NUTRITIONAL MARASMUS IN BANTU INFANTS IN THE PRETORIA AREA

PART II. CLINICAL AND PATHOLOGICAL ASPECTS

P. J. PRETORIUS, M.MED. (PAED.), M.D., *National Nutrition Research Institute, CSIR, and Department of Paediatrics, University of Pretoria* AND H. NOVIS,* M.B., CH.B., *Department of Paediatrics, University of Pretoria*

In a previous report[1] some observations were made concerning the aetiology of the marasmus syndrome as observed in 80 Bantu infants studied at the Pretoria General Hospital.

The present paper is concerned with some of the clinical and pathological features of the disease. The other aspects studied, including certain biochemical findings and the results of nitrogen and fat-balance studies, will be dealt with in a subsequent report.

When a study was made of the literature it soon became evident to us that the term 'marasmus' had different meanings for different investigators. In most of the available reports no attempt has been made to define the term, and often no distinction is made between marasmus and kwashiorkor. The interpretation of results described in such reports is therefore rendered difficult—if not impossible.

We feel that the diagnosis of nutritional marasmus could be based on the following 4 criteria: (1) wasting, (2) body weight below the 'malnutrition line',[6] (3) absence of oedema and (4) absence of disease which may cause severe wasting. For the purpose of the present investigation, however, only one criterion, severe wasting, was used. In 16 of the 80 patients in the original series the wasting was thought to be primarily due to illness rather than underfeeding, and these will not be considered in the present discussion.

CLINICAL FEATURES

The typical clinical picture (Fig. 1) was that of an emaciated infant with muscle atrophy and loss of subcutaneous fat.

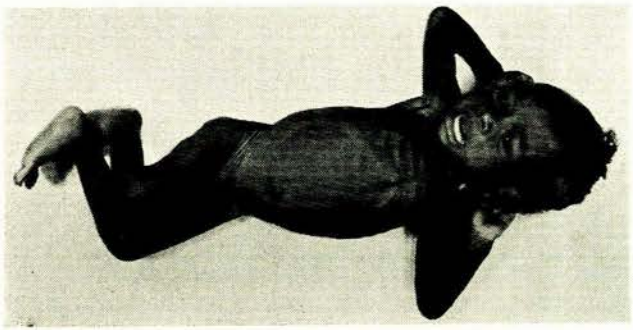

Fig. 1. Typical clinical appearance in nutritional marasmus. This patient, aged 18 months, weighed 3·82 kg. The expected weight (50th percentile for American children[4]) was 11·43 kg.

*Present address: 109 S. Elmwood Ave., Oak Park, Illinois, USA.

With the exception of 2 patients who had slight swelling of the dorsa of the feet, no oedema was detected in any of these children. Slight hyperpigmentation of the skin, sometimes associated with scaling, was observed in 12 (19%) of the 64 patients. Among kwashiorkor patients in this area such hyperpigmentation and scaling has been found to occur in over 90%.[2] The incidence of mucous membrane lesions (angular stomatitis and/or cheilosis) in kwashiorkor patients has been found to be 66% as compared with 14% in the marasmic infants of the present series.

Hair changes are considered to be rare in marasmic infants.[3] In our series, reddish discolouration of the hair, so commonly seen in kwashiorkor, was observed in only 4 patients, but in about half of the patients the hair appeared to be abnormally sparse.

As was mentioned in the previous report,[1] signs of infection, especially bronchopneumonia, gastroenteritis and otitis media were often present on admission.

In Figs. 2-4 the values for weight, height and head circumference of marasmic infants are compared with those of kwashiorkor patients admitted to the same ward. The percentile lines were plotted from values reported for children in the USA.[4] The use of the American values seems justified since it has been shown that values obtained in well-fed, privileged African children, at any rate for weight and height, are comparable with those of American children.[5]

Weight. In Fig. 2 the age/weight relationship of the marasmic infants is compared with that of kwashiorkor patients admitted to the same ward during the period of the study. It is evident that the patients with marasmus belonged to a younger age group (mean age 8·7 months) than the kwashiorkor patients (mean age 22·6 months), and are more underweight. Even if they were to be compared with kwashiorkor patients who had lost their oedema, the marasmic patients would still be noticeably more underweight.

With the exception of one patient, the body weights of all the marasmic infants fell below a line representing values two-thirds as great as the 50th percentile values for American children, designated by Ford *et al.*[6] the 'malnutrition line.'

Length (Fig. 3). As is the case in kwashiorkor patients, severe retardation of longitudinal growth was present in most of the marasmic infants, the measurements being below the 3rd percentile for American children[4] in the

great majority of cases.

Head circumference, (Fig. 4). Head circumference was measured in 40 marasmic infants. In Fig. 4 the values are compared with those of 43 kwashiorkor patients. Most of the values obtained in both groups fell below the third percentile for American children.[4] Growth of the skull appeared to be more retarded in the marasmic than in the kwashiorkor patients, since the values of only 5 marasmic infants (12·5%) fell above the 3rd percentile, whereas the corresponding number in the kwashiorkor group was 15 (35%). This difference may possibly be ascribed to the fact that marasmus occurs as a rule at a younger age, when the size of the head increases more rapidly than is the case in children of 'kwashiorkor age'. Arrest of growth of the head would therefore have a more striking effect in marasmus than in kwashiorkor.

The adverse effect of malnutrition on brain growth, as evidenced by the reduction in head circumference, has been commented on by other workers.[7,8] Stoch and Smythe[7] have adduced evidence which suggests that mental retardation may result from malnutrition.

PROGNOSIS AND COURSE

Since nutritional marasmus is a serious disease, it is not surprising that 22 of our patients (34%) died, the mortality rate being about 3 times as high as that of kwashiorkor patients in our ward.

In the vast majority response to treatment was slow, necessitating a long period of hospitalization. The average length of stay in hospital in the patients who recovered was 86 days, or about 3 times as long as the usual period of hospitalization in the case of kwashiorkor patients.

In most patients gain in weight was very slow, the average gain being 0·57 kg. during the first 4-week period after admission in the patients who eventually recovered. Kwashiorkor patients in our ward usually gain between 1 and 2 kg. over this same period.

Recovery was retarded by frequent episodes of infection, especially bronchopneumonia, of gastroenteritis and otitis media. Hypothermia, at times associated with hypoglycaemia, was frequently observed in the present series. This phenomenon, a common finding in undernourished laboratory animals[9] and human infants[10,11] is of serious prognostic importance. It was a terminal phenomenon in 9 of the 22 patients who died, death having occurred in these patients within a period of a few hours to 2 days after the onset of the hypothermia.

POSTMORTEM FINDINGS

Postmortem examinations were performed on 8 of the 22 patients who died.

A noteworthy finding was the presence of bronchopneumonia in all 8 patients. In one case the bronchopneumonia was complicated by empyema.

The cardiovascular system was normal in all patients except one whose heart showed a slight atrophy of the myocardial fibres.

Slight atrophy of the pancreatic acinar cells was found in 5 patients. Histological examination of the liver showed marked fatty change in only one case. The livers of 2 other cases showed slight fatty changes, while in the remaining 5 cases the liver histology was considered to be normal. This is in agreement with the well-known finding that the livers of marasmic infants, in contrast to those of

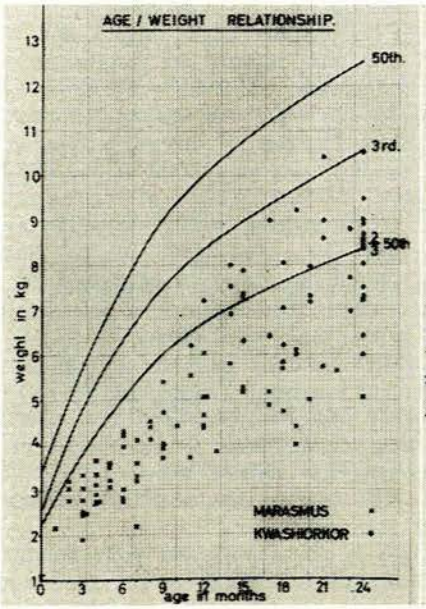

Fig. 2

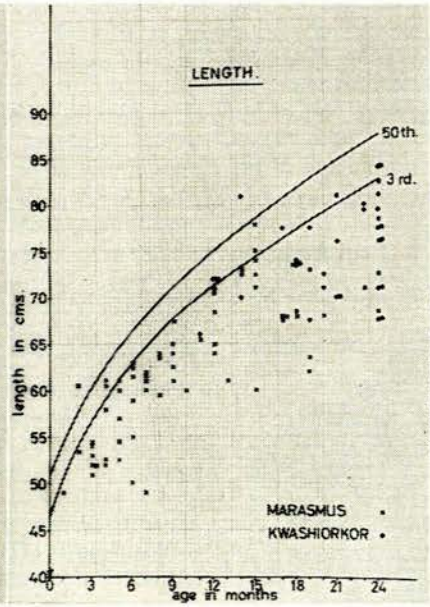

Fig. 3

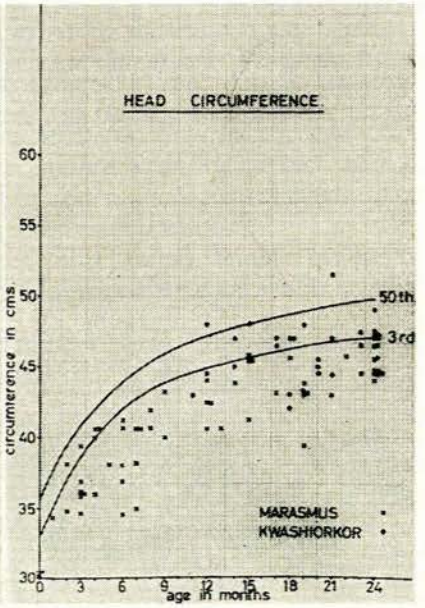

Fig. 4

Fig. 2. Age/weight relationship of patients with nutritional marasmus (crosses) and kwashiorkor (dots). The percentile lines represent American children.[4]
Fig. 3. Age/length relationship of patients with nutritional marasmus (crosses) and kwashiorkor (dots). The percentile lines represent American children.[4]
Fig. 4. Age/head-circumference relationship between nutritional marasmus (crosses) and kwashiorkor (dots). The percentile lines represent American children.[4]

kwashiorkor patients, usually show only slight fatty changes or none at all.[3]

Other lesions found, included hyperplasia of mesenteric lymph nodes (2 cases), acute renal tubular necrosis (1 case), mild atrophy of the suprarenal glands (1 case) and acute ulcerative colitis (1 case). One patient had widespread haemorrhagic cortical and subcortical infarction in the cerebral hemispheres and cerebellum. No evidence of vascular occlusion was demonstrated, and despite careful search, no morphological cause for the infarction could be found. The widespread infarction may be explainable on the basis of a functional vasoconstriction similar to that which may operate in renal tubular necrosis.

The livers, brains and lungs were weighed in 5 of the patients. It has long been known that the tissues of marasmic infants are often reduced in mass, but retain their essential structure.[3] Unfortunately the scale used for weighing the organs was not sensitive enough to register low weights accurately. The weights recorded for the smaller organs (heart, spleen, kidneys) are therefore too inaccurate to allow interpretation.

The lungs of all 5 patients were heavier than those of normal American children of corresponding age.[12] This finding is probably a reflection of the bronchopneumonia that was present in every case. As can be seen from Table I, the weights of the livers and, with one exception, of the brains of all the patients, were well below the average values for normal American children.[12] The values for normal African infants are not known and the number of patients studied was small, but these findings nevertheless suggest that there was atrophy of these organs. The assumption[7] that brain mass is proportional to head circumference is therefore given support. Unfortunately head circumference was not recorded in the one patient whose brain weight exceeded the average.

TABLE I. LIVER AND BRAIN WEIGHTS OF 5 CASES

Case	Age (months)	Weight in grams	
		Liver	Brain
1	3	110 (140)*	450 (516)*
2	4	150 (160)	— (540)
3	6	130 (200)	520 (660)
4	7	210 (227)	720 (691)
5	23	320 (380)	870 (1059)

*The bracketed figure is the average weight for normal American children of corresponding age.[12]

RESPONSE TO TREATMENT

Dietary Treatment

It is widely believed that marasmic infants tolerate milk fat poorly,[3] and a low-fat diet is therefore often prescribed.[3,5,13] This was not done in our patients. Most of them received whole milk containing 3% sunflower-seed oil; the mixture, which provided about 94 calories per 100 ml. formula, being tolerated very well. The usual calorie intake varied between 170 and 180 c. per kg. per day, but in several patients exceeded 200 c. per kg. per day. As a rule the feeds were taken well; if anorexia was present—an uncommon finding—the patients were fed by means of an indwelling polyethylene intragastric tube. Food intake was measured in most of the patients during the first 4 weeks after admission.

A distinctive feature of the disease was that some patients failed to gain weight despite a high calorie intake. This finding is illustrated by the weight gain curve of a patient shown in Fig. 5. During the first 26 days after admission the weight of this patient remained unchanged on an average calorie intake of 195 c. per kg. per day. Thereafter the intake was increased to an average of 256 c. per kg. body weight per day without producing any effect on weight gain. After the patient had received the high-calorie diet for 22 days he developed bronchopneumonia and died. Comparable observations were made in many other patients. Weight may remain constant for weeks or even months before the patient suddenly starts gaining. The reason for this strange phenomenon is unknown. Poor absorption of nutrients does not seem to be the cause, since the balance studies which we carried out on a considerable number of our patients usually showed only slight impairment in the absorption of either nitrogen or fat. (The details of these balance studies will be published in a later article.)

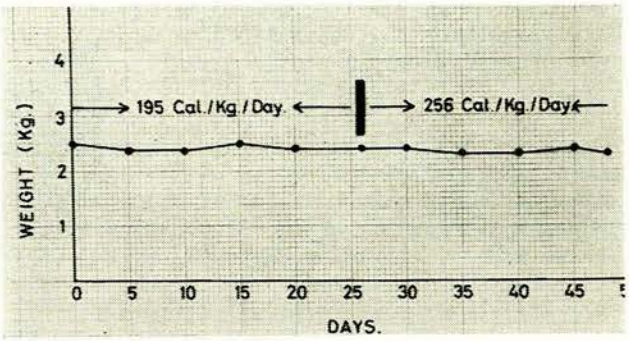

Fig. 5. Weight chart of a patient with nutritional marasmus. Weight remained constant on an average daily intake of 195 calories per kg. body weight. The weight curve remained unchanged after the average intake was increased to 256 c. per kg. body weight per day.

Supportive Treatment

All patients received multivitamin supplements daily and, if anaemic, iron and additional folic acid were prescribed. Antibiotics were not given prophylactically, but only when considered to be indicated. Hypoglycaemic patients were treated with intravenous glucose. In many instances the appearance of hypoglycaemia was a preterminal event. Hypoglycaemic patients who had become stuporose almost invariably died despite glucose administration. In this respect our experience differs from that of Kerpel-Fronius,[10] who found glucose administration effective in most of his hypoglycaemic patients.

Attempts were made to keep the patients warm so as to minimize loss of heat through the skin, and several seriously ill patients were treated in incubators. Fluids and electrolytes were given intravenously to dehydrated patients, and plasma and/or blood was administered on 15 occasions to patients who either appeared to be shocked or who had become anaemic. Repeated small transfusions of plasma and blood, given to 3 patients who were not responding well to treatment, did not appear

to be of particular benefit. Anabolic steroids were administered at weekly intervals to 7 patients and appeared to be without effect.

Efficacy of Therapeutic Measures

In general the results obtained with the therapeutic regimen used were disappointing. Although a high caloric intake could easily be achieved, the mortality rate was high and response to treatment slow. However, the disease is at present being studied intensively in several centres, and it seems likely that research will result in the discovery of more effective therapeutic measures.

DISCUSSION

Chilean workers[14] have advanced the theory that the frequent failure of marasmic infants to gain weight is the result of decreased secretion of growth hormone. These investigators administered 2 mg. of human growth hormone to each of 6 marasmic infants at weekly intervals for 4 consecutive weeks. This resulted, on the average, in a fourteenfold increase in weight gain, while a considerable increase in retention of nitrogen, potassium and phosphorus also occurred. When the injections of growth hormone were stopped, weight gain promptly ceased. The authors came to the conclusion that growth hormone secretion may be diminished in severe undernutrition. They suggest that a decrease in hypophyseal function may be an adaptive mechanism developed in response to the chronically diminished caloric intake. This mechanism might then permit survival in spite of a greatly lowered caloric intake by causing decreased bodily activity, a lowered BMR and diminished or arrested growth. A return to normal of hypophyseal function would allow growth to commence again.

This interesting theory appears to be strongly supported by the experimental evidence cited. Direct confirmation from experiments with growing animals is not available, but experiments performed on adult animals suggest that undernutrition is accompanied by hypophyseal depression. Mulinos and Pomerantz[15] found that prolonged inanition of the rat produced effects, particularly on the endocrine organs, which resembled those of hypophysectomy. It is difficult to understand, however, why even the deposition of subcutaneous fat, which is not known to be in any way dependent on the secretion of growth hormone, should sometimes be delayed in marasmic infants for weeks or even months after the intake of calories and other nutrients has become optimal. It is of interest in this regard that severely undernourished adult laboratory animals respond to a satisfactory diet by immediately gaining weight and increasing the body temperature.[16]

If undernutrition does indeed cause hypophyseal depression with a reduction in the secretion of growth hormone, a lowered basal metabolic rate (BMR) should be a constant feature of undernutrition in growing individuals. However, although the BMR has been found to be lowered in undernourished adult experimental animals[16] and also in undernourished human adults,[17] the results obtained in undernourished infants have not been consistent. In some instances the oxygen consumption per kg. body weight of malnourished infants has proved to be *higher* than that of healthy infants.[18] However, as oxygen consumption in these malnourished infants tended to be subnormal in relation to surface area, it has been suggested that in view of the abnormal preponderance in these children of organs which are most active metabolically, notably the brain, this finding is consistent with an actual depression of respiratory activity in the individual organs.[18]

A characteristic feature of marasmus is a marked reduction in the fat content of the body. As fat tissue has a low oxygen consumption, fat depletion will cause an increase in oxygen consumption relative to body weight.[18,19] According to Mönckeberg *et al.*[19] height is better correlated with oxygen consumption than weight. They found that the oxygen consumption of malnourished infants, expressed in litres per hour per 100 cm. height, was constantly and significantly lower than that of normal infants.

As is the case in undernourished adult experimental animals,[16] the BMR of undernourished infants invariably rises during recovery.[18] According to Montgomery,[18] gain in weight will not occur unless caloric intake per kg. body weight exceeds the BMR by 60 to 85 calories. The BMR of 8 marasmic infants in his series varied between 49 and 74 calories per kg. per day. If these values also apply to the patients in our series, intakes varying between 109 and 159 calories per kg. body weight per day should have been sufficient to ensure gain in weight. In most of our patients the intakes, usually varying between 170 and 180 c. per kg. body weight per day, were well above this range, but in many instances did not result in any weight gain whatsoever.

In our experience, if no gain in weight occurs on an intake of about 180 calories per kg. body weight per day, it is unlikely to be brought about by a still higher intake. If no progress is made the patient should again be carefully examined to exclude the presence of chronic infections and organic diseases, e.g. anomalies of the urinary tract, brain tumours,[11,20] cerebral cortical atrophy,[21] and inborn errors of metabolism (galactosaemia, congenital renal acidosis, fructose intolerance, etc.). If no such causes can be found one can only wait for the day when the patient will start to gain weight. Unfortunately many patients die before such a stage is reached, either from secondary infection (usually bronchopneumonia) or from some other complication such as hypoglycaemia or perhaps some undiagnosed metabolic disorder.

SUMMARY

A study of the clinical and pathological features of nutritional marasmus was carried out on 64 patients with a mean age of 8·7 months.

The typical clinical picture was that of an emaciated infant showing severe retardation of growth as reflected by a marked reduction in body weight, length and head circumference. With one exception the body weights of all patients fell below a line representing values two-thirds as great as the 50th percentile values for American children.

Twenty-two (34%) of the patients died. Response to treatment was slow, necessitating a long period of hospitalization. Recovery was also retarded by frequent episodes of infection, especially bronchopneumonia, gastroenteritis and otitis media.

Evidence of bronchopneumonia was found in the lungs of all 8 patients on whom autopsies were carried out. Histological examination of the liver showed marked fatty changes in one patient, slight changes in 2, and no change in the other 5. The weights of the livers and, with one exception, the brains of all

8 cases were well below the mean values for normal American children.

Most of the patients received whole milk containing 3% sunflower-seed oil. The mixture, 100 ml. of which provided about 94 calories, was tolerated extremely well. The usual caloric intake varied between 170 and 180 c. per kg. body weight per day, but in several patients exceeded 200 c. A distinctive feature of the disease was that some patients failed to gain weight despite high caloric intakes. A possible explanation for this phenomenon is discussed.

We wish to express our thanks to the Medical Superintendent of the Pretoria General Hospital for permission to publish this report; to Prof. J. G. A. Davel for the provision of clinical facilities and for advice; to Dr. I. W. Simson, Acting Head of the Department of Pathology, University of Pretoria, for permission to use the autopsy reports, and to Dr. M. L. Neser and Dr. G. H. Findlay for their advice in connection with the preparation of the manuscript.

REFERENCES

1. Pretorius, P. J. and Novis, H. (1965): S. Afr. Med. J., **39**, 237.
2. Pretorius, P. J. (1956): ' 'n Ondersoek oor die Invloed van Voedings met verskillende Samestellings op die Genesing van Kwashiorkor', M.D. thesis, University of Pretoria.
3. Trowell, H. C. *in* Trowell, H. C. and Jelliffe, D. B., eds. (1958): *Diseases of Children in the Subtropics and Tropics*. London: Edward Arnold.
4. Nelson, W. E. (1964): *Textbook of Pediatrics*, 8th ed. Philadelphia: Saunders.
5. Kahn, E. and Freedman, M. L. (1959): S. Afr. Med. J., **33**, 934.
6. Ford, F. J., Lurie, G. M., Wittman, W. and Harris, F. (1961): *Ibid.*, **35**, 1081.
7. Stoch, M. B. and Smythe, P. M. (1963): Arch. Dis. Childh., **38**, 546.
8. Pharaon, H. (1962): Turkish J. Pediat., **4**, 169.
9. McCance, R. A. and Mount, L. E. (1960): Brit. J. Nutr., **14**, 509.
10. Kerpel-Fronius, E. (1957): Mod. Probl. Pädiat., **2**, 146.
11. Cronjé, R. E., Pretorius, P. J. and Davel, J. G. A. (1963): S. Afr. Med. J., **37**, 867.
12. Coppoletta, J. M. and Wolbach, S. B. (1933): Amer. J. Path., **9**, 55.
13. Jelliffe, D. B. and Dean, R. F. A. (1959): J. Trop. Pediat., **5**, 96.
14. Mönckeberg, F., Donoso, G., Oxman, S., Pak, N. and Meneghello, J. (1963): Pediatrics, **31**, 58.
15. Mulinos, M. G. and Pomerantz, L. (1940): J. Nutr., **9**, 493.
16. Mount, L. E., Lister, D. and McCance, R. A. (1963): Brit. J. Nutr., **17**, 407.
17. Keys, A., Brozek, J., Henschel, A., Mickelsen, O. and Taylor, H. L. (1950): *The Biology of Human Starvation*, Vol. 1. Minneapolis: University of Minnesota Press.
18. Montgomery, R. D. (1962): J. Clin. Invest., **41**, 1653.
19. Mönckeberg, F., Beas, F., Horwitz, I., Dabacens, A. and Gonzáles, M. (1964): Pediatrics, **33**, 554.
20. Aas, K. (1963): Acta pediat. (Uppsala), **52**, 161.
21. Smythe, P. M. and Bouchier, I. A. D. (1960): Arch. Dis. Childh., **35**, 328.