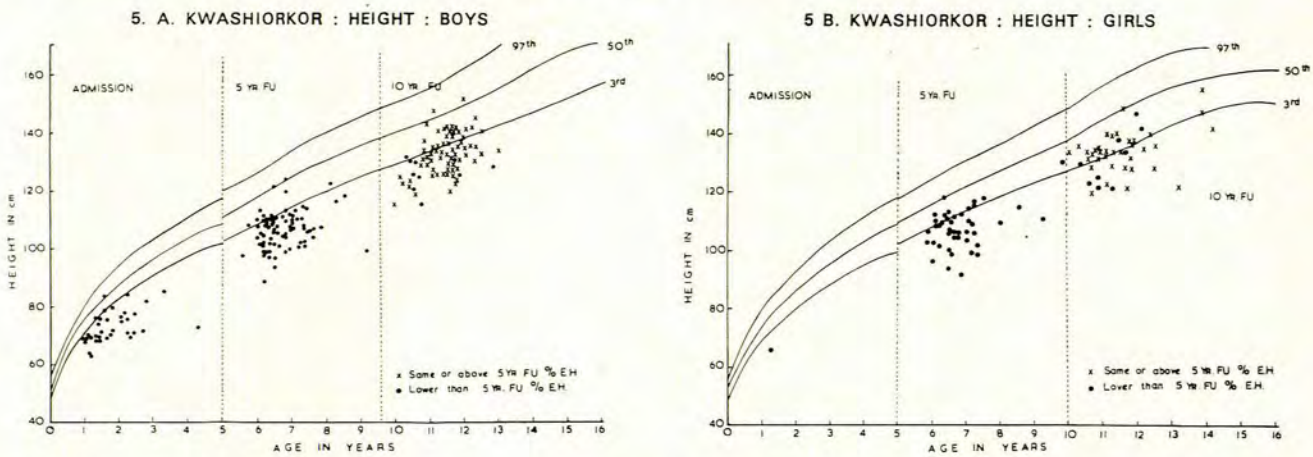


Fig. 5 A and B. Heights of ex-patient boys (A) and girls (B) in relation to the 3rd Boston percentile, on admission, at 5 and 10 years.

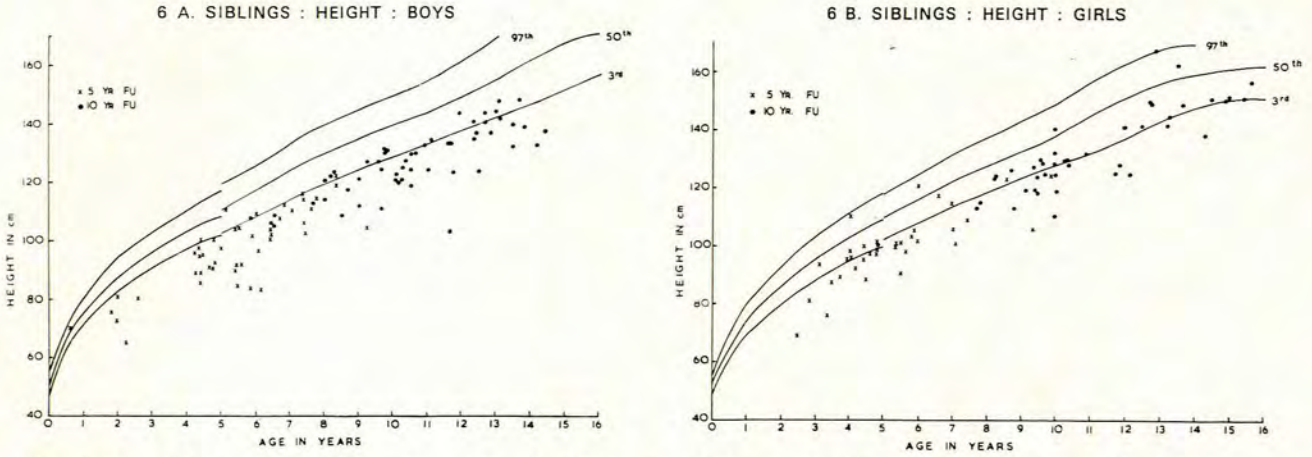


Fig. 6 A and B. Heights of sibling boys (A) and girls (B) in relation to the 3rd Boston percentile at 5 and 10 years.

reached the 3rd Boston percentile in height and those who had not. The results are illustrated in Figs. 5A and 5B (ex-patients) and Figs. 6A and 6B (siblings).

During the episode of kwashiorkor only very few of the boys were above the 3rd percentile. Girls' heights were not available. There was a considerable improvement at 5 years and a further improvement at 10 years, when 42·3% of children had reached the 3rd percentile. At both 5 and 10 years the percentage of girls who were at the 3rd percentile was about double the percentage of boys.

The siblings showed figures similar to those of the ex-patients at 5 and 10 years, the girls again far overshadowing the boys.

Individual ex-patients showing improvement in percentage of expected height: Figs. 5A and 5B also indicate the ex-patients who had improved in expected height from the 5- to the 10-year follow-up examination, i.e. 68 of 77 boys (86%) and 36 of 45 girls (80%). As with weight, however, this increase in expected height does not

TABLE VI. HEIGHT: EX-PATIENTS AND SIBLINGS: PERCENTAGE OF CHILDREN ABOVE THE 3RD BOSTON PERCENTILE

		Percentage of children above third percentile	
		Ex-patients	Siblings
Admission	**M + F**	—	**19·0**
	M	**8·6**	**20·0**
	F	—	**18·0**
5-year follow-up	**M + F**	**22·1**	**22·2**
	M	**16·9**	**13·0**
	F	**31·1**	**34·3**
10-year follow-up	**M + F**	**42·3**	**45·4**
	M	**33·3**	**33·3**
	F	**57·8**	**60·5**

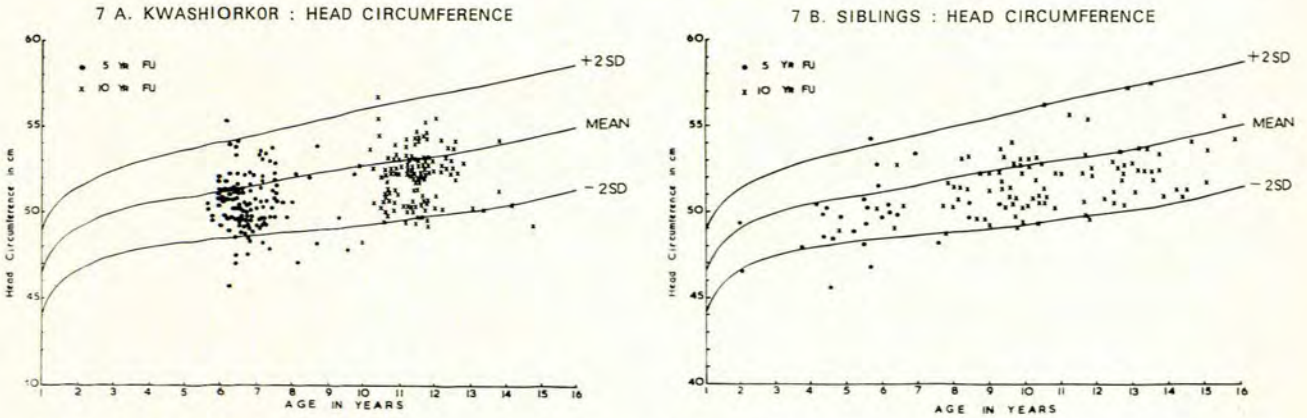


Fig. 7 A and B. Head circumference of ex-patients (A) and siblings (B) plotted against age. The graph was constructed and smoothed from head circumference values as given by Watson and Lowrey.[54]

necessarily imply that the children had reached the 3rd Boston percentile.

Head Circumference

The mean percentage of expected head circumference did not differ significantly between the ex-patients and siblings at 5 and 10 years (Table VII). There was no significant increase in mean percentage of expected head circumference from 5 to 10 years. With few exceptions, head circumference values in both ex-patients and siblings were within the normal range of head circumference for age (Figs. 7A and 7B).

Skinfolds, Mid-upper Arm Circumference (MUAC) and Mid-upper Arm Muscle Circumference (MUAMC) (Table VIII)

The differences in the values of the ex-patients and siblings were not statistically significant. All the mean values were below the standard values used for the calculations. MUAC and MUAMC values in the ex-patients were significantly better in girls than in boys ($p<0{\cdot}05$) but not in the siblings.

In Figs. 8 and 9 the skinfold values of the ex-patients and the siblings are plotted against the standards of Tanner and Whitehouse.[50] Only a minority of the values fall below the 3rd percentile, in spite of the low mean values.

TABLE VII. HEAD CIRCUMFERENCE

	Ex-patients		Siblings		
	Mean % of expected head circumference ± 1 SD	Number of cases	Mean % of expected head circumference ± 1 SD	Number of cases	Significance
5-year follow-up	**97·9 ± 3·4**	**122**	**97·3 ± 3·4**	**28**	**NS**
10-year follow-up	**98·3 ± 3·4**	**123**	**97·6 ± 3·8**	**97**	**NS**

TABLE VIII. SKINFOLDS, MID-UPPER ARM CIRCUMFERENCE (MUAC) AND MID-UPPER ARM MUSCLE CIRCUMFERENCE (MUAMC)

		Ex-patients		Siblings		
		Mean % of standard value ± 1 SD	Number of cases	Mean % of standard value ± 1 SD	Number of cases	Significance
Triceps skinfold	**M**	**78·4 ± 22·2**	**78**	**8·:·1 ± 19·6**	**54**	**NS**
	F	**79·6 ± 19·3**	**45**	**84·2 ± 37·2**	**43**	**NS**
Subscapular skinfold	**M**	**83·5 ± 16·3**	**78**	**82·9 ± 16·9**	**54**	**NS**
	F	**80·1 ± 25·8**	**45**	**90·4 ± 57·3**	**43**	**NS**
MUAC	**M**	**89·9 ± 7·1**	**72**	**91·2 ± 6·9**	**52**	**NS**
	F	**93·0 ± 7·1**	**40**	**92·8 ± 10·7**	**36**	**NS**
MUAMC	**M**	**91·9 ± 7·3**	**72**	**92·2 ± 7·1**	**52**	**NS**
	F	**95·1 ± 6·7**	**40**	**95·1 ± 10·6**	**36**	**NS**

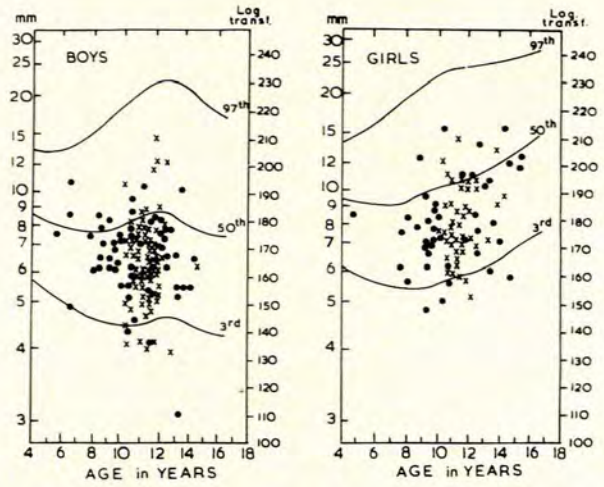


Fig. 8. Triceps skinfolds of ex-patients (X) and siblings (•) plotted against the standards of Tanner and Whitehouse[80]

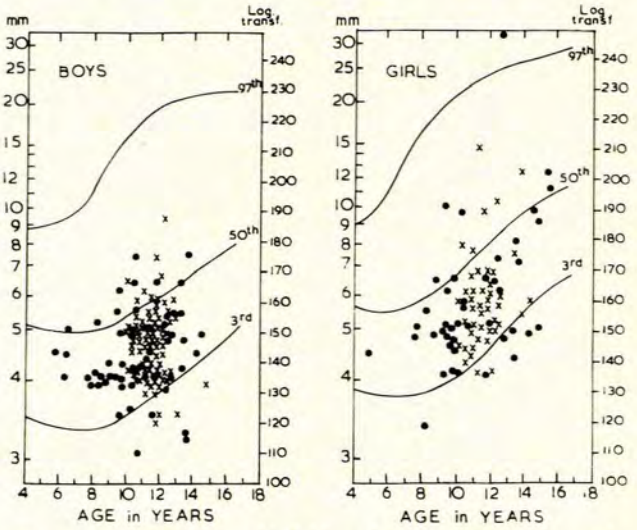


Fig. 9. Subscapular skinfolds of ex-patients (X) and siblings (•) plotted against the standards of Tanner and Whitehouse.[80]

Bone Age

From Figs. 10A (ex-patients) and 10B (siblings) it is seen that bone age was retarded in the majority of cases at 5 and 10 years. In some cases the retardation was as much as 6 years.

On substituting bone age for chronological age in the Boston height and weight percentile charts,[82] and then plotting each child's weight and height against his or her bone age (Figs. 11 - 14), the weights and heights showed a much better scatter through the percentiles than found in Figs. 2, 3, 5 and 6, where weights and heights were plotted against chronological age. In a few children, however, weight and height values were still below the 3rd percentile when plotted against bone age, indicating that their weights and heights were more retarded than their bone ages.

In order to compare the exact degree of difference in retardation of weight, height and bone age, the weight age, height age and radiological bone age of each child was expressed as a percentage of its chronological age and designated Developmental Quotient for weight, height and bone age respectively.[32] Mean values for the various De-

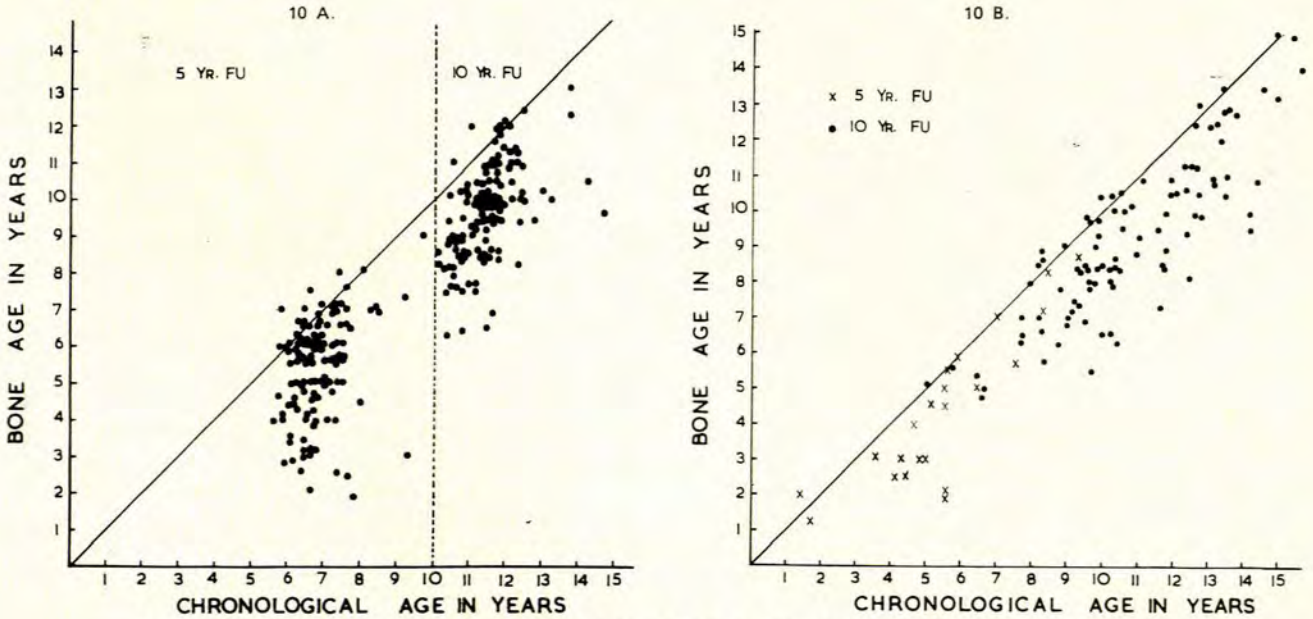


Fig. 10 A and B. Bone ages in ex-patients (A) and siblings (B) plotted against chronological ages.

velopmental Quotients of the ex-patients and siblings are shown in Table IX.

It is seen that bone age was less retarded than weight and height and that the status of the siblings was similar to that of the ex-patients, except for female bone age. Female ex-patients and siblings showed better Developmental Quotients than male ex-patients and siblings.

TABLE IX. MEAN DEVELOPMENTAL QUOTIENTS (DQ) AT 10-YEAR FOLLOW-UP EXAMINATION.

Developmental quotients		Ex-patients		Siblings		
		Mean ± 1 SD	Number of cases	Mean ± 1 SD	Number of cases	Significance
Weight	**M + F**	**73·6 ± 12·5**	**123**	**74·0 ± 12·1**	**97**	**NS**
	M	**71·0 ± 13·1**	**78**	**70·8 ± 11·4**	**54**	**NS**
	F	**77·9 ± 10·3**	**45**	**78·1 ± 11·8**	**43**	**NS**
Height	**M + F**	**76·4 ± 11·8**	**123**	**77·1 ± 13·0**	**97**	**NS**
	M	**74·1 ± 11·7**	**78**	**72·8 ± 10·7**	**54**	**NS**
	F	**80·4 ± 11·0**	**45**	**82·4 ± 13·6**	**43**	**NS**
Bone age	**M + F**	**84·8 ± 9·7**	**123**	**85·7 ± 11·4**	**97**	**NS**
	M	**84·6 ± 10·1**	**78**	**82·6 ± 12·2**	**54**	**NS**
	F	**85·2 ± 9·0**	**45**	**89·6 ± 9·0**	**43**	**$p<0{\cdot}05$**

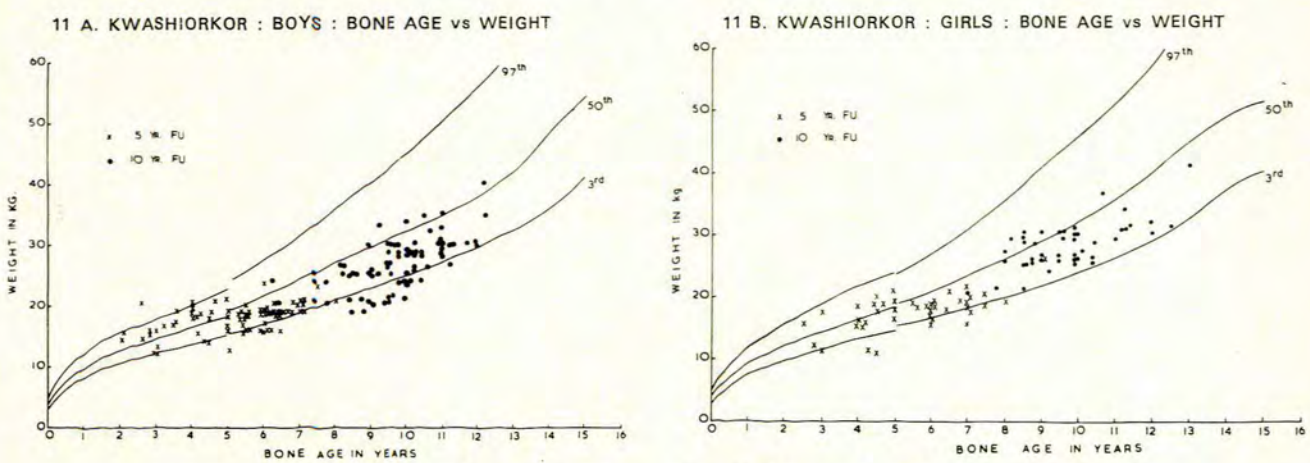


Fig. 11 A and B. Weight in ex-patient boys (A) and girls (B) plotted against bone age.

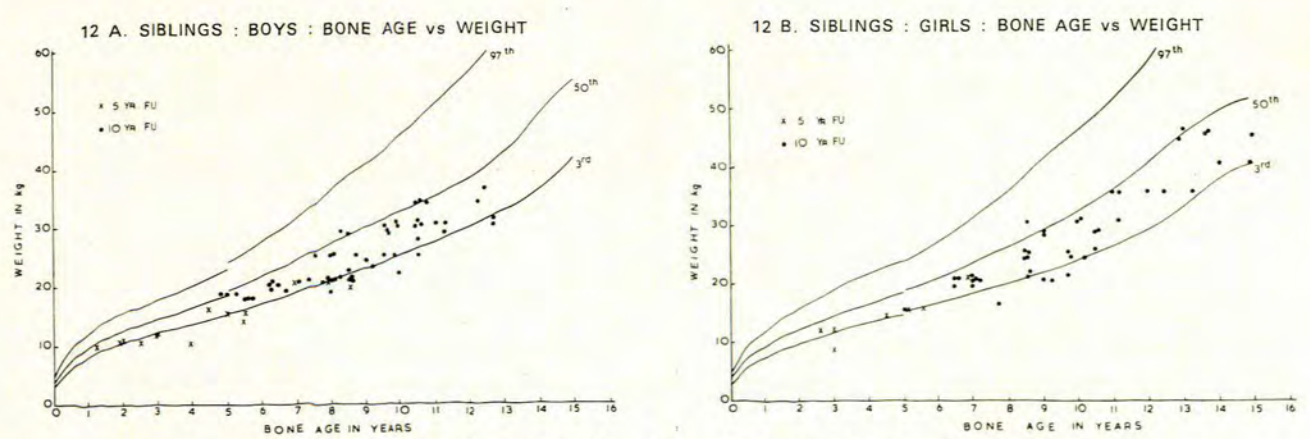


Fig. 12 A and B. Weight in sibling boys (A) and girls (B) plotted against bone age.

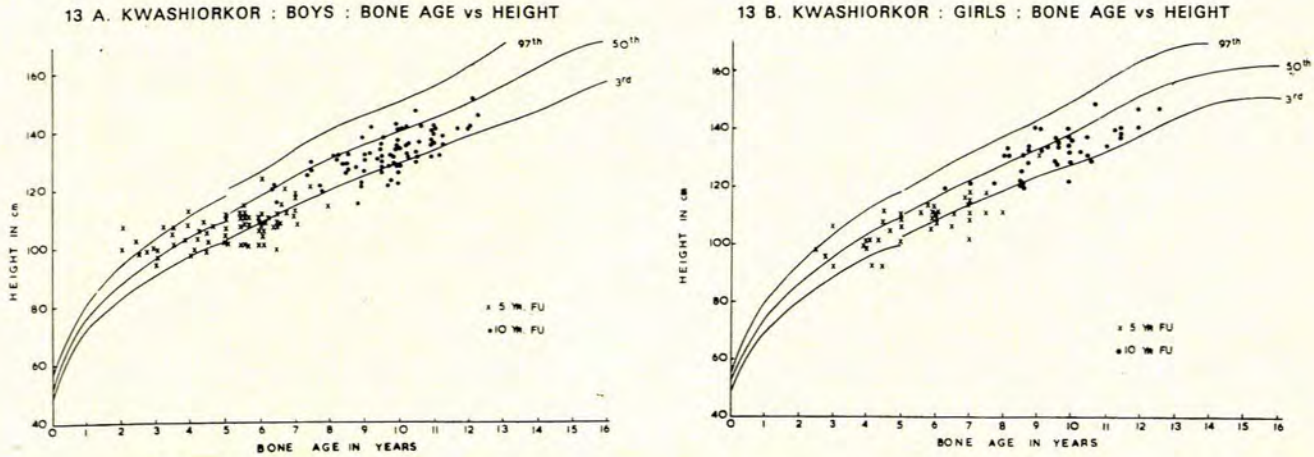


Fig. 13 A and B. Height in ex-patient boys (A) and girls (B) plotted against bone age.

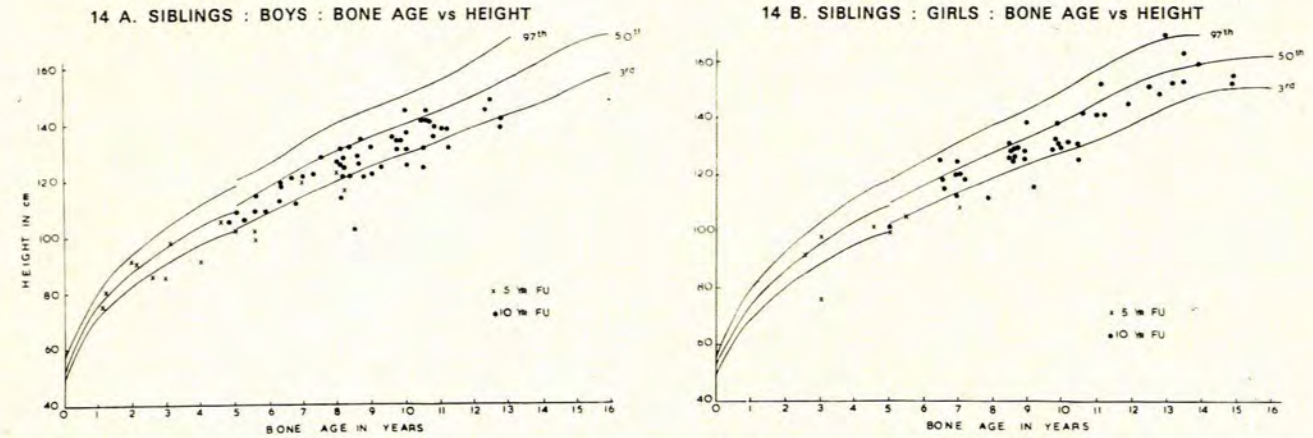


Fig. 14 A and B. Height in sibling boys (A) and girls (B) plotted against bone age.

Serum Albumin and Globulin

The mean values of serum albumin and globulin in g/100 ml at 5 and 10 years are shown in Table X. Surprisingly, the mean albumin level at the 5-year follow-up examination for the siblings was only 3·43 g/100 ml, which is significantly lower than that of ex-patients, but the results of only 22 cases were available. These 22 blood specimens were, however, obtained from the very poorest families, who formed the basis for a feed-up trial project (to be published). At 10 years there was no significant difference between the mean value of serum albumin between the ex-patients and siblings. The serum globulin values were high in both ex-patients and siblings at 5 and 10 years. The increase in serum albumin and globulin values from 5 to 10 years was statistically significant in both ex-patients and siblings (p at least $<0·05$).

TABLE X. SERUM ALBUMIN AND GLOBULIN: MEAN VALUES

	Ex-patients		Siblings		
	Mean ± 1 SD	Number of cases	Mean ± 1 SD	Number of cases	Significance
Albumin g/100 ml					
5-yr follow-up	**3·65 ± 0·35**	**109**	**3·43 ± 0·42**	**22**	**$p<0·05$**
10-yr follow-up	**3·77 ± 0·40**	**121**	**3·81 ± 0·34**	**95**	**NS**
Globulin g/100 ml					
5-yr follow-up	**3·27 ± 0·49**	**109**	**3·20 ± 0·50**	**22**	**NS**
10-yr follow-up	**3·66 ± 0·52**	**120**	**3·65 ± 0·40**	**94**	**NS**

TABLE XI. SERUM ALBUMIN: ANALYSIS ACCORDING TO LEVELS OF SERUM ALBUMIN: PERCENTAGE OF CHILDREN

		Number analysed	Percentage of children			
			<2·8 g/100 ml	2·8 - 3·49 g/100 ml	3·5 - 4·24 g/100 ml	>4·25 g/100 ml
5-year follow-up						
Ex-patients	**M + F**	**109**	**4·6**	**30·3**	**60·6**	**4·6**
	M	**69**	**5.8**	**27·5**	**62·3**	**4·4**
	F	**40**	**2·5**	**35·0**	**57·5**	**5·0**
Siblings	**M + F**	**22**	**0**	**63·6**	**27·3**	**9·0**
	M	**15**	**0**	**66·7**	**33·3**	**0**
	F	**7**	**0**	**57·1**	**14·3**	**28·6**
10-year follow-up						
Ex-patients	**M + F**	**121**	**1·6**	**19·7**	**70·5**	**7·4**
	M	**78**	**1.3**	**21·8**	**66·7**	**10·3**
	F	**43**	**2·3**	**16·3**	**79·0**	**2·3**
Siblings	**M + F**	**95**	**0**	**17·9**	**76·9**	**5·3**
	M	**53**	**0**	**24·5**	**71·7**	**3·8**
	F	**42**	**0**	**9·5**	**83·3**	**7·1**

In Table XI the children are further divided into subgroups according to serum albumin levels. About one-third of the ex-patients and about two-thirds of the siblings were hypoalbuminaemic (serum albumin <3·5 g/100 ml) at 5 years but at 10 years the incidence of hypoalbuminaemia was similar in expatients and siblings. Female ex-patients and especially female siblings, showed better albumin values than males.

From Figs. 15 and 16 it is seen that the lower serum albumin levels were mostly found in the lower weight children.

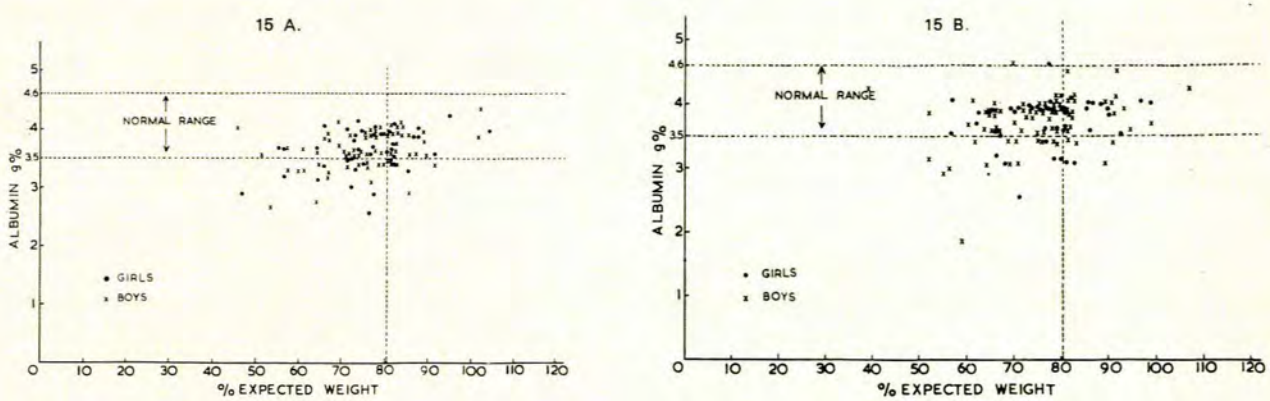


Fig. 15 A and B. Ex-patients: Serum albumin plotted against percentage of expected weight at the 5-year (A) and 10-year (B) follow-up examinations.

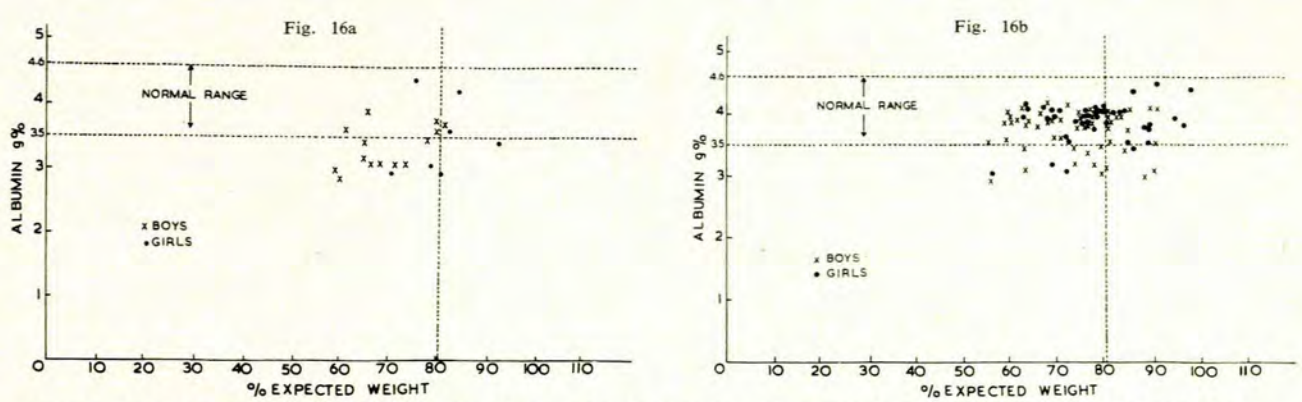


Fig. 16 A and B. Siblings: Serum albumin plotted against percentage of expected weight at the 5-year (A) and 10-year (B) follow-up examinations.

TABLE XII. HAEMOGLOBIN (Hb), PACKED CELL VOLUME (PCV) AND MEAN CORPUSCULAR HAEMOGLOBIN CONCENTRATION (MCHC)

	Ex-patients		Siblings		
	Number of cases	Mean ± 1 SD	Number of cases	Mean ± 1 SD	Significance
5-year follow-up					
Hb Boys	69	12·57 ± 1·31	14	11·99 ± 1·07	$p<0·05$
Girls	42	12·86 ± 1·29	7	11·90 ± 1·14	$p<0·025$
PVC Boys	68	35·67 ± 2·63	14	35·13 ± 2·41	NS
Girls	42	36·00 ± 2·78	6	34·48 ± 2·62	NS
MCHC Boys	68	35.37 ± 2·71	14	34·17 ± 2·25	$p<0·05$
Girls	42	35·78 ± 2·81	6	34·78 ± 2·48	NS
10-year follow-up					
Hb Boys	78	13·56 ± 0·97	53	13·47 ± 0·96	NS
Girls	45	13·53 ± 0·91	42	13·74 ± 0·92	NS
PVC Boys	78	38·01 ± 2·77	53	38·23 ± 2·88	NS
Girls	44	38·17 ± 2·73	42	38·33 ± 2·44	NS
MCHC Boys	78	35·75 ± 1·97	53	35·50 ± 2·10	NS
Girls	44	35·58 ± 2·26	42	35·88 ± 1·83	NS

TABLE XIII. SERUM UREA AND CHOLESTEROL

	Mean % EW ± 1 SD	Mean serum urea ± 1 SD	Mean serum cholesterol ± 1 SD
40 Ex-patients + siblings	75·88 ± 13·88	26·18 ± 9·37	175·08 ± 38·87
20 Ex-patients only	74·93 ± 15·99	26·47 ± 10·28	166·16 ± 40·21
20 Siblings only	76·73 ± 11·59	25·89 ± 8·31	184·50 ± 35·03
20 Ex-patients + siblings < 3rd percentile in weight	64·40 ± 9·09	26·33 ± 7·51	179·67 ± 30·62
20 Ex-patients + siblings > 3rd percentile in weight	87·36 ± 6·24	26·05 ± 10·85	170·74 ± 44·90

Haemoglobin, Packed Cell Volume (PCV) and Mean Corpuscular Haemoglobin Concentration (MCHC) (Table XII)

The mean values of haemoglobin, PCV and MCHC were near normal limits at 5 and 10 years in both ex-patients and siblings. At 5 years the ex-patients' haemoglobin values were better than those of the siblings, but at 10 years there were no significant differences between ex-patients and siblings. At the 5-year follow-up examination one ex-patient's haemoglobin was 8·5 g/100 ml but all other haemoglobin estimations were above 10 g/100 ml.

Lactose Tolerance Tests

Thirty of the 40 children examined showed flat lactose tolerance curves, i.e. a rise of blood sugar of less than 20 mg/100 ml. Flat curves occurred with equal frequency in ex-patients and siblings and in children of normal and subnormal weight. The mean 24-hour stool weight after lactose ingestion in the 30 children with flat curves was 453 g (SD 230 g, range 73-973 g). In the 10 children with rising curves the mean 24 hour stool weight after lactose ingestion was significantly lower i.e. 249 g (SD 178 g, range 18 - 382 g) ($p<0·01$). Several children with flat curves complained of severe abdominal pain during the test, but none of those with rising curves had abdominal pain.

Stools and Urine

In 36 of the 38 stools examined intestinal parasitic ova, either *Ascaris lumbricoidis* or *Trichuris trichuria* or both were found, and in one child's stool cysts of *Entamoeba hystolitica* were seen. The urine was chemically and microscopically normal in all 40 children examined.

The values of serum urea and cholesterol were within normal limits and did not differ significantly in any of the groups studied (Table XIII).

Parents' Heights

In the 55 instances where both parents' heights were available, the midparental height[25] was calculated. The mean midparental height in the series was 161 cm (5 ft $3\frac{1}{2}$ ins).

Social Circumstances

Changes during the first 5 years of follow-up have been reported.[59,60] Social circumstances in the next 5 years are summarized below:

Environment: Families continued to move frequently, only 15 remaining at one address for 10 years while 108 moved on at least 253 occasions. Contact, which had been difficult to maintain at the outset, became somewhat less so as housing conditions improved and the numbers of shack-dwellers diminished. While only 6 families were in Council houses at the start of the study, the number had increased to 28 at 5 years and to 64 at 10 years. Almost half the series, however, were still outside the housing estates, many of them in very poor surroundings. Even in the Council houses low standards of hygiene often prevailed due to the density of overcrowding. Only 20 homes in the whole series were not overcrowded according to the standard applied.

Economic status: Fig. 17 shows a slight if only relative economic improvement in 10 years. Twenty-four children had moved into other home care and in many cases this raised their standard of living. The number of wage-earners in some of the households increased and there were better work opportunities in this time of industrial growth. On the other hand 42% of the fathers had had very little education (Std. II or less) a fact which affects earning capacity.[91] In addition there were more children to feed than before since families had increased in size, as shown in Table XIV, from a mean of 4·2 at the start to 6·6 children after 10 years. A family of 10 children was not uncommon. Altogether there were 70% of the households that were still below or only slightly above subsistence level, i.e. the Poverty Datum Line.

TABLE XIV. FAMILY SIZE: CHANGE IN 10 YEARS (101 FAMILIES)

		Mean family
Total children alive at start	430	4·2
Total children alive at 5 years	595	5·9
Total children alive at 10 years	671	6·6

Diet: Judged by key protein foods half the children (61) appeared to be getting what was graded either as an 'average' or as a 'fairly good' diet, i.e. one which included meat, fish or poultry at least once daily, eggs or cheese at least once weekly and a minimum of 2 cups of milk each week. Roughly a quarter of the diets (29), however, fell short of this standard, the 10 worst of which did not apparently include animal protein in any form on every day of the week. Bulk was provided throughout by bread, potatoes and other vegetables, rice and a certain amount of maize meal.

Family stability: Social pathology was considerable, including illegitimacy, alcoholism and marital breakdown. There was an incidence of 40% of illegitimacy which was greater than that generally prevailing in the community (23·5% in the City Council area in 1958).[2] Alcohol was taken to the extent of creating a problem in 40% of the households. There were 'broken' homes, i.e. changes in the parental background of half the children (61) in the 10 years owing to death or separation of parents, change of consorts, desertion, placement in foster care or other

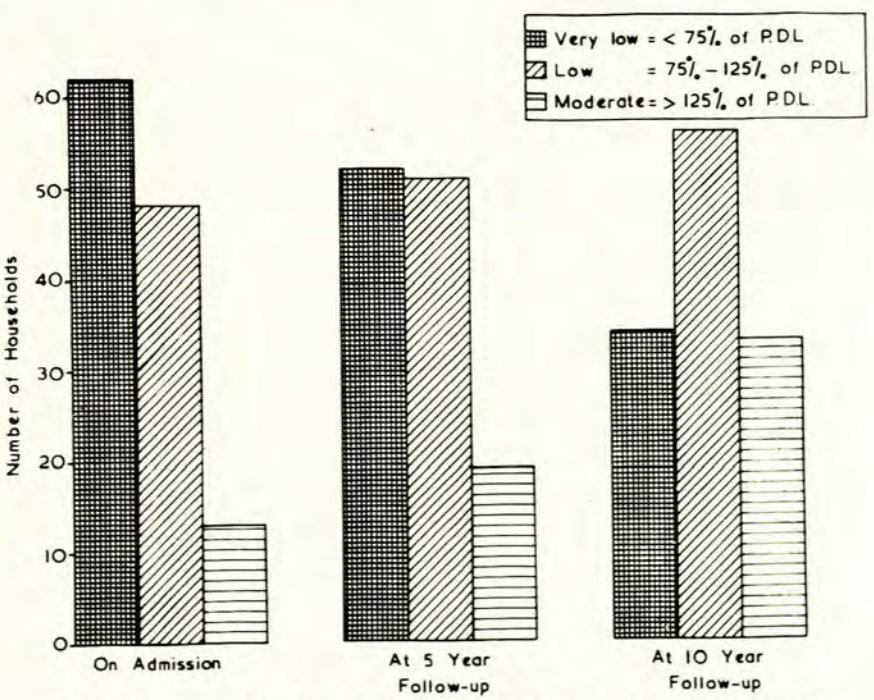


Fig. 17. Income of 123 families in relation to Poverty Datum Line (PDL).

causes, i.e. only 62 children remained with the same parents throughout and even this did not necessarily imply that the home was happy or peaceable. The effect of this instability on relapse had already been noted at the 5-year follow-up: In 70 'unbroken' homes, only 2 children relapsed with kwashiorkor (one relapsed twice) but in 61 'broken' homes, 17 children relapsed (4 on 2 occasions and one 5 times).

The mean percentage scores and ranges given for each of the above 4 factors and for the Multiple Social Index are shown in Table XV.

TABLE XV. PERCENTAGE SCORES FOR SOCIAL CIRCUMSTANCES IN 123 EX-PATIENTS

	Mean ± 1 SD	Range
Housing space	41·09 ± 39·78	0 - 100
Economic status	58·94 ± 18·96	20 - 100
Dietary adequacy	60·20 ± 25·15	17 - 100
Family stability	51·87 ± 23·99	0 - 100
Multiple social index	53·15 ± 18·14	16 - 95

Scholastic Progress

Among the 95 pairs of children only 37 ex-patients and 42 siblings had never failed a grade in their first few years at school.

Correlation Coefficients

Table XVI shows correlation coefficients which were calculated between some of the variables.

There was a good correlation between percentage of expected weight and percentage of expected height at the 10-year follow-up examination in both ex-patients and siblings. The children were therefore well-proportioned.

In the 54 ex-patients in whom weights after loss of oedema on admission were available, a significant correlation between percentage of expected weight on admission and percentage of expected weight after 10 years was found (r = 0·62). Similarly, siblings' weights on admission correlated well with weights after 10 years (r = 0·55). The children lightest for age on admission were therefore still the lightest for age after 10 years.

Percentage of expected height on admission also correlated significantly with percentage of expected height after 10 years (r = 0·63 for ex-patients and r = 0·57 for siblings). The shortest children therefore tended to remain the shortest.

Age on admission showed significant negative correlation with percentage of expected weight after 10 years, but although admission age correlated negatively with percentage of expected height after 10 years, this correlation failed to reach statistical significance. This indicates that the child who was older on admission tended to show the greater weight deficit after 10 years.

Serum albumin at 10 years showed a significant correlation with percentage of expected weight in the ex-

TABLE XVI. CORRELATION COEFFICIENTS>

	Ex-patients			Siblings		
	r	No.	p	r	No.	p
% EW* at 10 years and % EH at 10 years	0·8086	123	<0·001	0·8221	96	<0·001
% EW on admission and % EW at 10 years	0·6220	54	<0.001	0·5597	62	<0·001
% EH† on admission and % EH at 10 years	0·6390	35	<0.001	0·5709	42	<0·001
Age on admission and % EW at 10 years	−0·2124	123	<0·05	—	—	—
Age on admission and % EH at 10 years	−0·1619	123	NS	—	—	—
% EW at 10 years and serum albumin g/100 ml	0·2836	121	<0·01	0·1371	95	NS
% EH at 10 years and serum albumin g/100 ml	0·1455	121	NS	0·1128	95	NS
% EH at 10 years and midparental height	0·4025	55	<0·01	0·3991	49	<0·01
% ESF‡ at 10 years and % EW at 10 years						
boys	0·3731	78	<0·001	0·3989	54	<0·01
girls	0·3690	45	<0·05	0·4524	43	<0·01
% ESF at 10 years and % EH at 10 years						
boys	0·1903	78	NS	0·2566	54	NS
girls	−0·0912	45	NS	0·3188	43	<0·05
% EH at 10 years and % housing space	0·1269	123	NS	0·1775	96	NS
% EH at 10 years and % economic score	0·1671	123	NS	0·0972	97	NS
% EH at 10 years and % dietary score	0·1831	123	<0·05	0·2177	97	<0·05
% EH at 10 years and % family stability	0·1694	123	NS	0·0646	97	NS
% EH at 10 years and MSI¶	0·2574	123	<0·01	0·2042	97	<0·05

* % EW = percentage of expected weight
† % EH = percentage of expected height
‡ % ESF = precentage of expected skinfolds (triceps and subscapular combined)
¶ MSI = Multiple Social Index

patients. Serum albumin did not, however, correlate with percentage of expected height in the ex-patients, neither did it correlate with weight nor with height in the siblings.

There was a significant correlation between midparental height and percentage of expected height in both ex-patients and siblings at 10 years. The taller parents therefore had the taller children 10 years after the episode of kwashiorkor.

The combined values of triceps plus subscapular skinfolds (both of these values being expressed as a percentage of the standard value for age and sex) correlated significantly with the percentage of expected weight in ex-patients and siblings, in both boys and girls. The children heaviest for age therefore had the thickest skinfolds. The correlation of the skinfold values with percentage of expected height was significant only in ex-patient girls.

Socio-economic factors. The percentage of expected height in the ex-patients at 10 years did not correlate significantly with housing space, economic status or family stability, but there was a significant correlation between percentage of expected height and dietary adequacy. The correlation between expected height of the children and the MSI, however, was more significant, indicating that the influence of a summation of adverse social factors was greater than that of any one of these tested separately.

In the siblings, the percenatge of expected height also correlated significantly with dietary adequacy and the MSI.

DISCUSSION

Most of the children appeared clinically well and happy, their weights and heights showed good correlation ($r = 0{\cdot}8$ for percentage expected weight and height) and, with few exceptions, their skinfold thicknesses were within normal limits. This gave the impression that they were in a good physical state. On analysing the data it was indeed found that 53% and 42% of ex-patients had reached international weight and height standards respectively. This is convincing evidence that growth retardation can be completely reversible after an episode of kwashiorkor in the age group studied.

Patterns of Catch-up Growth in This Study

Weight and Height: Children whose growth has been slowed by illness show a greater than normal rate of growth upon correction of the disorder. This rapid phase of growth may continue until the child has caught up to its pre-illness or normal growth curve and is therefore called 'catch up' growth.[86]

In this series, there was considerable 'catch up' growth in weight during the first 5 years after the episode of kwashiorkor. Most of this improvement in weight had probably already occurred by 3 years after discharge from hospital, as was indicated by Brock and Hansen.[11] Although a few individual children further improved their weight status during the second 5-year period, the weight status of others deteriorated, and the mean percentage of expected weight of ex-patients remained stationary at 76% from the 5- to the 10-year follow-up examination. This is the same weight as that achieved by the siblings at the 10-year follow-up examination. The siblings' expected weight during the 10-year period declined slightly from 80% to 76%. These findings call to mind Tanner's views on 'catch up' growth. He stated: 'A most striking characteristic of mammals is that it is self-stabilizing, or to take another analogy, "target seeking". Children, no less than rockets, have their trajectories, governed by the control systems of their genetical constitution and powered by energy absorbed from the natural environment. Deflect the child from its natural growth trajectory by acute malnutrition or a sudden lack of hormone, and a restoring force develops so that as soon as the missing food or hormone is supplied again, the child catches up to its original curve. When it gets there, it slows down to adjust its path to the old trajectory once more. The question is how the child "knows" that it has reached its old trajectory and so slows down."[79]

Can 76 - 80% of expected weight therefore be considered the 'trajectory' for weight for this group of children? It would seem so, under their present environmental conditions, which are by no means ideal. This present 'trajectory' may of course not be the true potential 'trajectory' of these children, but the only one compatible with the present 'natural environment'.

In contrast to weight, height had steadily increased. At the 5-year follow-up examination, ex-patients' and siblings' mean percentage of expected height was 88%, but at the 10-year follow-up examination, height had increased significantly in both ex-patients and siblings, as was reflected in mean percentage of expected height, the frequency distribution curves and the doubling of the percentage of children reaching the 3rd percentile in height.

Most of the ex-patients are now at an age where the pubertal growth spurt becomes evident. It can only be speculated as to whether this increase in height is still to be ascribed to continuing 'catch-up' in height or whether the hormonal forces governing pubertal height growth now override (to an extent at least) the deleterious environmental factors. Although the numbers of children who have reached puberty in this study are too small to draw conclusions, it is interesting to note that only 2·8% of female ex-patients had started to menstruate in contrast to 13·9% of siblings. Whether this fact can account for the higher mean percentage of expected height in the female siblings cannot be answered at present. (See also discussions on The Future).

Sex differences: At 10 years female ex-patients and siblings were superior to boys in weight, height, skinfold thickness, MUAC, MUAMC, Developmental Quotients for weight, height and bone age, and albumin status.

This superiority of the females cannot be ascribed to the usual earlier pubertal growth spurt in females, because all the values have been expressed as a percentage of standard value for age and sex. Moreover, this superiority in weight and height was already evident at the 5-year follow-up examination. It has been shown repeatedly that the growth processes of girls are more resistant to stress than those of boys[22,33,50,77] and animal experiments, too, have shown that males are more vulnerable than females to both calorie and protein deficiency.[84]

Bone age: According to the Developmental Quotients of bone age, weight and height, these children are less retarded in bone age than in weight and height. This may indicate that these children are not going to reach their full potential height as adults.

Growth Retardation Following Kwashiorkor

Although about half of the children have reached adequate growth standards 10 years after the kwashiorkor episode, 'catch up' growth has been unsatisfactory in 47% of the children with respect to weight and 58% of the children with respect to height. The mean values of all the anthropometric measurements of the ex-patients are also below Western standards, and reasons for this growth retardation have to be found. With few exceptions, the children did not suffer from chronic non-nutritional debilitating disease. Intestinal parasitic ova and lactose intolerance were found with equal frequency in children who had grown well and those who had not. The question arises as to whether the episode of kwashiorkor could specifically have affected the growth of some children. The significant correlation between percentage of expected weight and height on admission and percentage of expected weight and height respectively at the 10-year follow-up examination, suggests that the severity of the original episode might have had this effect. However, there is evidence of current poor nutrition and it is logical to assume that those children who were originally most severely deprived nutritionally would be more likely than the others to continue to be so deprived. It is therefore not possible to separate the effects of the original severe deficiency from the effects of continuing poor nutrition. The fact, however, that the ex-patients' physical status was similar to that of their siblings at 10 years is sufficient proof that the episode of kwashiorkor *per se* cannot account for the present growth retardation.

The negative correlation between age on admission and 10-year follow-up weight and height implies that it was the child who was older during the kwashiorkor episode who showed the more severe growth retardation 10 years later. This does not conflict with the finding that severe malnutrition in rats in the first 3 weeks of life precluded normal growth thereafter:[43,57,58] the mean age of the study children on admission was 18·8 months, which is not comparable to the first 3 weeks of life of the rat. One could also argue that the children who presented with kwashiorkor when they were older, had probably suffered from malnutrition for a longer period than the children who presented at a younger age. If this assumption is true, the negative correlation between admission age and present physical status may indicate that the duration of the original malnutrition had a deleterious effect on subsequent growth.

Growth hormone and pancreatic function were not evaluated in the present study. It has been shown, however, that growth hormone levels are raised and not suppressed by glucose in severe protein calorie malnutrition.[64,65] In a separate study Becker and Pimstone[6] found normal growth hormone levels, not suppressed by glucose, in 12 randomly selected children from this series. Pancreatic function may be damaged irreversibly in chronic protein calorie malnutrition.[3]

Because the growth retardation was of equal severity in the ex-patients and siblings, however, a cause operating in both groups had to be found. The following possibilities had to be considered:

The anthropometric standards used were too high for local non-White children: The fact that the ex-patients did not differ from the siblings, that the mean midparental height (161·4 cm) was low and that there was a significant correlation between midparental height and the height of the children strongly suggest a genetically short stature. It was found by Lurie and Ford[49] that healthy Cape Coloured children lagged far behind South African White children in weight and height. More recently Sloan and Hansen[73] found that weights and heights of Cape Coloured school children fell within the normal range for British children although their mean values were well below those of local White and British children. On the other hand, two recent studies in Cape Town have shown[42,91] that, at least in the preschool children, local healthy non-White children reach growth standards equivalent to those of Western children. In Uganda, MacWilliam and Dean[50] found no good reason to suppose that their African children, if perfectly nourished, would be smaller than their European or American counterparts. Similar conclusions have been reached by others.[8,36,47,51,70] Under ideal circumstances the growth of children should probably be judged by local standards,[27] but present environmental conditions are not ideal. The children in this survey are school-attenders, and it is quite conceivable that similar children have been included in the school surveys mentioned, thus lowering the local mean anthropometric measurements.

Furthermore, we do not know whether the parents themselves have reached their own potential genetic height. It is quite likely that as children they themselves suffered from chronic malnutrition. The literature[40,57] suggests that improved nutrition improves the height of the whole population. On the whole, therefore, while genetic inheritance cannot be disregarded as a possible cause of the apparent growth retardation of the children, neither can the possibility of environmental factors operating on the parents themselves be so disregarded.

Continuing chronic malnutrition: The skinfold values in both ex-patients and siblings were mostly in the normal range for British children. Severe calorie deficiency is therefore an unlikely cause of the growth retardation. Evidence of protein deficiency, however, was found, as judged by the presence of hypoalbuminaemia in 21% of the ex-patients and 18% of the siblings. Serum albumin correlated significantly with percentage of expected weight in the ex-patients. Serum albumin levels have frequently been used as an index of protein deficiency.[39,12,38,45,72,90] It can therefore be concluded that the children in the present series were not starved with regard to calories, but that some of them were still protein deficient.

Other circumstantial evidence for continuing malnutrition is the grossly retarded bone ages and the fact that females consistently fared better in all anthropometric measurements. Finally, the patients come from a socio-economic population in which malnutrition is common.

It has been shown locally that the poorer income groups purchase less high protein foods.[93]

Recurrent infections: The histories of these children did not suggest that they had suffered from severe recurrent infections between the 5- and 10-year follow-up examinations. However, on examination, superficial skin infections and tooth decay were common and the serum globulin showed a significant rise during this period. This could indicate excessive exposure to an infective environment and a probable high incidence of subclinical infections.

Adverse socio-economic factors: For obvious reasons no continuous human study can be carried out under controlled experimental conditions. This is particularly difficult with growing children because of the dynamic nature of family life; it is even more difficult when the family belongs to a group which is itself in an accelerated state of social change. This change is due in part to the growth of industry and in part to the replacement of slums by housing estates. While the former calls for increased numbers of factory hands, the latter also offers good employment in the banks, post-offices, shops, schools, clinics and other amenities. The study families are among those that are not yet fully caught up in this whorl of development, but they are not unmoved by its currents. Hampered by economic, educational and social shortcomings, many of them are unable to take advantage of the new opportunities for employment.

This is the varied background against which the growth and health of the ex-patients and their siblings during 10 years must be seen. It explains the need that was felt for a multiple social index embodying a number of variables to account for differences in growth. Multiple social indices have been used elsewhere in relation to child growth and health.[14,55,68] In previous work in Cape Town[91] subjective criteria were applied to such factors as social stability, maternal capacity and standard of hygiene. In the present study the need for a more objective assessment of the social component was met, in the first place, by the selection of four areas considered to be relevant to the progress of local children with an early history of severe malnutrition, viz. environmental hygiene, economic status, habitual diet and family life. Characteristic features of these four which could be measured were then identified although the fallibility of such a method was recognized. Thus an estimation of available income might bear no relation to the actual use that was made of it; the adequacy of housing space included nothing of the outer environment nor of cleanliness of habits; the key protein foods used excluded the protein derived from vegetable sources and did not include an estimate of quantity; and the adverse factors characterizing family instability omitted, except by inference, such subtle realities as ignorance and maternal incapacity.

In spite of these limitations the MSI proved a useful tool which demonstrated again the fact that malnutrition in children is of multiple aetiology.[15] In Cape Town 10 to 15 years ago, kwashiorkor was occurring frequently among the children of the most socially degraded unskilled workers who were living on low incomes in sordid surroundings. Since then modern town planning with the provision of tap-water and waterborne sanitation has done much to reduce the infection which is intimately associated with malnutrition. It has also made many of the homes more accessible to preventive health work, brought the children nearer to the schools and helped to raise the standard of living. Delay in rehousing and continued low wages for unskilled workers, coupled with over-large families and old habits of irresponsibility, still degrade this, however, and the home life of many of the study children has remained debased and insecure. Although some have improved their standard of living, others have brought their old habits into new homes, while others again are still in the same sordid dwellings as before or in shacks in the bush.

Nevertheless they have certain advantages over their counterparts in the slum tenements of Western cities. Even the illegitimate children (known by the kindly term of 'voorkinders') are generally absorbed into their own or other families so that the isolated self-centred family unit, familiar elsewhere, is hardly known here. The 'battered baby' is not yet a feature of this society, nor is maternal rejection in morbid form. A mother's possible revulsion against a constantly ailing child that causes her to be reprimanded for negligence, is a transitory thing—if for no other reason than that he is shortly supplanted by another child equally difficult to rear. Once past the hazards of the toddler age, he becomes part of a family or playmate group and tends to rear himself, mainly out of doors, sharing with others the parental censure or indulgence as it comes. It may be that he will develop some of the characteristics of children in 'multi-problem hard-to-reach families' described by Malone,[52] i.e. deprived of constant maternal care and exposed to the dangers and excesses of their surroundings, they become over-alert and deceptively mature at the expense of rational thought and behaviour.

School learning may suffer as a result and, in fact, as shown above, many ex-patients and controls are failing to pass their grades every year. There are, however, many other social causes that contribute to slow progress at school. In the first place, ill-fed children do not make eager pupils. Secondly, education, although free, is not compulsory and admission to school may be late because of parental ignorance or negligence. The parents themselves may be illiterate so that the child hears only the most functional use of a colloquial mixture of languages. Intellectual stimulation and emotional security have, from the earliest years, almost always been lacking and there is neither the inducement to study nor, in most cases, the space in the home for it. Creative ability and abstract thinking are not encouraged by the possession of books and playthings. The social milieu has, indeed, such a pervading effect on the child that it precludes, at the present stage, a clear indictment of factors such as genetic inheritance or very early malnutrition as the root causes of low intellectual attainment.

Likewise with regard to growth, Chase and Martin[14] writing of longterm undernutrition in more circumscribed family units, coin the term 'psycho-nutritional' to explain failure in growth and development. Although many of the problems they encounter are problems familiar in the Cape Town setting also, tne term 'socio-nutritional' would

seem more nearly to describe the reasons for growth failure in the children studied here. The result obtained by using the Multiple Social Index supports this assumption but does not rule out the likelihood that, when social action has done all that is possible to reduce the incidence of malnutrition and its after-effects, there may still remain a hard core of families in need of intensive personal care.

It is, however, the wider spread of children who are at present in a less severe but definitely suboptimal state of physical and, probably, of intellectual development that rouses the gravest concern. Their very number in many of the emergent populations, obscures the immediacy of the problem they present.

COMPARISON WITH OTHER LONGTERM FOLLOW-UP STUDIES

The most pertinent results of other longterm follow-up studies in the literature are summarized in Table XVII. Only two of these studies were done prospectively.[32,75] The ages of these children during the malnutrition episode, and the type of malnutrition they suffered from, varied in the different studies. No attempt has been made to determine the differences in subsequent growth of the two sexes, except by Krueger[45] who presents separate weight and height charts for boys and girls but does not comment on differences in growth. Little attention has been given to diet and social circumstances subsequent to discharge from hospital, with the notable exception of the study by Chase and Martin,[14] and it must be assumed that children returned to the same environmental circumstances as before. Conclusions that stunted growth in later life is due to irreparable damage inflicted by the original episode of malnutrition may therefore be unwarranted. This was readily admitted by Graham[32] and Giok *et al.*[31]

Siblings were used as controls in only one study.[30] In the other reports 'local healthy children' and/or Boston standards of growth were used.

It is not surprising, therefore, that the conclusions in the different studies vary, eg. Garrow and Pike[30] found the ex-patients' physical status slightly superior to that of their siblings 2 - 8 years after an episode of severe malnutrition. Others[13,69,76] found the ex-patients' status similar to that of controls who were local healthy children, while the status of ex-patients was inferior to that of control children in several instances.[32,14,17,45,75]

MacWilliam and Dean,[50] using the Boston percentiles as a standard, found that children had reached 82% of expected weight and 90% of expected height after 3 years. In the present study the children were 76% of expected weight and 87% of expected height at the 5-year follow-up examination, i.e. slightly inferior to the Uganda children. The study most comparable to the present one is that of Garrow and Pike,[30] who used siblings as controls. They found ex-patients small by North American standards, but not when they were compared with their siblings. Their study has been criticized, in that the siblings were probably also malnourished,[63] and it was pointed out by Latham[46] that probably neither group had reached its full growth potential. In the present study it is readily admitted that some ex-patients and control siblings suffered from continuing adverse environmental circumstances (dietary and socio-economic) and these factors are considered of major importance as a contributary cause of the stunted growth in some of the children. Nevertheless, in spite of the poor environmental milieu, about half of the children did reach adequate growth standards, showing that the potential for growth is present and that complete recovery is possible after kwashiorkor.

In this respect, it is interesting to note that MacWilliam and Dean[50] found that maternal instruction improved the subsequent status of the children.

On the other hand, it would seem from the reported studies, the present study and animal experiments, that there are certain factors, during the original episode, which may have an effect on subsequent growth. Thus Garrow and Pike[30] found a significant correlation between percentage of expected weight on admission and at follow-up ($r = 0{\cdot}46$), although a similar significant correlation for height was not found. Graham[32] indicated that severity of malnutrition on admission as judged by Developmental Quotients for weight, height and head circumference adversely affected follow-up status, and MacWilliam and Dean[50] stated that the smallest and shortest children stayed the smallest and shortest. In the present study the correlation between percentage of expected weight on admission and after 10 years ($r = 0{\cdot}62$) was even higher than that of Garrow and Pike,[30] and in addition, a significant correlation ($r = 0{\cdot}63$) was found between percentage of expected height on admission and after 10 years. Whether these correlations would still be significant if genetic and subsequent environmental influences could be excluded, is a question which cannot be answered by our present data. Carefully controlled experiments on Rhesus monkeys showed that, provided a full diet was given subsequently, complete recovery is possible even after early severe malnutrition.[44]

The effects of age on admission and duration of malnutrition are difficult to separate from each other, because a child who has been malnourished for a long time, must of necessity be an older child. Graham,[32] however, concluded that younger children who were malnourished for a longer time fared the worst. Chase and Martin[14] found that children admitted to hospital under 4 months of age were less severely affected subsequently and Cabak's children,[13] who were mostly under the age of 12 months when admitted, did not differ physically from control children at follow-up examination. In the present series children who were older on admission, showed greater weight deficits than children who were admitted at a younger age.

SPECULATION ON FUTURE GROWTH

Acheson[1] stated that 'if, during a period of undernutrition skeletal maturation is slowed but growth is slowed even more, the growth potential will not be realized (unless compensation occurs subsequently) and the child will as a result become a smaller adult than he would otherwise have been'. In the present study, according to the Developmental Quotients for bone age and height,

TABLE XVII. LONGTERM FOLLOW-UP STUDIES

Country. Year of report. Reference	Number of cases	Type of case	Age original admission	Duration of follow-up	Controls	Conclusions	
						Anthropometric and biochemical	Other
India 1955[69]	51	Nutritional oedema	?	Up to 5 years	Normal healthy children	Weight, height and serum proteins same as controls	
S. Africa 1957[76]	27	Kwashiorkor	15·9 m	5 years	Normal healthy children	Weight, height, head circumference, bone age same as controls	No cirrhosis. No anaemia
S. Africa 1963[75]	21	Severe malnutrition	10 - 36 m	2 - 7 years	Normal healthy children	Weight, height, head circumference lower than controls	Lower IQ in test group
Yugoslavia 1965[13]	36	Marasmus	4 - 24 m most 12 m	Up to 14 years	Normal healthy children	Weight and height same as controls	Lower IQ in test group
Uganda 1965[50]	130	Kwashiorkor	19 m	3 years and longer	Boston	Weight 82%, height 90% of Boston standards. Bone age lagged further behind after discharge	Maternal instruction improved children's subsequent status
Jamaica 1967[30]	65	Severe malnutrition	3 - 24 m (from graph)	2 - 8 years	Siblings and local children	Small by North American standards, but slightly better in weight, height, chest width, tibia widths, muscle width than controls	% weight for age on admission and % weight for age at follow-up correlated significantly (r = 0·46) but % height for age on admission and at follow-up did not (r = 0·23)
Uganda 1967[17]	50	Kwashiorkor	1·8 year	4 - 11 years	Local healthy children	Weight and height lower than controls	No cirrhosis
Indonesia 1967[31]	46	29 Malnourished, 17 Vit. A deficient	2 - 4 years	5 - 7 years	Local healthy children and Boston	Weight and height lower than controls	Vitamin A deficient children fared poorly
Peru 1968[32]	60	14 Kwashiorkor, 46 severe malnutrition	12·3 m range 3 - 41 m	29 - 98 months	Boston	Weight, height, head circumference and bone age lower than controls	Severe calorie deprivation during most of 1st year of life likely to cause permanent stunting. Episode of severe protein deficiency unaccompanied by prolonged and severe calorie deficiency is much less likely to leave permanent effects
Uganda 1969[45]	152	Mostly kwashiorkor		6 - 11 years	Local healthy children	Weight and height lower than controls	
USA 1970[14]	19	Generalized undernutrition	1·5 - 2·4 m	3 - 4 years	Siblings and local children	Weight, height and head circumference lower than controls	Test children mentally poorer

bone age is less retarded than height, implying that these children are not going to reach their full potential for height. There are, however, many fallacies in interpreting bone age. By the Greulich-Pyle method[35] skeletal age is about one year less than that judged by the Tanner-Whitehouse[51] method.[3] Had we thus used the latter method of estimating bone age, the children would have been more mature skeletally, giving an even greater discrepancy between bone age and linear height and indicating an even greater probability of future stunting in height. On the other hand, Dreizen *et al.*[21] could find no appreciable difference in adult stature between 30 malnourished and 30 well nourished girls. In the present study boys are included and bone ages seem to be more retarded than in the cases of Dreizen *et al.*[21] The adult statue of the children in the present study is therefore unpredictable. They are still being followed and an answer should be available within a few years.

CONCLUSION

There has been speculation recently on whether it is worth admitting children to hospital for the treatment of malnutrition because of the high mortality, even after discharge[71] and the possible longterm effects on survivors such as learning difficulties and poor psychosocial adaptation.[9] Some even go so far as to say that the limitations produced make it difficult for these children to be incorporated into the socio-economic development of the country.[58]

While it is correct that the vast numbers of children in the emergent populations who are in a suboptimal state of physical and probably of intellectual development should arouse the gravest concern, it is not correct that they should be regarded as being beyond help.

Our findings in this series and those of Garrow[29] and of Garrow and Pike[30] do at least establish that it is possible for complete or near complete recovery from severe kwashiorkor to occur. Since about half the children had reached adequate if not ideal growth standards after 10 years, despite their environmental conditions, it is clearly worthwhile to continue to give every malnourished child the benefit of active clinical treatment. It is equally clear that health supervision of all children during the growing period, together with well-planned and fundamental 'social uplift' of families will reduce the number of those who stand in need of such treatment. While nothing should obscure the gravity of the problem, much will be lost by considering it insoluble.

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