MALNUTRITION IN CHILDREN
A CLINICAL AND BIOCHEMICAL STUDY *

K. C. Chaudhuri, M. D. ** and A. Chaudhuri, M. D.

Malnutrition in children has been described in the literature under a series of confusing names, such as: protein malnutrition, marasmus, kwashiorkor, mahlnahrschaden, hunger edema, etc. True malnutrition must be distinguished from under-nutrition as seen in starvation and famine. It would be more rational to consider malnutrition as a syndrome or symptom complex caused by a variety of factors rather than as a disease due to lack of a single food factor or a mere caloric deficiency. Diseases due to lack of a single food factor are very rarely seen as a natural event in human subjects, for most foods consist of a variable combination of nutrients.

The problem of malnutrition due to long term effects of a multiple dietary deficiency, sometimes complicated by the relative excess of one or another nutrient (producing an imbalance) is considered in this paper. In many instances, this syndrome is conditioned by other causes unrelated to the deficiency in the diet such as infections, parasitic infestations, disturbances of metabolism, diarrhea, etc. These contributory factors may be either the cause or the effect of malnutrition and can thus lead to a vicious circle.

Clinical Material

During the year 1960, 15,681 children were treated in the outpatient department of the Institute of Child Health, Calcutta; 637 in the Institute proper and 600 children were observed in the community health service. About 25 per cent of the children suffered from malnutrition and diarrhea. A series of 50 unselected cases admitted by one of us (K.C.) during the period April 1959 to June 1960 is discussed in this paper. It is thought appropriate for the purpose of clinical study to divide them into two groups: 1. those with edema, and 2. those without edema. Table 1 shows the number, age and body weight of the two groups of children.

---

* Paper presented at the Second Middle Eastern-Mediterranean Pediatric Congress, Ankara, 1961.

** Director, Institute of Child Health, Calcutta, India.

TABLE 1

BODY WEIGHT OF MALNOURISHED CHILDREN IN DIFFERENT AGE GROUPS

	EDEMATOUS		NON - EDEMATOUS	
Age groups	Number	Weight	Number	Weight
0 - 12 months	5	5.1 Kg.	22	3.5 Kg.
13 - 24 months	10	6.3 Kg.	7	5.3 Kg.
25 - 42 months	6	8.3 Kg.	—	—
TOTAL	21		29	

In the edematous group there were 21 children between the ages of 6 months and 3 1/2 years. Only 5 children were below one year of age. Minimum weight was 3.1 Kg. for an infant of 6 months and the maximum 8.8 Kg. for a child of 2 1/2 years.

In the non - edematous group there were 29 children between the ages of 3 months and 2 years. Only 7 children were above the age of one year and none was over 2 years. The minimum weight was 2.3 Kg. for an infant of 8 months and the maximum was 6.2 Kg. for a two year old child. It is obvious that the weight loss in both groups was profound. The height is not shown in the table but it is remarkable to note that height was not affected and was within normal limits.

Figures 1 and 2 depict a typical example in each group. As is obvious the marasmic infant was skin and bones. His weight was 2.8 Kg. at 6 months, his skin was wrinkled at the folds and he had a total loss of subcutaneous tissue, musculature and turgor. In the edematous child, although the weight loss was masked by edema, his weight was below that of the normal range at this age. His weight on admission was 5.9 Kg. which dropped to 5.3 Kg. after the institution of appropriate therapy. The edema fluid was rapidly lost and the true picture of emaciation manifested itself in all its ugliness.

It is not possible to go into detailed description of each case within the limits of an article. Since the clinical picture is more or less known to all pediatricians working in this field in any case mention of the common features will suffice. The disease generally makes its appearance about weaning time when the formula is changed from one kind to another, ultimately ending with barley water or some other kind of cereal water. As a natural sequel to inadequate or improper feeding there follow the loss of weight, retardation of growth, apathy and peevishness, loss of appetite, cold and clammy

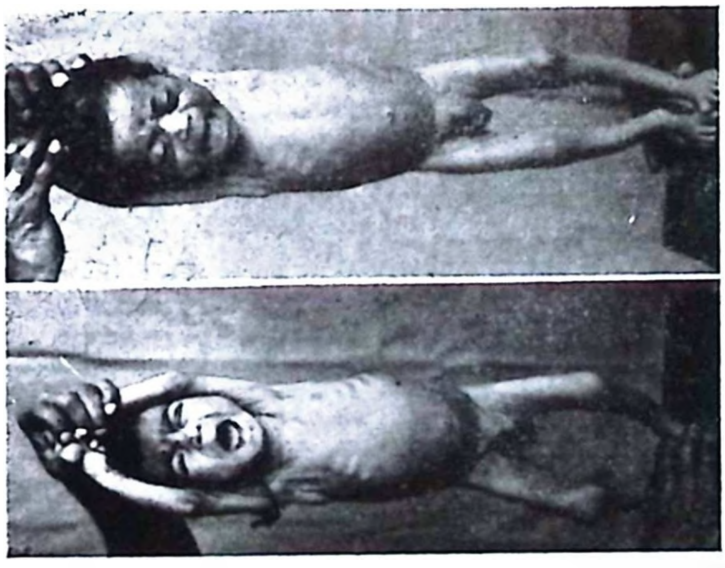

Fig. 1. Case no. 1.

K. B., age 6 months. Weight 2.8 Kg. on admission. Weight on discharge, 6 weeks later, 3.1 Kg.

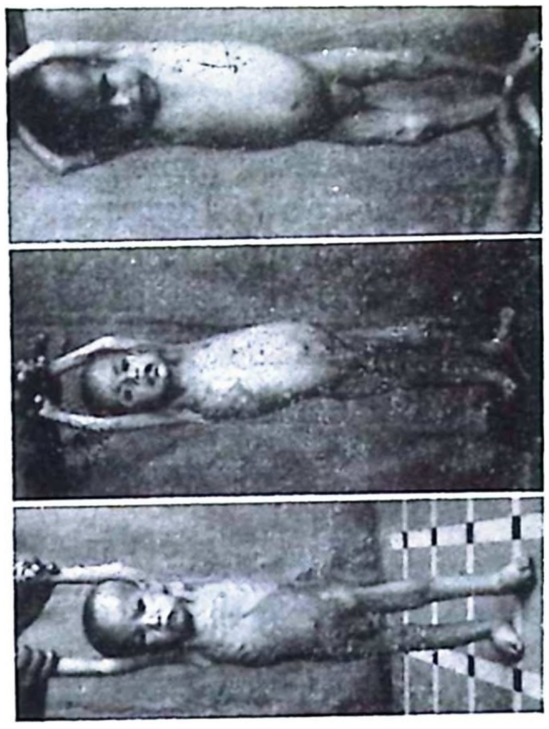

Fig. 2. Case no. 2.

D. D., age 1 year, 8 months. Weight 5.9 Kg. on admission, 5.3 Kg. during treatment, and 5.7 Kg. on discharge.

extremities, sleeplessness and irritability, petechial hemorrhages, skin changes and edema. It is noteworthy that in our series of cases clinical signs of frank deficiency diseases such as angular stomatitis, pellagrous skin changes, and hemorrhage were present in only 5 cases; signs of rickets or scurvy were absent.

The predisposing factors of this disease are the social status, economic group, etc. The majority of our cases belong to low income groups in which living conditions are bad, there are too many children to look after, parents can hardly afford a medical consultation and the children are brought to the hospital *in extremis*. All these contributory factors indicate that malnutrition is a social disease.

Associated with the appearance of clinical signs and symptoms is the occurrence of biochemical and pathological lesions, commonly hypoproteinemia, electrolyte and blood sugar disturbances, enlargement of the liver, general fatty degeneration, anemia, retardation of growth and skeletal development.

Intercurrent infections are not infrequent. In our series stool and urine examination results were usually negative; in a few cases we detected cysts of Ascaris lumbricoides and Giardia lamblia in the stool and a few pus cells in the urine. The red blood cell count was low - 1.1 to 4.1 millions per c.mm. and hemoglobin was 4.0 to 12.1 Gm. per 100 ml. In one case tubercle bacilli were observed in gastric lavage and suspicious hilar shadows were noticed in a few cases. In about 25 per cent of cases the tuberculin test was positive.

Biochemical Investigations

The results of paper electrophoretic examination of serum proteins and protein fractions done in 19 cases are shown in table 2.

TABLE 2

ELECTROPHORETIC PATTERN OF TOTAL PROTEIN AND PROTEIN FRACTIONS IN NORMAL AND MALNOURISHED CHILDREN

GROUP	T. P.	Alb.	Gl.	$Alp._1$	$Alp._2$	Beta	Gam.
Edematous	5.5 Gm. Per. 100 ml.	60.5%	39.5%	4.9%	9.9%	7.7%	11.3%
Non - edematous	6.8 Gm. Per. 100 ml.	50.8%	49.2%	4.0%	12.0%	7.0%	12.5%
Normal [1]	6.7 Gm. Per 100 ml.	55.0%	45.0%	5.0%	9.0%	13.0%	11.0%

The total protein was reduced in the edematous group but not in the marasmic. Hypo albuminemia, on the other hand, was present in both groups and also the beta globulin factors were reduced.

Paper chromatographic study for urinary amino acid excretion was done in 10 cases. Total nitrogen excretion was estimated by the Micro - Kjeldahl method and amino - nitrogen and ammonia nitrogen excretion was done by the formol titration method (Sörensen). Results of these investigations are shown in tables 3 and 4.

TABLE 3

CHROMATOGRAPHIC PATTERN OF URINARY AMINO - ACID EXCRETION IN NORMAL AND MALNOURISHED CHILDREN

AMINO ACID	NORMAL	MALNOURISHED
Alanine	Present	Present
Aspartic acid	Nil	Present
Cystine	Nil	Present
Glycine	Present	Present
Glutamic acid	Nil	Present
Lysine	Nil	Present
Serine	Nil	Present
Threonine	Nil	Present
Tyrosine	Nil	Present
Valine	Nil	Present

TABLE 4

TOTAL NITROGEN, AMINO - NITROGEN AND AMMONIA NITROGEN EXCRETION IN URINE OF NORMAL AND MALNOURISHED CHILDREN

	NORMAL	MALNOURISHED
Total Nitrogen	414.0 %	528.7
Amino - Nitrogen	31.3 %	54.8
Ammonia Nitrogen	32.02%	48.5

In normal children only glycine and alanine were excreted, whereas in malnourished ones, alanine, aspartic acid, cystine, glycine, glutamic acid, lysine, serine, threonine and valine were excreted. The spots of glycine, threonine and lysine were very dense. Excretion of total nitrogen, amino nitrogen and ammonia nitrogen was appreciably greater in the malnourished children.

Pyruvic acid and alpha - ketoglutaric acid levels in blood and urine were estimated by paper electrophoresis, the results of which are shown in table 5.

TABLE 5

PYRUVIC ACID AND ALPHA - KETOGLUTARIC ACID LEVEL IN BLOOD AND URINE OF NORMAL AND MALNOURISHED CHILDREN

	PYRUVIC ACID		ALPHA - KETOGLUTARIC ACID	
	Normal	MALNOURISHED	Normal	MALNOURISHED
Blood	0.26 %	0.36 %	0.14 %	0.33 %
Urine	0.42 %	0.23 %	0.53 %	0.30 %

The level of both pyruvic acid and alpha - ketoglutaric acid was high in blood and low in urine in the malnourished children.

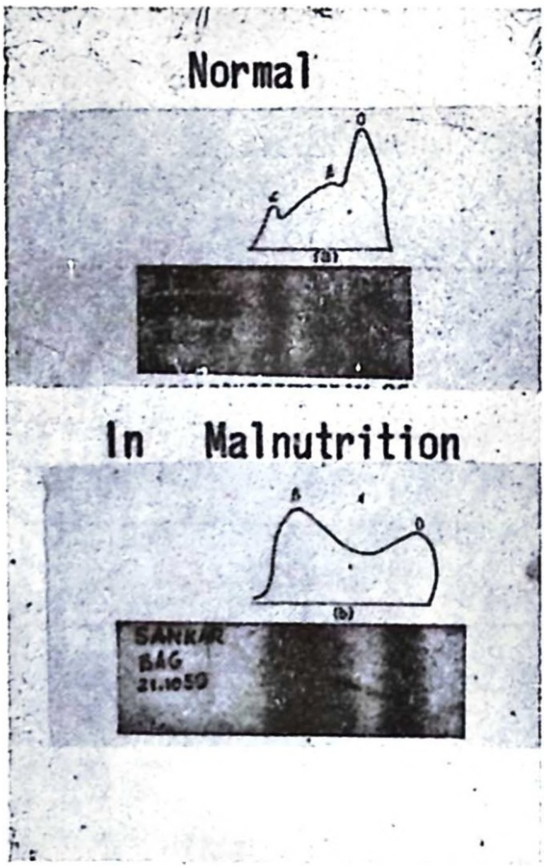

Fig. 3. Electrophoretogram of serum lipo-proteins.

A. In a normal child. B. In a malnourished child.

An electrophoretogram of lipo - proteins in blood is shown in fig. 3 and the results of investigation done in 6 cases are shown in table 6.

TABLE 6

ELECTROPHORETIC PATTERN OF LIPO-PROTEINS IN SERUM OF NORMAL AND MALNOURISHED CHILDREN

	NORMAL	MALNOURISHED
Total Protein	6.6 Gm. per 100 ml.	5.6 Gm. per 100 ml.
Alpha lipo protein	21.3 %	4.2 %
Beta lipo protein	27.5 %	51.3 %
Gamma lipo protein	51.1 %	44.3 %

Alpha lipo proteins were reduced considerably and as a matter of fact were totally absent in 2 out of 6 cases analyzed. The beta lipo protein level was raised and the gamma slightly reduced in the malnourished children.

Discussion

Complex manifestations of malnutrition, both clinical and biochemical, are not limited to or due to disease of any one or more organs, but are the results of a changed metabolism affecting the whole body. Our knowledge of cellular metabolism in malnutrition has many gaps and therefore the interpretation of the biochemical findings and their correlation to the clinical is not easy.

Gillman and Gillman state, «In the absence of any detectable excretion of proteins marked depression of albumin production is apparently the most characteristic effect of chronic malnutrition on plasma protein synthesis in human subjects.» Although it is widely believed that edema develops when the concentration of serum albumin falls below 3 per cent, in our series of cases this relationship could not be established. In a previous report we found that hypoproteinemia was not invariably associated with edema. Karpel-Fronius showed that plasma volume was reduced in malnutrition and that the reduction of plasma volume tended to keep the serum protein concentration at about the normal level. It is quite likely that the normal level of total protein in our marasmic group may be accounted for in this way. Plasma volume estimation was not done in these cases. Low serum protein values may also be attributed to disturbances of the gastrointestinal tract (which were present in the majority of our cases) through the lack of absorption of proteins by the bowel, or through a perverted metabolism which facilitates the excretion of nitrogen in the feces. The exact mechanism of the production of edema is still unexplained. In our series younger infants did not de-

velop edema but the older children did although the deprivation of proteins in the diet as judged by careful history of feeding was more or less of the same degree.

If both proteins and calories are diminished below the quantity required, the amount of tissue proteins lost is considerable. Increased excretion of amino acids, total nitrogen, amino - nitrogen and ammonia nitrogen may be a reflection of this altered protein metabolism. Increased elimination of amino acids may also cause disturbances in other organs, notably in the liver. In a previous report we showed that fatty degeneration of the liver was not infrequent and was sometimes followed by fibrosis. In the present series of our cases, the enlargement of the liver was a common finding. It is possible that altered amino acid metabolism may be responsible for these changes in the liver.

As in our cases, Colles also found a high level of keto acids in blood in kwashiorkor and demonstrated that the limiting amino acid may be methionine since the keto acid level tends to return to normal when methionine is added to the diet. The role of keto acids in malnutrition is not clearly understood. Keto acids appear to be the end product of deamination. A most important process in the metabolism of all amino acids is the removal of the amino group and its replacement by oxygen with the formation of keto acids. For example, glutamic acid on oxidative deamination yields alpha - ketoglutaric acid and alpha - ketoglutaric acid is one of the intermediaries between citric acid and oxalo - acetic acid in the Kreb's cycle. Further, in the breakdown of glucose a key stage is the formation of pyruvic acid. Pyruvic acid can enter Kreb's cycle by two pathways - by decarboxilation or forming oxalo - acetic acid. In a previous report we discussed this problem in some detail.

The alpha lipo - protein level was found to be low in our cases : Magioni also found that the alpha lipo - protein level in malnourished children was low. Angelopoulos and Beschranka reported normal values of lipo proteins and stated that up to the sixth month, both alpha and beta lipo - protein values are high and they assume adult values after this age. Salk and Wolf showed that alpha lipo - proteins were greatly reduced in cirrhosis of the liver and the level of beta lipo - proteins was raised. Alpha $_1$ lipo - protein is a known component of alpha $_1$ globulin, alpha$_2$ lipo protein of alpha$_2$ globulin and beta lipo - proteins of the beta globulin. It is known that syntheses of these components take place in the liver and any pathological lesion of the liver may cause an altered level of lipo - proteins and plasma

proteins in general. Further, any change in the globulin fraction may bring about a change in the lipo-protein level. However, the exact mechanism is not fully understood. Our biochemical studies once again indicate that malnutrition causes profound disturbance in cell metabolism. Only during the last 15 years have biochemists studied cell metabolism. Those of us who qualified in an earlier period find it both fascinating and intricate.

REFERENCES

1. Angelopoulos, B., and Bechrakis, G.: Electrophoretic analysis of serum proteins, lipo-proteins and glucoproteins in healthy newborn infants, older infants and children in Greece, J. Pediat. **57**: 66, 1960.
2. Chaudhuri, K. C.: Malignant malnutrition bei kindern in Indien, Oesterr. Ztschr. f. Kinderh. **8**: 153, 1952.
3. Chaudhuri, K. C., et al.: A study of alpha-keto acids in protein malnutrition, Indian J. Pediat. **16**: 399, 1959.
4. Ibid: Pattern of amino-acid excretion in urine of children with nutritional dystrophy, Indian J. Pediat. **27**: 389, 1960.
5. Ibid: Nutritional disorders in childhood, Indian J. Pediat. **28**: 409, 1961.
6. Chaudhuri, A.: Morbidity pattern of children, Personal communication.
7. Chaudhuri, A., et al.: Infantile cirrhosis of the liver (Sen's syndrome) with particular reference to the sulfur-containing amino-acids, J. Pediat. **57**: 230, 1960.
8. Collis, W. K. F.: Nutrition, quoted by Holt, J. Pediat. **57**: 119, 1960.
9. Gillman, Z., and Gillman: Perspectives in Human Malnutrition, New York, Grune and Stratton, 1951, p. 349.
10. Hassan, F., and Gunther, M.: The serum proteins at 6 months of age in infants fed on human or cow's milk or on both, Arch. Dis. Childhood **33**: 30, 1958.
11. Karpel Fronius, E.: Metabolic disturbances in infantile malnutrition, Mod. Prob. Pediat. **2**: 146, 1957.
12. Magioni, G.: Beobachten uber die gesamte proteine in kreislauf, die lipoproteine und die urin ausscheidung per amino-sauren bei der eiweissnahrungmangel-dystrophie, Mod. Prob. Pediat. **2**: 161, 1957.
13. Misra, R. P.: Protein metabolism in marasmic children, J. Indian M. A. **34**: 481, 1960.
14. Mitchell and Nelson: Textbook of Pediatrics, New York, Saunders, 1960, p. 1403.
15. Payne, H. C., and Forsyth, C. V.: Paper electrophoresis of serum proteins in children, Arch. Dis. Childhood **33**: 60, 1958.
16. Salk, H. B., and Wolf, O.: Proceedings in B.P.A., Arch. Dis. Childhood **34**: 187, 1959.
17. Trowel, H. C., Davies, J. N. P., and Dean, R. F. A.: Kwashiorkor, London, Ed. Arnold, 1954, p. 166.