GASTROENTERITIS AND MALNUTRITION

W. WITTMANN AND J. D. L. HANSEN, *Departments of Medicine and Child Health, University of Cape Town*

Diarrhoea is an important cause of illness throughout the world and remains a leading cause of death among infants and young children.[1] Since the turn of the century the industrially developed countries have experienced a rapid and consistent decline in mortality from diarrhoea.[2-5]

In the industrially underdeveloped countries, however, deaths from gastroenteritis remain high on the whole.[2,6-8] In these countries diarrhoea is still often the main cause of death. In a recent review Ordway[3] pointed out (1) the high morbidity and mortality among infants and young children, (2) the association with malnutrition, (3) the low socio-economic status of the affected population groups, and (4) the multiple and often obscure aetiology of the disease.

In South Africa mortality from gastroenteritis remains high among non-White children. During the first 5 years of life it overshadows all other causes of death.[9,10] Several workers have indicated the striking association of the disease with malnutrition.[10-12]

To further clarify some aspects of the disease, this study was done in the Outpatient Department of the Red Cross War Memorial Children's Hospital in Rondebosch, Cape, where the bulk of the work revolves around diarrhoeal disease.[13,14] In this communication the findings relating to nutritional status and infection in children with severe gastroenteritis will be discussed. Other aspects of the study will be dealt with in subsequent publications. In a later issue Moodie and colleagues will report on the findings of the socio-economic investigation on the study group.[49]

MATERIAL AND METHODS OF INVESTIGATION

The study was undertaken in 2 parts.

Trial I was conducted between March and June 1962 (autumn and early winter).

Trial II was conducted between November 1962 and February 1963 (summer).

The trials consisted of 50 and 51 non-White children respectively. The criteria for selection of cases and the methods of investigation were identical in the 2 trials.

Criteria for Selecting the Patients

1. *Diarrhoea* as the presenting complaint.
2. *The presence of clinically detectable dehydration.*

Patients were *excluded* if they (*a*) had received intravenous fluid therapy on any occasion during the previous month; (*b*) showed clinical signs of kwashiorkor, e.g. oedema or typical skin lesions; (*c*) had gross underlying illness, e.g. parenteral infection, tuberculosis or other defects, or (*d*) were moribund or too ill to warrant investigation.

The first 2 patients fulfilling the above criteria that were admitted to the resuscitation room in the outpatient department each week-day before noon, were taken into the series. Beds were reserved for these cases for the duration of each study period.

A detailed medical history was taken and a full clinical examination carried out personally by the investigator (W.W.) in every case.

Each child was weighed on 3 occasions:

1. On admission—before any treatment was given.
2. After completion of intravenous fluid therapy.
3. 24 hours after fluid therapy had been completed.

The following samples were obtained for analysis:

1. *Blood.* Blood was taken by venipuncture, usually from an external jugular vein, for the estimation of serum proteins, haemoglobin and PCV. Serum proteins were estimated by a biuret method.[15]

Three blood samples were taken from each patient:

1. Before the intravenous fluid administration was started.
2. Within an hour of completion of the intravenous fluid therapy.
3. 24 hours after fluid therapy had been completed.

In the second trial some of the blood from the first sample was sent for culture.

2. *Stool.* A fresh sample of stool was collected for microscopy and culture from every case before any treatment was given and repeated on the 3rd day.

Control subjects. Concurrently with each trial a group of control children were studied. There were 11 controls in the first trial and 32 in the second.

These were healthy non-White children without diarrhoea who visited the surgical outpatient department with minor surgical conditions. Alternatively, they were examined at the time of a routine visit to the municipal child welfare centres in the areas from which the patients were drawn.

The following procedure was adopted:

(*a*) Body weight and age were recorded.
(*b*) One blood sample was taken for serum proteins and haemoglobin and PCV.
(*c*) One fresh stool sample was obtained for microscopy and culture.

Weight Analysis

Normal standard. The Boston percentile charts[16] for weight were used as representing the normal expected range. For illustrations of weight distribution all weights were plotted against the Boston percentile chart for boys.

Correction for dehydration. All weights were corrected for dehydration in the patients who were dehydrated on admission. In the absence of oedema the best recorded weight after rehydration on day 2 or 3 was used. If oedema developed 11% was added to the dehydrated weight and this calculated weight was used in the assessment of weight for age.[12]

Degree of Low Weight

1. The degree of low weight for age was graded according to the standard suggested by Gomez.[17] The Boston 50th percentile was used as the theoretical mean ideal weight for age. The weight of the patient was expressed as a percentage of this mean.

The percentage was calculated separately for boys and girls and the grading was as shown in Table I.

TABLE I. DEGREE OF LOW WEIGHT

Normal	*Above 90% of expected weight*
1st degree malnutrition	90 - 76% ,, ,, ,,
2nd ,, ,,	75 - 60% ,, ,, ,,
3rd ,, ,,	below 60% ,, ,, ,,

2. When using only 2 grades, i.e. normal weight and low weight for age, the Boston 3rd percentile weight was used as the dividing line. This line coincides almost exactly with 80% of the expected weight (see results). For ease of calculation the weight was considered normal at 81% or more, and abnormal at 80% and less.

RESULTS

Combined Results

The results of the 2 trials were combined. Few differences were noted between the groups and these will be indicated in the text.

Racial distribution. In this study no attempt was made to study the relative incidence of the disease between the different ethnic groups, nor were the characteristics of the disease compared between these population groups. The control subjects were Cape Coloured with very few exceptions. The study groups (total 101) happened to include members of the 3 non-White racial groups as follows: Cape Coloured 68, Asiatic 13, Bantu 20.

Age distribution. The age distribution of all patients is demonstrated in Fig. 1.

The majority of patients were younger than 1 year. Of the patients under a year old, more than half were younger than 7 months and 20% were under 4 months old. A fair number of cases occurred up to the age of 18

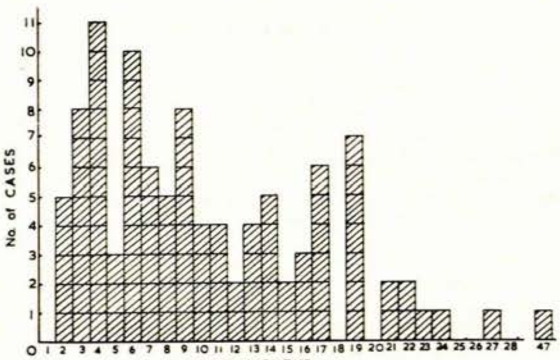

Fig. 1. Age distribution of 101 patients with gastroenteritis.

months, but thereafter the incidence dropped sharply. Only 2 patients were over 2 years old.

There were more children under 3 months old in the second trial than in the first. Otherwise the age distribution was similar for the 2 groups. The ages of the control subjects matched the cases fairly closely (Fig. 2).

Sex distribution. There were more male than female patients. The figures are shown in Table II.

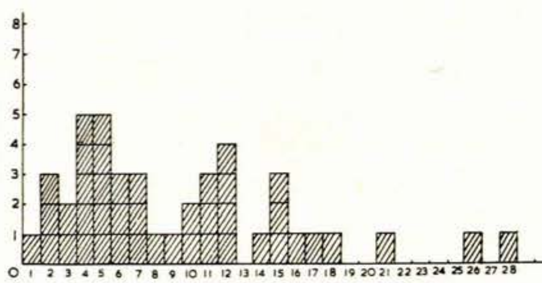

Fig. 2. Age distribution of 43 control cases.

The difference in the sexes was only apparent in the younger patients under 1 year old. Over the age of 1 year the sexes were equally represented.

TABLE II. SEX DISTRIBUTION OF 101 PATIENTS WITH GASTROENTERITIS

	Male	*Female*
All ages	62%	38%
Under 1 year old	66%	34%
Over 1 year old	51%	49%

Weight for age. The proximity of 90% of expected weight and 80% of expected weight to the 10th and 3rd Boston percentile lines respectively is illustrated in Fig. 3.

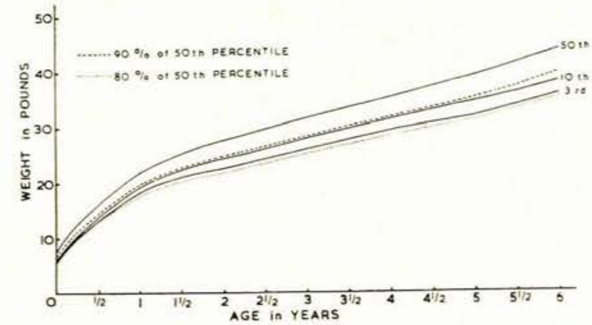

Fig. 3. Boston percentiles to indicate proximity of 80% and 90% of 50th percentile to 3rd and 10th percentile lines respectively.

In the analysis of results 'below the 3rd percentile' was used as 80% of expected weight and less. 'Above the 10th percentile' was used as 90% of expected weight or more.

The corrected weights of the 101 patients are shown in Fig. 4. Each patient is represented by a cross against the

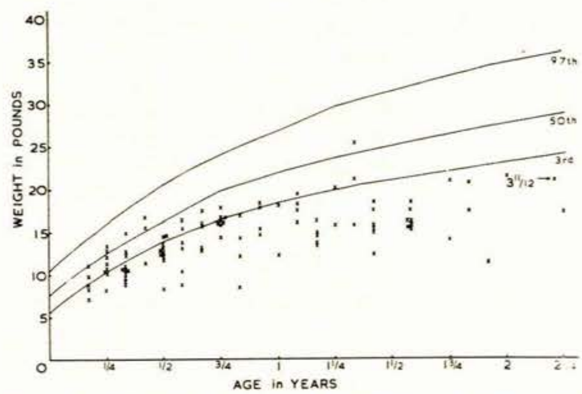

Fig. 4. Corrected weights of patients plotted against Boston standard.

Boston normal weight range for age. There were 64 patients below normal and 37 patients were within normal range. Only very few cases were above the mean expected weight. Note how the younger children tend to be normal in weight and the older children are below normal. The deviation from normal is greater with advancing age.

In Fig. 5 the weight distribution of the 43 control subjects is demonstrated. Here the majority of children are within the normal weight range. This distribution does not represent a random sample of the population because the children were selected from the more privileged sections of the society in general.

In Table III the degree of malnutrition by weight is indicated for patients with gastroenteritis and controls. Just less than half the patients were 2nd or 3rd degree malnourished and only 11% were above 90% of expected weight for age. The majority of controls were normal.

Low weight for age was more common and more gross in the older children. Fig. 6 demonstrates the significant progressive *incidence* of low weight with advancing age. The percentage of low weight children is indicated for each of the 4 age groups.

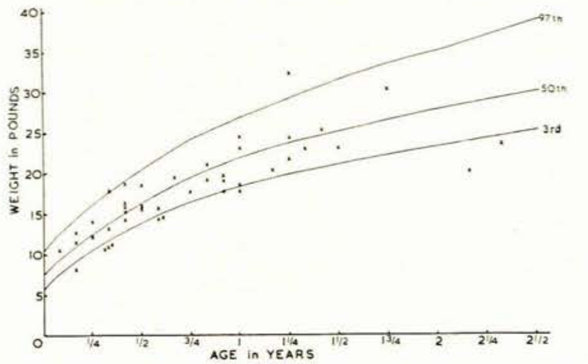

Fig. 5. Weights of controls plotted against Boston standard.

TABLE III. DEGREE OF MALNUTRITION BY WEIGHT IN PATIENTS AND CONTROLS

Degree of malnutrition		*Patients*		*Controls*	
Normal	90% expt. wt.	10·9%		67%	
1st degree	90—76%	41·6%		28%	
2nd degree	75—60%	37·6%	47·5%	5%	5%
3rd degree	below 60%	9·9%		0%	

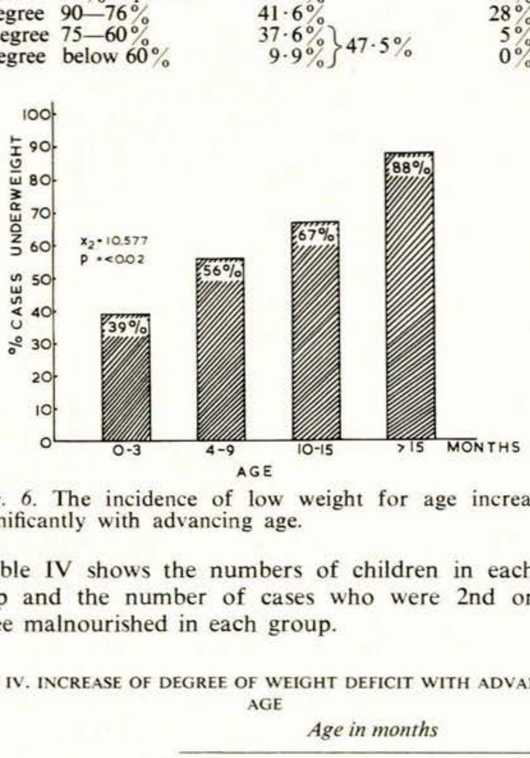

Fig. 6. The incidence of low weight for age increased significantly with advancing age.

Table IV shows the numbers of children in each age group and the number of cases who were 2nd or 3rd degree malnourished in each group.

TABLE IV. INCREASE OF DEGREE OF WEIGHT DEFICIT WITH ADVANCING AGE

	Age in months			
	0—3	*4—9*	*10—15*	*Over 15*
Total no. of patients	13	43	21	24
2nd and 3rd degree malnutrition ..	3	14	13	18
Mean % expected weight	85±4	80±4	71±4	69±4
		p=<0·30	p=<0·01	p=<0·005

After the age of 9 months the majority of patients were grossly underweight. The progressive weight loss with advancing age is statistically significant. Applying the Student 't' test, the difference between the means of the first group and each of the subsequent groups becomes increasingly more significant.

Conclusion. The majority of patients with severe gastroenteritis were below the normal weight for their age. Increasingly more of the older children were below the normal weight range and the weight loss was progressively more marked with advancing age.

SERUM PROTEINS

1. Serum Albumin in Relation to Dehydration

All 3 blood samples were obtained in 82 patients with gastroenteritis. The results of these are shown in Table V to demonstrate the fluctuation with the state of hydration of the patients. (Less than 3 samples were obtained from 19 patients and they are not included in this analysis.) While dehydrated (1) the mean serum albumin was significantly higher than immediately after intravenous therapy, (2) (t=9·624, p=<0·001).

TABLE V. SERUM ALBUMIN IN RELATION TO DEHYDRATION

	Albumin G/100 ml.	
Blood sample	*Mean*	*Range*
1	4·02±·80	2·31—5·60
2	3·02±·53	1·74—3·92
3	3·30±·60	1·88—4·64

Blood obtained on the 3rd day (3) showed a significant rise over the previous day (t=3·164, p=<0·01) but was still significantly lower than that of the first sample.

This 3rd day sample was considered to give the best reflection of the albumin concentration, and was therefore used to calculate the incidence of hypo-albuminaemia in relation to body weight.

There were 3 low albumin values on the first day. Blood was not obtained from these cases subsequently. These results are included in calculations where merely the *incidence* of hypo-albuminaemia is concerned.

2. The Incidence of Hypo-Albuminaemia in the Patients with Gastroenteritis

Blood was obtained from 84 patients on the 3rd day and the results are shown in Table VI together with control values. All values that were more than 2 standard deviations below the mean of the controls were considered abnormal (3·37 G/100 ml.).

One of the control subjects had a value lower than this.

TABLE VI. SERUM ALBUMIN IN GASTROENTERITIS AND CONTROL SUBJECTS

	Albumin G/100 ml.	
	Mean	*Range*
84 patients	3·25±·61	1·88—4·64
42 controls	3·89±·26	3·28—4·42
	t=6·504	p=<0·001

Of the 84 patients there were 42 with serum albumin concentrations below 3·37 G/100 ml. and a further 3 had low values of the first-day sample. Hypo-albuminaemia thus occurred in 45 of 87 patients (52%). The mean albumin of the patients was significantly lower than the controls.

3. Hypo-Albuminaemia in Relation to Age and Body Weight

Age. Comparing 3 age groups it became clear that hypo-albuminaemia, like low weight, occurred with increasing frequency in the older age groups. In Table VII

TABLE VII. OCCURRENCE OF HYPO-ALBUMINAEMIA

	Age in months		
	0—3	*4—9*	*Over 10*
Total no. patients ..	11	35	41
Low albumin ..	3	15	27
	$x^2 = 7 \cdot 019$	$p = < 0 \cdot 05$	
Mean albumin ..	$3 \cdot 57 \pm \cdot 52$	$3 \cdot 44 \pm \cdot 44$	$3 \cdot 00 \pm \cdot 67$

the incidence of hypo-albuminaemia (i.e. albumin below 3·37 G/100 ml.) is shown for each of the 3 age groups.

The incidence of hypo-albuminaemia increased significantly with advancing age. It can also be seen in the table that the highest mean serum albumin occurred in the youngest group of patients. After the age of 9 months the serum albumin of the cases was well below the lowest normal limit.

Low weight. The serum albumin after rehydration of 84 patients was compared with the percentage of expected weight of these patients. There were 54 low weight and 30 normal weight patients in the group. Hypo-albuminaemia occurred in 59% and 33% respectively. The mean serum albumin of the low-weight children was significantly lower than that of the normal-weight children as shown in Fig. 7 ($t = 2 \cdot 705$, $p = < 0 \cdot 01$).

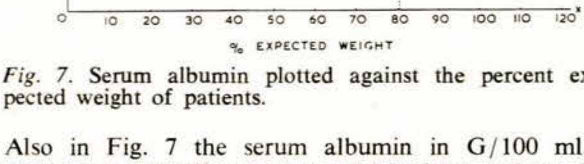

Fig. 7. Serum albumin plotted against the percent expected weight of patients.

Also in Fig. 7 the serum albumin in G/100 ml. is plotted against the % expected weight of the patients. The association of hypo-albuminaemia with low weight is very clearly demonstrated. Above 90% of expected weight the serum albumin was always within the normal range. The quadratic regression line shows very strikingly how the albumin drops with increasing weight loss. In the normal weight range the albumin and weight vary independently. The association of low weight and low serum albumin was highly significant ($F\ 81 = 41 \cdot 836$, $p = < 0 \cdot 01$).

The albumin and weight of the control subjects are shown in Fig. 8. The only abnormal albumin value was in a child who was above the mean expected weight for age.

Hypo-albuminaemia and a low weight for age were thus very common in these children with severe dehydrating gastroenteritis. There was a striking correlation between

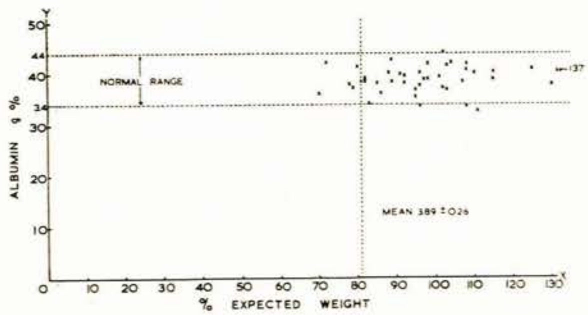

Fig. 8. Serum albumin plotted against the percent expected weight of controls.

low weight and low serum albumin. Both occurred more frequently in the older children than in the younger patients in the series.

Other signs of nutritional deficiency. These signs are listed in relation to weight for age in Table VIII.

TABLE VIII. SIGNS OF NUTRITIONAL DEFICIENCY

	Weight for age	
	Below 80% expt.	*Above 80% expt.*
Total no. of patients ..	64	37
Skin lesions	14	5
Marasmus	4	0
Pre-kwashiorkor	2	0
Anaemia	26	13
Rickets	6	3

Clinical Diagnosis of Protein-Calorie Malnutrition

Apart from low weight for age (64%), a clinical diagnosis of protein deficiency could have been made in only 25% of cases, i.e. by virtue of skin lesions or the appearance of marasmus or pre-kwashiorkor. When present skin lesions were minimal and consisted of angular stomatitis, dry scaling over the legs and arms, slight hyperpigmentation in exposed areas or 'crazy-paving' over the shins. Five normal weight patients showed skin lesions. Marasmus was present in 4 children who showed obvious wasting and absence of subcutaneous fat. Some of the underweight children looked deceptively well by virtue of the presence and normal distribution of subcutaneous fat. Pre-kwashiorkor was diagnosed in 2 patients with growth failure, angular stomatitis, sparse hair and 'moon facies'. Hair changes were not accurately recorded in all cases but were never gross.

Rickets. This diagnosis was made clinically in 2 patients and radiologically in a further 7 children. The lowest weight at which rickets occurred was 72% of the expected.

Anaemia. A haemoglobin level below 10 G/100 ml. after rehydration was considered an indication of anaemia at all ages in this study. At this conservative estimate 39% of patients had anaemia. (Anaemia was fully investigated in the second series in conjunction with Friedman *et al.*[18] A high incidence of iron deficiency and folic-acid deficiency was found. Vitamin-B_{12} deficiency did not occur.)

The difference in incidence of anaemia and rickets was not striking between the 2 weight groups. Clear-cut clinical signs of malnutrition other than low weight were not commonly present in the group of patients studied.

The History of Diarrhoea in Relation to the Nutritional Status

If diarrhoea had occurred previously more than twice it was considered to be recurrent.

A history of recurrence was significantly more frequent in the low-weight patients. The figures are given in Table IX. Almost half the low-weight patients had a recurrent history and this was true in less than one-fifth of the normal weight cases.

TABLE IX. SIGNIFICANT ASSOCIATION BETWEEN RECURRENT DIARRHOEA AND LOW WEIGHT FOR AGE

	Weight for age	
	Below 80%	*Above 80%*
Total no. of patients	64	37
Recurrent diarrhoea	30	7
	$x^2 = 7 \cdot 898$	$p = < 0 \cdot 005$

The patients with recurrent diarrhoea showed a higher incidence of hypo-albuminaemia (21/34) than those with no history of recurrence (24/53), but these differences were not significant by the Chi square test ($p = < 0{\cdot}20$).

The incidence of hypo-albuminaemia was also not significantly more frequent in the patients who had diarrhoea for longer than 7 days (13/23) than in those with a shorter history (32/64). The mean serum albumin did not differ significantly between the 2 groups ($3{\cdot}28 \pm 0{\cdot}61$ G/100 ml. and $3{\cdot}17 \pm 0{\cdot}63$ G/100 ml.). Of the 23 patients with diarrhoea for longer than 7 days, there were 20 who had a history of 14 - 21 days.

INFECTION

Interpretation of Results

The interpretation of microscopy and culture results is not always easy. The following notes explain the interpretation of the results in this study:

Bacteria. Enteral infection was accepted when shigella, salmonella, specific *E. coli,* abundant pus cells or abundant yeasts were found.

Pus cells. During microscopic examination of the stools, pus cells were recorded by 4 grades of plus signs— + + + +. 'Abundant pus cells' here recorded represent the last 2 grades. In all the patients with shigella, and in all but 2 of the salmonella cases, pus cells were present in these amounts. 'Abundant pus cells' was accepted as evidence of enteral infection. Microscopic blood was usually present together with abundant pus in the stool but macroscopic blood was not seen.

Entero-bacteria other than the above were not considered here to have a causal relationship to diarrhoea and they were not accurately identified.

Staphylococcus aureus was looked for in the second trial but was not identified in large numbers in any of the stools examined.

Massive numbers of yeast spores and hyphae in the stools were considered pathogenic even if *Candida albicans* was not identified on culture. Lesser numbers were not considered as a cause of diarrhoea.

Giardia. A causal relationship was accepted for *Giardia lamblia* and other parasites were 'doubtful' causes.

Cause unknown. The diarrhoea was labelled 'cause unknown' only if the stools were totally negative and the patient had no parenteral infection.

Multiple infection refers to the presence of more than 2 pathogens in each stool.

The findings in this section are recorded for the total number of patients of both trials.

General Observations

The following general observations are necessary before an analysis of the results is given:

Seasonal incidence. The isolation of shigella was twice as common in summer (Trial II) as in Trial I, which was done during the colder season of the year.

E. coli was only looked for in 45 patients and 32 control subjects of the second trial. The percentage incidence is given from these numbers.

Incidence of infection. Excluding the above differences, the 2 trials were comparable regarding the incidence of infection.

Virus studies were not done in any of the groups investigated.

TABLE X. FINDINGS ON STOOL CULTURE AND MICROSCOPY

Total no. of cases	*Patients* *101*	*Controls* *43*
Salmonella	7	5
Shigella	13	0
E. coli	31	19
Abundant yeasts	6	0
Abundant pus cells	55	5
Giardia lamblia	17	16
Ascaris	22	5
Trichuris trichiura	10	0
Trichomonas hominis	26	0
Double infection	28	5
Multiple infection	15	0
Totally negative	13	60

The findings of stool microscopy and culture are given in Table X for all the patients and control subjects.

Patients Differed from Controls

There were some differences between patients and controls that were very striking:

Shigella was isolated in 13% of patients and in none of the control subjects.

Pus cells were found in 55% of patients and only 5% (2 cases) of the controls. One control patient with pus had a salmonella and the other had pus cells only.

Parasites. There was also a striking difference in the incidence of parasites between patients and controls, excluding *Giardia lamblia.*

Multiple infection did not occur in the controls but it was present in 15% of patients.

Bacteriological examination was totally negative in 60% of control subjects and in only 13% of patients.

It is interesting to note that salmonella and *Giardia lamblia* occurred with almost equal frequency in patients and control subjects. Although *E. coli* occurred more frequently in the patients, the difference in incidence between patients and controls was not statistically significant by the Chi square test.

The most striking feature of the patients with gastroenteritis was the small percentage of stools that were totally negative.

The occurrence of a large number of pus cells was a striking find. It was almost invariably present when shigella or salmonella was isolated, but none of the other findings could be significantly associated with the presence of pus in the stools.

Trichomonas hominis, although frequently present, was found by itself in only 6 patients and could not be assessed separately.

Relating the incidence of positive stool findings to the nutritional status of the patients showed up some differences.

In Table XI these findings together with the incidence of parenteral infection are indicated in relation to the degree of malnutrition by weight.

TABLE XI. INFECTION IN RELATION TO NUTRITIONAL STATUS

	Degree of malnutrition by weight				
	3rd	*2nd*	*1st*	*Normal*	*Total*
Total no. patients	*10*	*38*	*42*	*11*	*101*
Enteral infection ..	9	24	29	7	69
Worms	3	13	7	1	24
Worms and/or giardia	4 (40%)	21 (55%)	10 (24%)	1 (9%)	36
Trichomonas ..	2	14	7	3	26
Multiple infection ..	4 (40%)	8 (21%)	3 (7%)	0	15
Oral thrush	2	3	6	0	11
Herpes stomatitis ..	1	0	0	0	1
Septicaemia	1	0	0	0	1
Tuberculosis ..	1	0	0	0	1
Pneumonia	1	3	1	0	5
URT infection ..	0	3	0	0	3
Skin sepsis	1	0	2	0	3

The small number of children of normal weight makes it difficult to draw comparisons with the malnourished, but this can be done between the more grossly abnormal and those less abnormal in weight.

Enteral infection as defined, occurred in 69% of patients. It was not more frequently found in malnourished than in the well-nourished patients. Multiple infections and intestinal parasites, however, did occur with much greater frequency in the more grossly underweight patients.

Parenteral infection was not common in this series (14%) but tended to be more frequently present in those who were malnourished. Septicaemia was present in only 1 patient. It so happened that all the patients with parenteral infection also had a positive finding in the stools. It did not therefore increase the overall incidence of infection. In Table XII the incidence of some findings is shown for the different age groups of patients.

E. coli and parasites. Differences were apparent in the incidence of *E. coli* and parasites. *E. coli* occurred in the younger patients and was isolated only once in children over 1 year.

TABLE XII. INTESTINAL PARASITES AND PATHOGENS IN RELATION TO AGE

	Age in months				
	0—3	*4—9*	*10—15*	*Over 15*	*Tota*
Total no. patients ..	*13*	*43*	*21*	*24*	*101*
Enteral infections ..	8 (61%)	30 (88%)	12 (51%)	19 (79%)	69
E. coli	1	9	3	1	14
Ascaris	0	3	5	14	22
Trichuris trichiura ..	0	1	2	7	10
Giardia	1	4	4	8	17
Worms and/or giardia	1	7 (16%)	8 (38%)	20 (83%)	36

Worms and flagellates occurred with increasing frequency in the older children. After the age of 15 months only 17% of patients were free of worms and giardia. Giardia occurred once under 4 months.

Age and nutrition. The influence of age and nutritional status cannot be clearly separated in relation to infection. In general the older patients were more malnourished and had a high incidence of enteral plus parasitic infection.

Of the 36 patients with worms and giardia, 28 were of low weight and 23 of these were older than 9 months. Of the 8 children of normal weight in this group, 5 were older than 9 months.

Conclusions. Enteral infection thus seemed to be fairly evenly distributed between the ages and weight groups. Parasites were much more common in the older patients and possibly more common in the malnourished, regardless of age.

Of the 14 *E. coli* isolations, 9 were in the young children of low weight. The significance of this finding is doubtful, due to the small number of cases.

DISCUSSION

Assessment of the Nutritional Status of the Patients

Kwashiorkor and nutritional marasmus represent the extreme grades of protein-calorie malnutrition. They have become well-known and easily recognized clinical entities.[19,20] The term protein-calorie malnutrition as suggested by Jelliffe and Dean[21] includes all grades of deficiency of these nutrients. Kwashiorkor and marasmus represent only a fraction of the total group which has been likened to an undersea mountain with only the tip protruding above the surface of the water.[22] The mild—moderate and easily reversible forms of the disease are as yet not generally appreciated or recognized by most medical men. Adequate treatment is consequently frequently delayed until the children present with a severe degree of the illness with a high morbidity and mortality. Clinical and biochemical signs usually appear late.[23,24]

Growth retardation is a constant early sign of the deficiency[23,25] and weight for age is a readily available measure of nutrition.[26] A grading of malnutrition by weight as proposed by Gomez[17] has been internationally accepted.[26] Ideally a growth record over a period of time should be compared to locally applicable standards,[23] but such standards are not always available and, where malnutrition is prevalent, local growth charts are not likely to reflect the optimum growth potential of the population affected. That normal standards of other population groups could be applied more generally has been suggested by a number of studies. Under improved nutritional and environmental conditions the growth of the classically small Japanese can become comparable with American standards.[27] A socio-economic gradient of weights and heights has been demonstrated within ethnic groups where weights and heights of the more favoured sections are comparable with European standards while the other are much lower.[28,29] In poor or underdeveloped communities, growth during early months of infancy is often comparable with Western European standards but starts deviating below them when diet becomes less adequate after weaning.[19,30]

From the data presented in this study it is suggested that the American growth charts are applicable to the population studied and that the vast majority of children whose growth diverges from them are suffering from nutritional growth failure. *The major part of the problem of malnutrition is not reflected by the incidence of kwashiorkor but by the incidence of severe gastroenteritis in malnourished children.* Unless this association is appreciated, treatment and prevention programmes will remain inadequate.

Emphasis in this investigation was mainly on the protein nutritional status of the children studied. The associated deficiencies that were found, such as anaemia and rickets, serve to stress the general tendency for deficiency states to be multiple.[31,32]

Weight and Serum Albumin

Hypo-albuminaemia is an accepted measure of protein malnutrition.[27,33,34] It is, however, not a sensitive index and a low serum albumin probably reflects an advanced degree of depletion of the total albumin mass.[35,36] The fact that laboratory facilities are necessary for its estimation, further limits its general use in common with other biochemical indices of malnutrition.

Weight for age is generally available and, in addition, low weight occurs early and constantly in the presence of malnutrition.[23,26] The importance of low weight as an index of malnutrition was confirmed by this study.

Whenever the bodyweight of the patients was normal by American standards, the serum albumin was normal almost without exception. The incidence and degree of hypo-albuminaemia increased progressively with increasing weight loss. A similar association was subsequently demonstrated in a group of symptom-free children.[37] In gastroenteritis the serum albumin may be influenced by anorexia, with additional starvation and malabsorption. This may explain the fact that normal-weight patients with gastroenteritis had a lower mean serum albumin than the controls although they were still within the normal range. The duration of the illness, however, did not significantly influence the albumin but the correlation between hypo-albuminaemia and low weight was striking.

Additional evidence of nutritional growth failure was found in the close association between low weight and low protein intake.[49] Low weight and inadequate milk intake occurred with progressive frequency with advancing age. Previous workers have found the weight of the same population comparable with European standards during the early months of infancy and demonstrated a divergence after feeding became less adequate.[19,30] Jelliffe[8] indicated that malnutrition heads the list as a cause for this divergence.

Malnutrition and Infection in Gastroenteritis

A strikingly high incidence of severe malnutrition has been clearly demonstrated by the findings in this study.

Some differences in the morbidity of diarrhoea became apparent by comparing the normal-weight children with those who were below normal weight. Severe recurrent diarrhoea was strikingly more common in the low-weight children. Poor socio-economic circumstances[49] were closely associated with malnutrition and the condition of the child could, with a high degree of accuracy, be related to this factor. Milk intake, and therefore protein intake, was totally inadequate in the majority of low-weight children. A prolonged episode of diarrhoea alone did not make a significant difference in the serum albumin. These factors are strongly suggestive evidence that diarrhoea is severe and recurrent in a malnourished child and that the child is not primarily malnourished because he has recurrent diarrhoea. Each episode of diarrhoea would further increase the malnutrition, especially as these episodes so frequently are followed by prolonged periods of starvation.

In the younger age groups the disease was present in both malnourished and well-nourished children, but after the age of 15 months it occurred almost exclusively in the severely malnourished children.

Infection occurred with almost equal frequency at all ages and it was not more frequent in the malnourished patients. Although specific entero-pathogens were not isolated with any great frequency, suggestive evidence of infection was present in the majority of cases. There may have been a failure to isolate shigella in some of the patients who had pus, mucus, red cells and macrophages in the stools. A reduction in the positive culture rate may have been influenced by treatment before admission. An adequate assessment of this factor could not be made because the patients rarely knew what type of medicine had been prescribed. A higher incidence of infection may have become evident if (*a*) virus studies had been done, and if (*b*) *E. coli* had been looked for in both trials instead of only one.

However, in a recent study in Johannesburg, Kahn *et al.*[38] were unable to demonstrate a significant relation between diarrhoea and enteroviruses. When present, the disease is believed to be mild and of short duration.[39]

The incidence of *E. coli* in patients and controls in this study was not significantly different. A similar observation was made in an earlier study of diarrhoea in Pretoria.[40] Diarrhoea from *E. coli* had mostly been found in institutions among newborn babies and infants of under 1 year.[39,41] The disease is mild, and often infected babies have no symptoms. Little is known of the importance of E. coli in the diarrhoea of malnourished children.[42] From the small number of cases in this study conclusions cannot be more than tentative.

In general the findings fit in with previous reports. The infection occurred during the first year of life and the prognosis was good. In a diet trial done subsequently[37] the organism was not isolated in any of the patients investigated, indicating that the infection does not only vary from place to place but also from time to time.

A striking difference in the incidence of worms and giardia and multiple infections was found between the older malnourished patients and the younger less malnourished children. Here it was not possible to determine the relative importance of age and malnutrition. Age almost certainly is a factor, but in the light of previous work it is more likely that malnutrition was the deciding factor. Malnourished animals have been shown to have an increased susceptibility to helminthic infection[43] and multiple intestinal parasites in man are more commonly found in malnourished poorer classes.[44] Although the morbidity due to worms cannot be adequately assessed,[45] the additional nutritional hazard of infestation in malnourished children has been pointed out by Jelliffe.[8] An amazing number of adverse factors capable of aggravating malnutrition are concentrated upon these older patients with gastroenteritis.

Infection was so frequently present that it must be considered the most common precipitating cause of diarrhoea. It was, however, equally common in well-nourished and malnourished patients. The malnourished child had recurrent and often severe episodes of diarrhoea. This aspect needs to be emphasized. The important practical consideration is not whether infection or malnutrition is the more important factor in the causation of diarrhoea. The suggestion is that this type of diarrhoea occurs in malnourished children far more frequently than in well-nourished children.[2,42] This study supports such a view. Elimination of infection would obviously improve matters and perhaps reduce mortality. It would not restore normal growth in such children[22] and would not prevent similar subsequent episodes.

From this work it is not possible to define the relative importance of infection and malnutrition. Almost invariably the first attack of diarrhoea followed soon after the introduction of bottle feeds.[49] Adequate food intake dropped progressively and one attack of diarrhoea followed another. Infection and malnutrition, as it were, both have their origin in the feeding bottle and cannot be separated after this. A home environment which favours frequent infection also favours the development of malnutrition in its own right.

Multiple factors were involved in the production of this type of severe recurrent diarrhoea. The outstanding feature was the nutritional status of the host and this appeared to determine the course of the disease more than any other single factor.

Much confusion exists on the importance of infection as a cause of malnutrition quite apart from the controversy about its role in the causation of diarrhoea. Several aspects of this association are illustrated in a recent article by Ryan *et al.*[46] They indicated that 'it is generally accepted that marasmus is related to infection *or* underfeeding'. From their investigation they concluded that malnutrition in the majority of cases was precipitated by infection. Gastroenteritis is listed as one such infection without any evidence to show that the diarrhoea was infective in origin. 'Malnutrition', which covers a wide range of deficiency diseases,[21] was in this context confined to marasmus and kwashiorkor. In a very good discussion the authors then point out that malnourished children, as a result of infection, often develop a state of more profound malnutrition. This is the important concept. Malnutrition which already exists as the result of dietary deficiency is aggravated by infection. The infection may have a major influence on the prognosis of such severely malnourished children.[47,48]

It appears that severe gastroenteritis is often the result of an abnormal response of a malnourished host to infection or other stresses. In the treatment and prevention of diarrhoea emphasis must be on the basic malnutrition rather than on merely treating the infection when the patient presents with diarrhoea.

SUMMARY AND CONCLUSION

The nutritional status and incidence of infection in a group of non-White children with dehydrating gastroenteritis has been studied. The high incidence and often severe degree of malnutrition has been clearly demonstrated. It is suggested that a low weight for age is a valuable and important early sign of malnutrition which can be easily applied. Acute episodes of diarrhoea are apparently most frequently precipitated by enteral infection and recurrent episodes seem to be closely linked with the nutritional status of the child. In treatment and prevention of gastroenteritis, malnutrition deserves prominent attention.

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