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Brain Growth in Children with Marasmus

A Study Using Head Circumference Measurement, Transillumination and Ultrasonic Echo Ventriculography

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ABSTRACT

Brain growth was studied by making simultaneous measurements of head circumference, transillumination and lateral ventricle indices in 102 children aged 2–24 months suffering from marasmus. The head circumference was significantly reduced, transillumination showed a slight-to-moderate increase in the children 6–24 months of age, and echo encephalography showed a normal lateral ventricle index. The results indicate a reduction of brain size which (particularly after the first 6 months of age) goes slightly beyond what may be inferred from the head circumference per se. The interpretation of the results, especially the relation between head circumference and brain size, is discussed.

In cases of severe protein-calorie malnutrition (PCM) of the marasmus type, there is not only a severe reduction of weight in relation to age but also a retardation of height in relation to age, i.e. a true stunting of growth (4, 23). Furthermore, studies in recent years have indicated a marked retardation of brain growth, demonstrated both *in vivo* by measuring head circumference (15, 24) and at autopsy by measuring brain weight (1, 37).

Head circumference is claimed to reflect brain size fairly closely (35, 40). This is not always true, however. In cases of severe PCM, alterations in the thickness of the scalp and the skull bone may cause changes in the head circumference/brain size ratio (11, 28). This ratio may be further changed by abnormal accumulation of fluid on the surface of the brain (30) or by enlargement of the brain ventricles (38).

As part of the work done at the Ethiopian Nutrition Institute (ENI), Addis Ababa, various studies related to brain growth in young children were carried out between 1969 and 1972. The aim of the study to be presented in this article was twofold:

(1) To measure the brain size in marasmic infants and children by simultaneously recording the head circumference and performing transillumination and echo encephalography.

(2) To demonstrate whether or not, in infants with marasmus aged less than six months, a recordable improvement in brain size takes place during nutrition rehabilitation.

MATERIAL

Definition of marasmus

The criteria used for including children in the study were as follows:

(*a*) Weight for age below 60% of the Boston standard (50% percentile) and no apparent oedema, i.e. the definition of marasmus adopted at the Jamaica Conference in 1969 (6).

(*b*) No signs of any serious disease which could in itself be a major cause of severe malnutrition. Children with diarrhoea (arbitrarily defined as more than three loose stools a day) were also excluded.

Organization of the study and number of children examined

The total number of children with marasmus examined was 102. The age and sex distribution and the place of examination are given in Table I.

A *cross-sectional study* was devoted to analysing the situation in the total material of 102 children, aged 2–24 months, before any medical or dietary rehabilitation took place. Each examination included in principle anthropometric and clinical observations, transillumination and ultrasonic echo ventriculography.

A *longitudinal study* was carried out by performing follow-up examinations of the 53 children aged 2–6 months who were recruited from the Lidetta Mother and Child Health (MCH) Centre in the Bole area of Addis Ababa.

Each examination included in principle anthropometric and clinical observations, transillumination and ultrasonic echo ventriculography. The interval between

Table I. *Age, sex distribution and place of examination. Children with marasmus*

Place of examination	Boys								Girls								Total
		Age, months								Age, months							
	n	2–3	4–5	6–8	9–11	12–14	15–17	18–24	*n*	2–3	4–5	6–8	9–11	12–14	14–17	18–24	
Lidetta Mother and Child Health Centre	24	10	12	2	–	–	–	–	29	17	8	4	–	–	–	–	53
Nutrition Rehabilitation Clinic, ESPC	29	–	–	5	4	8	6	6	20	–	–	1	6	4	3	6	49
Total	53	10	12	7	4	8	6	6	49	17	8	5	6	4	3	6	102

two examinations was routinely 1 month±7 days. On a few occasions (four in all) transillumination and echo ventriculography could not be performed and the next complete examination then usually took place 1 month later.

The aim was originally to make at least three follow-up studies of each of the 53 children. Not unexpectedly, however, this proved impossible. Ten of the children dropped out even after the first examination (fatal outcome, home problems, unco-operative mothers). Another 14 were re-examined only one or two times. The majority of the children—29—were, however, re-examined five times or more, in some cases up to nine times.

Ages of the children

Records containing accurate information concerning dates of birth were available for 28 out of 53 of the children aged less than 6 months (all attending the Lidetta MCH Centre). For the 49 children aged 6–24 months (the majority attending the Nutrition Rehabilitation Clinic at the Ethio-Swedish Pediatric Clinic (ESPC) in Addis Ababa), birth records could be obtained in only 6 cases.

For the children without birth records, we had to rely on information given by the mothers concerning the date of birth. Thanks to the existence of a fairly detailed religious calender in Ethiopia, the birth dates of the majority of the children could be reconstructed with considerable accuracy. Cross-checking, when possible, indicated that the information was correct to the week, often even to the day.

It may be expected that a discrepancy between recorded age and true age will become greater with increasing age. Since, in this study, as in some others in this series, the main focus was on a limited age group (0–24 months), the errors are, in most cases, probably small, although in individual cases larger aberrations cannot altogether be excluded.

Birth weights of the children.

Children with low birth weights (≤2 500 g) represent a fairly large proportion of all the children born in developing countries (39). They also represent a considerable proportion of all the children who have low weights for age during the first few months of life. In order to eliminate as far as possible this category of children, the following measures were taken:

(*a*) No children under 2 months of age were included in the series.

(*b*) No children with available birth records indicating a birth weight ≤2 500 g or representing the outcome of a twin pregnancy were included.

Feeding pattern

No attempt was made to record a detailed dietary history in every case. In most population groups in Ethiopia, prolonged breast feeding—often up to ages of 18–24 months—is still the custom (19). This is true also of the area in Addis Ababa in which the non-privileged families of our study lived. For the children below 12 months of age, the marasmic disease could primarily be attributed to "starvation at the breast"; for the older children lack of suitable weaning foods played a major role. In some of the children, earlier diseases (repeated diarrhoea etc.) contributed to their marasmic condition.

Socio-economic background

The families to which the children with marasmus belonged, came throughout from the non-privileged stratum which has been defined in another publication of this series (8). In brief, this means an income below—often far below—US $13 per month, a period of education for the parents which did not exceed 2 years (the vast majority were illiterate), poor lodgings, very primitive living conditions and a high frequenty of unemployment and broken homes.

Nutrition rehabilitation program

Each of the 53 children aged 2–6 months included in the longitudinal study were also included in a nutrition rehabilitation program on an out-patient basis. The program comprised regular check-up, nutrition education and free distribution of an infant formula based on full-fat milk powder ("Baby FAFFA", produced at the Ethiopian Nutrition Institute). Each mother received 1.5 kg of Baby FAFFA once a week. This amount was

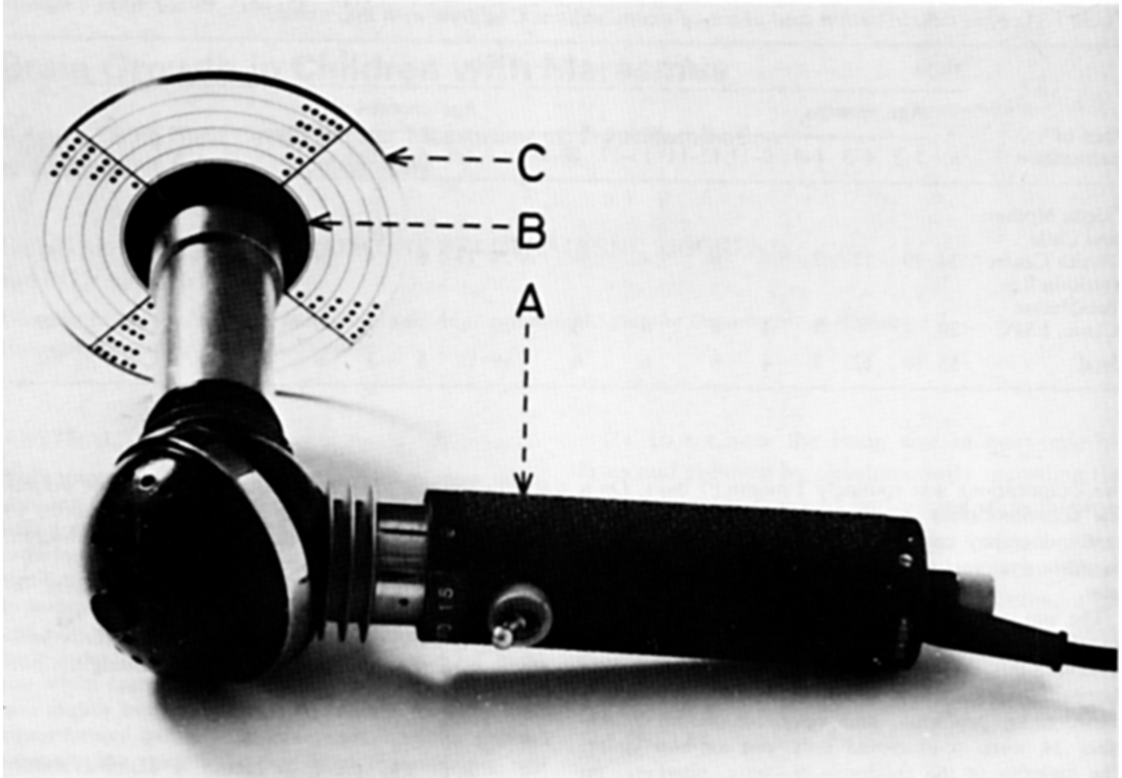

Fig. 1. An ordinary transillumination lamp (Oculus) (*A*) with a black rubber adapter (*B*) fixed to the rubber rim held against the baby's head, to which rim is attached a circular scale plate (*C*) (34).

liberal also taking into account the fact that some of the severely malnourished children needed at least 150 calories and 3 g of protein per kilogram of body weight and 24 hours. The mothers were carefully instructed in how to feed the baby, using either a cup or a carefully cleaned bottle.

METHODS

All the children were examined by one and the same pediatrician (G. E.). Interviews with the children's guardians, mostly their mothers, were carried out with an Ethiopian nurse or health officer acting as interpreter. The nurse or health officer also acted as an assistant at the examinations.

Anthropometry. Standard anthropometric data, including body weight, length, arm circumference, head circumference and skinfold thickness (triceps), were recorded. For the methodological details, see WHO Monograph Series No. 53 (17). Scales and tapes were regularly checked. A Harpenden caliper was used.

Head circumference was of particular importance in these studies. Great care was taken to obtain accurate and reproducible results. The measurement was made with a steel tape to the nearest 0.1 cm. The tape was placed so as to measure the greatest occipito-frontal circumference.

Transillumination. The transillumination examinations were performed by using a transillumination lamp of the Oculus type with a small 25-watt (7.5 V) lamp and a point scale fixed to the rim by a black rubber adapter (Fig. 1). The results of the examinations were expressed in scale points, according to the method described by Sjögren & Engsner (34).

The examinations were performed in a totally darkened room after the examiner had adapted to darkness for 3–5 minutes. As a routine, all infants were examined over the fronto-temporal and parieto-occipital regions, on the right as well as the left side of the head. In a minority of cases, a slight difference between the two sides was observed, but it never exceeded 0.5 scale points. If a difference was noted, the mean value of the two sides was used.

Normally, newborn infants should transilluminate fronto-temporally up to scale point 2 or less, and parieto-occipitally up to scale point 1 or less. Children aged more than 12 months should not illuminate the scale plate at all (34).

Ultrasonic echo ventriculography. The size of the lateral ventricles was measured by ultrasonic echo (31,

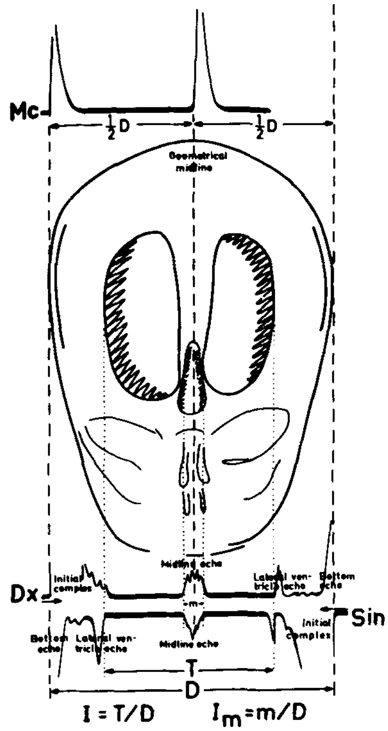

Fig. 2. Schematic pneumogram compared with enlarged schematic echo ventriculogram, where *Mc* is the midline control, *Dx* the echo encephalogram from the right, and *Sin* an inverted echo encephalogram from the left temporal region. The position of the lateral ventricle echoes correspond to the lateral surface of the lateral ventricles, and the echo-free zones to the widths of the lateral ventricles seen in the pneumogram (31).

32). The echo encephalograph used was a Siemens apparatus (Kraut-Krämer system) with a Polaroid Land camera for instant recording of the oscillographic tracings. The probe used had a frequency of 2 megacycles per second and a diameter of 24 mm. Liquid paraffin was used as a contact medium between the head and the probe. The head was not shaved prior to the examination.

The summarized width of the right and left lateral ventricles *(T)* was expressed in relation to the diameter of the child's head *(D)* as a lateral ventricle index *(I)* (Fig. 2).

Two or more echo ventriculograms were regularly photographed; if there was a slight difference between them, the mean value of the lateral ventricle indices was recorded. Normally this index should not exceed 0.33 or 33% ($M+1$ S.D.) of the diameter of the head in newborn babies and 0.29 in children aged 12 months (33).

Discussion of the methods

Some sources of error in the interpretation of the recorded data should be discussed. As regards the influence on *head circumference measurements* of the variation in thickness of scalp and skull bone, this question is dealt with at some length under "Discussion". The same factors (thickness of scalp and skull bone), as well as the degree of mineralization of the bone and the thickness of the hair covering, may exert some influence on the outcome of *transillumination*. Severe PCM may in itself cause, not only thinning, but also alteration of the mineralization of the bone (14). If rickets is also present, it may produce further demineralization and thinning of the bone. In a separate study it could be demonstrated that florid rickets with marked craniotabes may increase transillumination by 0.5–1.0 scale points (10). However, pronounced rickets is said to be uncommon in marasmic children with stunted growth and this proved true also in our material.

Dodge & Porter (5) made the observation on autopsy material the transillumination of the skull bone, as such, will disappear at a thickness of 6 mm but that, when scalp and skull bone are examined together, it seems to disappear at a thickness of the skull bone of 2.5–3 mm. According to Roche (29), the skull bone thickness in the naseon region will reach 6 mm around 18 months of age, whereas in other regions the thickness of the bone at this age amounts to only 2.5–3.0 mm. These observations would indicate an age limit for transillumination in practical work at 18 months rather than at 12 months, which is the figure most frequently mentioned.

As we shall see in the present material as well as in a material of children with kwashiorkor (9), transillumination, often of abnormal degree, could be observed in children up to 24–36 months of age. Indirectly, this is a proof that the translucency of the integuments due to the thinning of tissues (in cases of kwashiorkor perhaps oedema) and the demineralization of bone must have been of common occurrence. As for the hair covering, this is, on an average, thicker in an Ethiopian than in a Swedish infant but shows the same temporary thinning a couple of weeks after birth. Most Ethiopian families, apart from the privileged ones, still practice shaving the heads of their childern from the time of baptism, i.e. at 4 weeks for boys and 6 weeks for girls. Recordings in a limited number of infants of transillumination before and after hair shaving indicated an effect of the order of 0.3 scale points (10).

The lateral ventricle index measured by *ultrasonic echo ventriculography* is less influenced by the factors mentioned. Pronounced thinning of scalp and bone was estimated to give a maximum index deviation of 0.01–0.02 only.

RESULTS

Cross-sectional study

Anthropometry. The data are presented in Table II*a*. In addition to absolute figures, the percent age standard (17) is also given routinely for two parameters (weight/age and length/age). Cor-

Table II*a*. *Anthropometric data. Children with marasmus included in the cross-sectional study*

Age groups (months)	*n*	Weight (kg)	Weight/age % standard	Length (cm)	Length/age % standard	Weight/length % standard	Arm circumference (cm)	Triçeps skinfold (mm)
2– 3	27	3.02 [0.54][a]	56 [12]	54.0 [4.4]	92 [12]	70 [10]	8.2 [1.4]	4.6 [2.4]
4– 5	20	3.79 [0.72]	56 [12]	55.5 [6.2]	87 [11]	80 [8]	8.5 [1.2]	4.4 [2.0]
6– 8		4.20 [0.64]	52 [9]	60.0 [5.8]	89 [9]	74 [10]	8.0 [1.8]	4.0 [2.4]
9–11	10	5.04 [1.60]	54 [11]	61.2 [6.2]	85 [9]	83 [11]	9.2 [2.4]	3.8 [2.0]
12–14	12	5.34 [1.26]	53 [13]	64.2 [5.8]	85 [10]	77 [10]	8.5 [2.6]	4.0 [2.2]
15–17	9	6.05 [1.12]	56 [11]	66.0 [6.2]	83 [8]	80 [12]	8.8 [3,1]	4.4 [2.1]
18–24	12	6.68 [1.34]	55 [8]	67.1 [6.6]	78 [10]	86 [14]	8.6 [2.8]	4.8 [1.4]

[a] Figures in brackets are 2 S.D.

responding to the mode of selection (weight/age below 60% of standard; cf. above), the emaciation and the stunting of growth, as evidenced from the mean values for weight, length, head circumference, arm circumference and skinfold thickness, are very pronounced.

Head circumference. Mean values and standard deviations for head circumference in relation to age are given in Table II*b*, Fig. 3*a* and 3*b*. These figures include, as background information, the mean values and distribution for head circumference/age in healthy Swedish children (18). The mean values for head circumference/age for the marasmic children lie at or slightly below *M* −2 S.D. The variation is considerable, however. Even in the youngest age group, the deviation from normal is pronounced. In absolute values, the difference between means varies from 3.4 cm (age group 2–6 months, both sexes combined) to 2.8 cm (age group 18–24 months, both sexes combined).

Transillumination. The results are presented in Fig. 4. The controls were non-privileged Ethiopian children with no or only mild PCM (8). The character of the control group means that the deviations observed in the children with marasmus are, if anything, slightly minimized.

Only in the age groups above 6 months there is a clearcut tendency to increased values. Thus, as regards the values of fronto-temporal recordings, the differences between the marasmus group and the control group for the age groups 6–11, 12–17 and 18–24 months are highly significant ($p<0.001$) and, as regards the values of parieto-occipital recordings, these differences in the age group 6–11. 12–17 and 18–24 months are not significant ($p>0.05$).

Ultrasonic echo ventriculography. A positive identification of the lateral ventricle echoes was obtained in all of the 102 marasmic children examined. The results are presented in Fig. 5. It is obvious that the marasmic state does not in any way cause a deviation of the lateral ventricle index, thus implying that there is no change in lateral ventricle width in relation to head diameter. Also, when a correlation for the abnormally low head circumference/age is made (using "head circumference age" (16) rather than chronological age), the means for the lateral ventricle index do not show any significant deviation from normal.

Longitudinal study

Anthropometry. The anthropometric data, expressed as means of the percentage standard, are given in Fig. 6.

In addition to group observations, four individual cases are also briefly presented with respect to changes in anthropometric data during nutrition rehabilitation (Fig. 7). They are chosen so as to

Table II *b*. *Head circumference in relation to age. Boys and girls separately*

Age group (months)	Head circumference (cm)			
	n	Boys	*n*	Girls
2– 3	10	36.0 [2.8][a]	17	35.2 [2.2]
4– 5	12	37.6 [3.2]	8	38.0 [2.2]
6– 8	7	41.1 [2.4]	5	40.6 [2.6]
9–11	4	42.0 [3.2]	6	41.6 [2.4]
12–14	8	43.8 [3.2]	4	43.1 [2.0]
15–17	6	44.4 [2.8]	3	44.0 [2.4]
18–24	6	45.2 [2.8]	6	44.6 [2.4]

[a] Figures in brackets are 2 S.D.

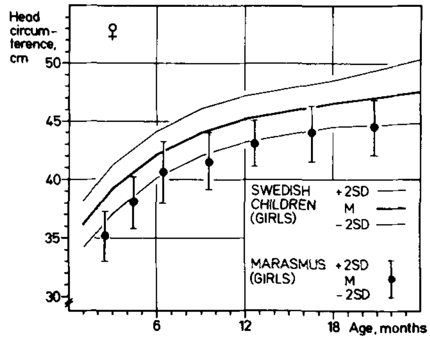

Fig. 3. (*b*) Head circumference related to age. Children with marasmus compared with normal range (18). Cross-sectional study. Girls only.

represent various types with respect to the success of nutrition rehabilitation.

Case B. Y.

A girl, first child of a 17-year-old mother married to a labourer. Delivery uncomplicated, birth weight 2950 g. Breast fed, no other food given. The father had been without income for the last 2 months. The mother stated that the family actually earned at most 10 US cents twice a week. She was favourable to the rehabilitation work and attended regularly.

Case S. W.

A girl, third child of a 21-year-old mother. Delivery uncomplicated, birth weight 3 150 g. Breast fed, no other food given. The mother had earlier worked as a bar girl but was now out of work, owing to the birth of the last child. She lived with a girl friend who worked at the same bar. The mother attended the nutrition rehabilitation program fairly regularly but probably gave some of the food to the other two children.

Case J. W.

A boy, the second child of a 19-year-old unmarried woman. Delivery uncomplicated, birth weight 2850 g. Breast fed, no other food given. The mother's first child died at the age of 1 year when the mother was 18 years old.

The mother lived with the child at a relative's house. The head of the extended family was a labourer, with a monthly income of about 5 US$. The mother was one of the most active members of the nutrition rehabilitation group.

Case W. H.

A boy, the first child of a 23-year-old, deserted mother. Delivery uncomplicated, birth weight 3 100 g. Breast fed, no other food given. The mother attended the nutrition rehabilitation program somewhat irregularly and was

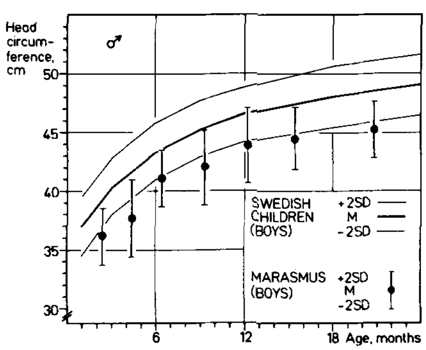

Fig. 3. (*a*) Head circumference related to age. Children with marasmus compared with normal range (18). Cross-sectional study. Boys only.

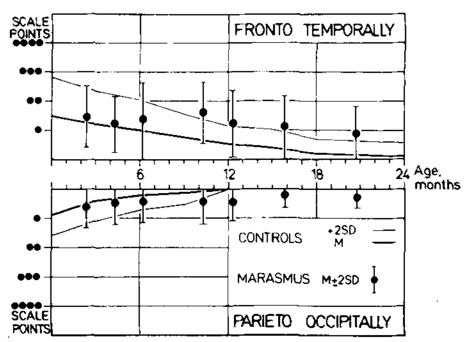

Fig. 4. Head transillumination related to age. Children with marasmus compared with a control group of Ethiopian children (8). Cross-sectional study. Boys and girls combined.

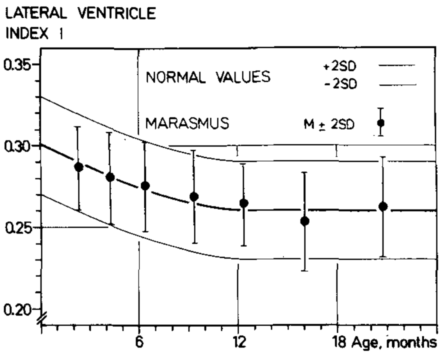

Fig. 5. Echo encephalography. Lateral ventricle index (*I*) related to age. Children with marasmus compared to normal range (33). Cross-sectional study. Boys and girls combined.

known to sell some of the food given to a neighbour. It was not possible to control or stop this practice. The mother had no other income.

Head circumference. The results are presented in Fig. 8*a* and 8*b*. These figures include, as background information, the mean values and distribution for head circumference in relation to age in healthy Swedish children (18).

The deviation of head circumference/age (Fig. 8*a* and 8*b*) from normal was less marked in the longitudinal group than in the larger cross-sectional one (excess mortality in children with the severest marasmus, who therefore were underrepresented in the longitudinal study). A slight tendency to catch up in head circumference during nutrition rehabilitation could be observed but was not very

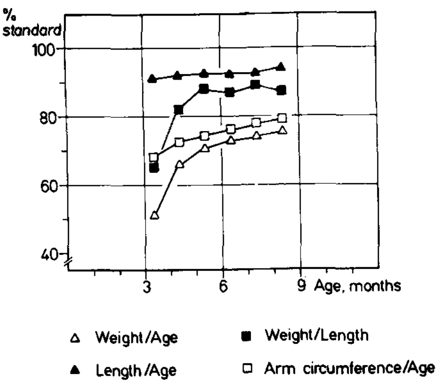

Fig. 6. Anthropometric data expressed as means of percentage of standard (17). Children with marasmus. Longitudinal study of 29 cases examined at monthly intervals during nutrition rehabilitation. Boys and girls combined.

impressive. This general rule was not without exceptions, however. In two of the individual cases (Fig. 7, B. Y. and J. W.) with better than average effects of nutrition rehabilitation, the catch up in head circumference was reasonably good.

Transillumination. The results of the follow-up examinations are presented in Fig. 9, which gives the means and standard deviations. The mean values do not differ significantly from those observed in non-privileged Ethiopian children with no or only mild PCM (8). There is a slight tendency for the values of the children with marasmus to move towards zero faster than in the group given for comparison.

Ultrasonic echo ventriculography. The results of the follow-up examinations are presented in Fig. 10. As was the case with the larger, cross-sectional material, the initial values come very close to those observed in Ethiopian children with no or mild PCM (8) and in Swedish children (33). During the follow-up period of nutrition rehabilitation for 6 months or more, the mean values for the lateral ventricle index manifest the same gradual slow decline as is typical of healthy children of this age group. Thus, no significant deviation from normal could be observed either initially or at follow-up.

DISCUSSION

Brain weight

An autopsy material of brain weights of children with severe PCM was first published from Uganda by Brown (1). He found in all the age groups examined (0–5 years) a numerical reduction in brain weight of the order of 15–20%. The differences were significant for the age groups above 1 year. Similar results have been presented by Winick & Rosso in a small series (9 cases) of children from Chile (40) and by Udani and coworkers from India (37).

Head circumference

In vivo, assessments of brain size have mostly been made by measuring head circumference. The reduction of head circumference observed in cases of marasmus differs in degree and also with respect to catch-up growth in longitudinal studies over longer time.

Stoch and Smythe (36) followed their group of initially grossly undernourished children up to the

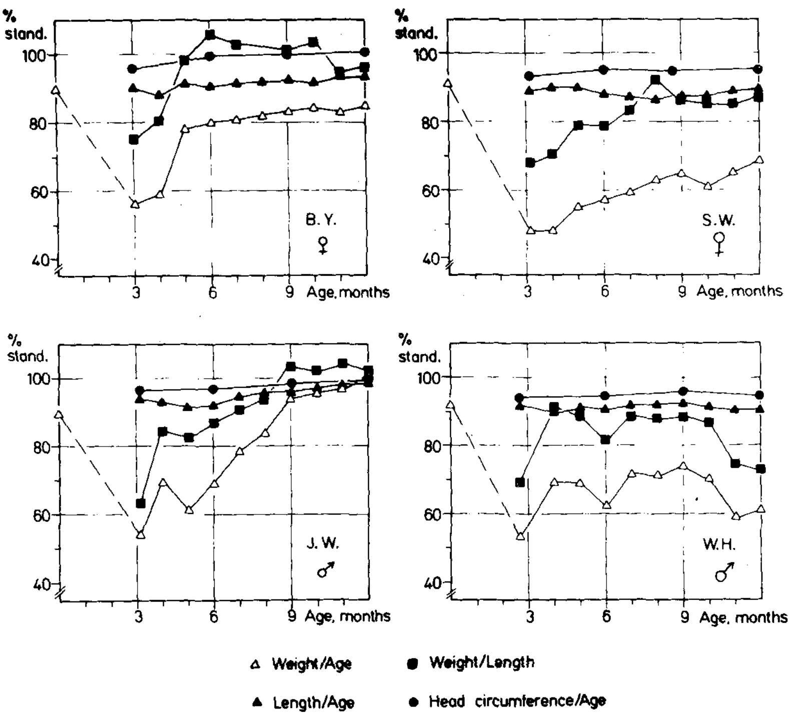

Fig. 7. Anthropometric data, expressed as percentage of standard (17) during nutrition rehabilitation. Four individual cases.

age of 10–11 years. At that time, there was still a significant difference in the head circumference/age relation (49.58 cm, as compared with 52.04 cm for American age mates). Since the children in the test group were still markedly stunted in growth, the head circumference/height relation was about normal.

Mönckeberg (25) followed 14 children aged 8–9 months, who had been admitted to hospital "with severe marasmic malnutrition". Renewed examination at the ages of 3–6 years showed values for head circumference definitely below normal. At the follow-up, the children were mainly normal, as regarded weight for age, but clearly subnormal, as regarded length for age; thus many of them were obese. The average head circumference/age

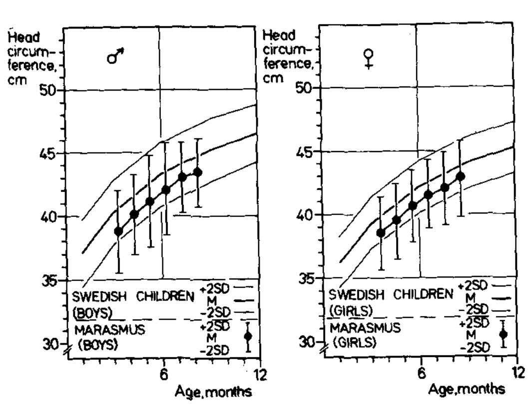

Fig. 8. Head circumference related to age. Children with marasmus compared with normal range (18). Longitudinal study of 29 cases examined at monthly intervals during nutrition rehabilitation. Boys and girls separately.

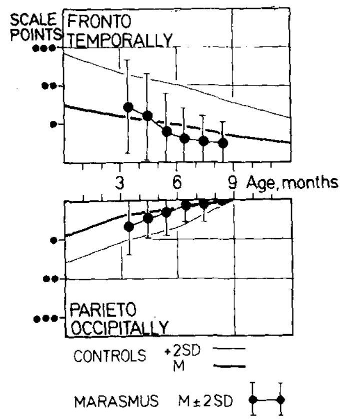

Fig. 9. Head transillumination related to age. Children with marasmus compared with a control group of Ethiopian children (8). Longitudinal study of 29 cases examined at monthly intervals during nutrition rehabilitation. Boys and girls combined.

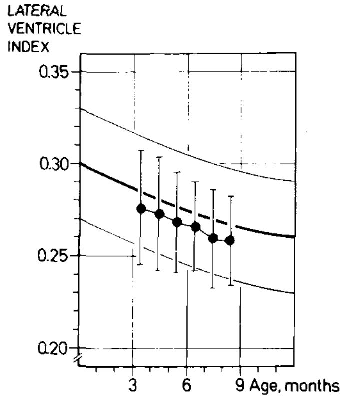

Fig. 10. Echo encephalography. Lateral ventricle index (*I*) related to age. Children with marasmus compared with normal range (33). Longitudinal study of 29 cases examined at monthly intervals during nutrition rehabilitation. Boys and girls combined.

relation was 2.4±1.4 cm below normal. The length deficit was 12.7±4%.

In a series of papers, Graham et al. (15, 16) have studied the growth and development of children of families living in the "septic fringes" of Lima, Peru. They followed over a number of years more than a hundred children afflicted at an early age with severe malnutrition, almost all of the marasmus type. Graham et al. do not give any absolute figures for head circumference etc.; they introduced the term "development age" and "development ratio", which make comparison with the results of other workers a bit complicated. For our purpose, the most interesting conclusion of their work is expressed as follows (16, Speculation): "Catch-up growth, both in height and in head size, can go on for many years after a period of severe malnutrition." Like many other workers in the field, they are of the opinion that "it may well be that the much slower rates of growth and the smaller statures achieved by children in adverse situations are a convenient adaptation for survival".

The head circumference measurements in *our material* show a reduction which for the cross-sectional material in its entirety is significant ($p<0.01>0.001$). For four out of six different age groups the difference is probably significant ($p<0.05>0.01$). In absolute values, the differences observed are of the same magnitude as those observed by Stoch & Smythe (36). For the longitudinal material with children in the age group 2–6 months, the difference in head circumference, to begin with, is less pronounced and not significant ($p>0.05$). During nutrition rehabilitation, which was, on an average, slow and irregular, only a slight tendency to catch up was observed.

Throughout in our studies, only the ratio of head circumference to age has been given. We have thus refrained from giving the ratio of head circumference to length. The patterns of growth increments for head circumference and for length differ markedly and there is only a weak correlation between the two.

Winick & Rosso (40) have given as equation for the relationship between head circumference and brain weight in normal children: total brain weight in g=(head circumference in cm $-20.5)^2+109.75$. Applying this equation to children with "neonatal malnutrition", they concluded that "reduction in head circumference accurately reflects reduction in brain weight". If so, it is hard to concieve that in cases of marasmus there could be a substantial increase of intracranial fluid with a corresponding further reduction of brain size. If a comparison is made between the observations by Stoch & Smythe on the head circumferences of South African children and by Brown on the brain weights of Ugandan children, it can be said that the two parameters tally reasonably well.

INTERPRETATION OF SUBNORMAL HEAD CIRCUMFERENCE VALUES

1. *What is the normal head circumference in Ethiopian children?*

There is good reason to postulate that in healthy Ethiopian children the same norms can be adopted as those noted in Swedish children. If ethnic differences were important, one would not expect privileged Ethiopian children to follow the same standards as those observed in Swedish children. But in fact, they do; at least this is true for the age groups under consideration here (7, 8).

2. *What is the definition of a subnormal head circumference value in an individual subject?*

The range of head circumference values in healthy individuals of one and the same age is considerable. This range is mainly genetically determined. It bears only a moderate relation to body size in general.

Normal intelligence is rarely found if the brain weight is below 1000 g in malde adults and 900 g in female adults (12). The corresponding head circumference can be assumed to be around 50 and 49 cm respectively. In growing subjects, as a border-line in relation to microcephaly, a head circumference of $M-3$ S.D. has been given (2, 3). For a one-year-old boy, this corresponds to *c.* 43 cm, as compared with a normal mean value of 46.5 cm. Other authors (26, 27) are of the opinion that even head circumference values below $M-2$ S.D. imply suboptimal intelligence.

It is obvious that also values "within the normal range" may be abnormal for a given child, e.g. if the genetic potential favours a $M+1$ S.D. development, whereas the actual value (or values) observed is $M-1$ S.D. However, only under special conditions (longitudinal observations, access to values in relatives, etc.) is it possible with some certainty to diagnose such a "relative subnormality".

3. *What do subnormal head circumference values observed in groups of children imply?*

The definition of subnormality in this case is simple; the mean value observed should be significantly below the standard (e.g. that of Swedish children). However, the interpretation of the mechanisms behind such a subnormality in mean head circumference is not always quite simple. This is true the more there are concomitant signs of severe malnutrition, perhaps of long standing (cf. below).

4. *How close is the correlation between head circumference and brain size?*

The interest in measuring head circumference stems mainly from the fact that in healthy individuals there is a fairly good correlation between head circumference and brain weight. However, this general rule has exceptions, particularly in sick and malnourished children. The four factors mentioned below (Table III) can all weaken the correlation. As sources of error, they act in different directions and it is not an easy task to find out *in vivo* to what extent the overall balance means an overestimation or an underestimation of the brain size.

5. *Attempts to quantify the effect of abnormal thinness of scalp and bone thickness on head circumference*

Our studies have only dealt with conditions *in vivo*. By making use of X-ray technique, it is possible to measure the thickness of the scalp (41) and the skull bone (29). on the one hand, and the volume of the skull cavity (21), on the other. However, neither time nor equipment were available and a convincing reason for exposing children to X-rays was lacking. Likewise, autopsy material was not accessible as a basis for comparison.

Earlier investigators, making use of radiographs, have made detailed studies of the thickness of the scalp (41) as well as of the bony cranium (29) in children of various ages. Such data make it possible to calculate how much of the head circumference measured by a tape reflects the thickness of the integuments and how much remains for the "skull cavity circumference" as such. The former component may be calculated to be roughly of the order of 10 per cent of the total, i.e. a child with a head circumference of 45 cm should have a "skull cavity circumference" of the order of 40.5 cm. This is not only a theoretical speculation. At the autopsy of two adults, a plaster cast was made of the calvarium. The head circumference was, on an average, 56.3 cm, and the "skull cavity circumference", measured as the circumference of the plaster cast, was 50.2 cm, i.e. a difference of 10.8 per cent.

On the basis of the data concerning thickness of scalp and bone (cf. above), a calculation has been made as to the effect on the head circumference of various degrees of reduction in thickness (Table IV). A simultaneous reduction of 50% of the scalp tissue and 25% of the bone thickness means a decrease of the head circumference by 1.7 cm (3.5%). An even more pronounced reduction of 75% of the soft tissue and 50% of the bone thickness means a decrease of the head circumference by 3 cm (6%).

The reduction of head circumference observed in our series of children with marasmus, i.e. an average of 3.4 cm in the age group 2–6 months, is almost certainly partially due to a thinning of the integuments. It is noteworthy that a decrease of the thickness of the scalp by 50% and of the bone by 25% may explain *c.* 50% of the reduction of head circumference observed.

It is evident that part of the reduction of head circumference values in cases of marasmus may be explained by emaciation, but even if this is pronounced, hardly more than 50%. It should be noted in this context that even after successful nutrition rehabilitation a head circumference/age relation below normal may remain for many years (36).

Table III. *Factors influencing the relationship between head circumference and brain size*

(*a*) Scalp tissue (and hair)	abnormally thin	Head circumference suggests erroneously *low* brain size
(*b*) Bone tissue	abnormally thin	Head circumference suggests erroneously *low* brain size
(*c*) Subdural/subarachnoidal fluid	abnormally increased	Head circumference suggests erroneously *high* brain size
(*d*) Cerebral ventricles	abnormally large	Head circumference suggests erroneously *high* brain size

6. *How can subnormality in head circumference be translated into subnormality in brain size?*

If the head circumference is assumed to reflect directly the cranial internal circumference and if the brain occupies the cavum cranii in the normal way, then it can easily be calculated that a reduction of head circumference at the age of one year from 46 to 44 cm will mean a corresponding reduction of the brain weight from *c.* 760 g to 660 g, i.e. a difference of 100 g (40). However, as we have seen, such a simple correlation may not exist, especially in cases of severe PCM. The reduction may be less if the thinning of integuments is pronounced or greater if the subdural/subarachnoidal space is abnormally enlarged (cf. above).

Table IV. *The effect on head circumference by alterations in thickness of scalp and/or skull bone*

Scalp-thickness reduction, % . . .		25	50	0	0	25	50	50	75
Skull-bone-thickness reduction, % . . .		0	0	25	50	25	25	50	50
Age *(months)*	Mean head circumference *(cm)*	Calculated effect on head circumference, cm[a]							
6	43.3	−0.5	−1.0	−0.5	−1.0	−1.0	−1.5	−2.0	−2.5
9	45.2	−0.6	−1.2	−0.6	−1.2	−1.2	−1.8	−2.4	−3.0
12	46.5	−0.6	−1.2	−0.6	−1,2	−1.2	−1.8	−2.4	−3.0
24	48.0	−0.5	−1.0	−0.7	−1.4	−1.2	−1.7	−2.4	−2.9

[a] The calculations have been made using the equation for a circle rather than that for an ellipse. The true shape of the skull may exhibit considerable individual variations. The approximation just mentioned will influence the result of the calculations only to a very limited extent.

Transillumination

The Mönckeberg group in Santiago (30) examined 32 children in the age range 3–12 months with severe "third-degree marasmic malnutrition", the growth deficit in all instances being more than 50% for their respective ages, according to Iowa standards.

Since photographic recording was the aim, a strong light source had to be used (800 W). The opening through which the 1-second flash of light was concentrated had a diameter of 5 cm. Around the opening a rubber ring was fitted. The transillumination was considered positive (abnormal) if the light also was more than 8 cm in diameter (five positions). By this criterion 28 out of 32 of the infants with marasmus had a positive finding, as compared with one (a border-line value) out of 30 nutritionally normal age matees.

In 26 out of 32 cases of marasmus, the existence of excess subarachnoidal fluid was verified by needle aspiration. A chemical analysis proved the fluid to have the same composition as the cerebrospinal fluid. Routinely, only *c*. 4 ml were aspirated, but in one case, in which aspiration was continued by mistake, 25 ml could be evacuated. The conclusion by the authors is "that malnutrition during the first months of life is associated with a brain size smaller than cranial capacity, which would result in a secondary increase in cerebro-spinal fluid".

As far as we are aware, no other similar series with systematic transillumination (possibly followed by aspiration) in cases of severe PCM has been published so far.

Our *own studies* indicated a slight-to-moderate increase of transillumination, in the age groups 6–24 months. It was demonstrable both from the fronto-temporal and parieto-occipital regions. The findings are by no means as dramatic as those just referred to by the Mönckeberg group.

How should the difference between our observations in Addis Ababa and those of the Mönckeberg group in Santiago be explained? Is there a true geographical difference or is the difference explained by the criteria for selection of material and/or technique? The severity of the PCM in the Santiago children may have been somewhat more pronounced than in ours. Furthermore, it is not quite clear to what extent children with low birth weights may have formed parts of the material. The technique using a very intense flash (800 W bulb) certainly exercised an influence. It is hard to see, however, that this could explain the results with very much more pronounced transillumination in the children with marasmus, as compared with normal children.

An important factor is the following. In the first year of life, the subarachnoidal space may be as wide as 0.5–1 cm also in children who are apparently normal. There is very little in the literature on this matter, but it is well known to pediatric neurologists and radiologists (Gamstorp, personal communication). The same phenomenon is observed also in foetal life (20). It prompts caution in interpreting X-ray pictures (pneumography), in order to avoid an erroneous diagnosis of "cortical atrophy". For the same reason, it seems justifiable to exercise caution also in the evaluation of positive needle aspiration in this age group.

Further studies from other regions are urgently needed to settle the question of the extent to which severe marasmus is accompanied by an abnormal accumulation of fluid in the subarachnoidal space. If such an abnormal accumulation of fluid is found, it would obviously mean that brain size is reduced to an even greater extent than head circumference *per se* indicates.

Ultrasonic echo ventriculography

We are not aware of any earlier studies with this technique, except for the preliminary data published by our own group (38).

Using chronological age, the mean values for the lateral ventricle index come very close to those of Swedish children and also the range of observations falls within normal limits. Using "head circumference age" (see above) instead, a considerable shift to the left would have occurred. However, as discussed under "Results", since the slope of the mean for the lateral ventricle index in healthy children which exists during the first year of life is rather modest, the change in position of the mean values of the marasmic children in relation to those of normal children is rather small and the difference in either case ("chronological age" and "head circumference age") from the normal is not significant.

It is of some interest in this context to recall that Stoch and Smythe (35) performed pneumography in two cases of severe marasmus and found the results normal. Furthermore, after the completion of our field work, we were informed of a multi-facetted study from Brazil (22; in Portuguese), involving also the taking of pneumoencephalogram in five children with marasmus, aged 4–14 months. The lateral ventricle size was normal in 4 of the 5 patients. This is in accordance with our own findings of normal lateral ventricle width measured by echo ventriculography.

However, the findings relating to the subarachnoidal space are different. All 5 patients showed "cortical atrophy", which was present also in 3 out of 4 patients on re-examination 4–5 months later. There are, however, definite difficulties in making X-ray diagnoses of "cortical atrophy", when it is not very pronounced. This is particularly true of children in the first year of life (cf. above). For these reasons, and because of the limited number of children involved, it is hard to evaluate the extent to which the observation made by the Brazilian investigators can be said to support the observations made by the Chilean scientists, using transillumination.

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