Effect of Kwashiorkor on Absorption and Excretion of N, Fat, and Minerals

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McCance, R. A., Rutishauser, I. H. E., and Boozer, C. N. (1970). *Archives of Disease in Childhood*, **45**, 410. **Effect of kwashiorkor on the absorption and excretion of N, fat, and minerals.** Balance experiments were carried out on 6 children being treated for kwashiorkor. The intakes and excretions of N, fat, Na, K, Ca, Mg, P, Cu, Zn, Mn, and Cr were measured. The absorptions were all thought to be in the normal range and the retentions were high. The stools were bulky and contained much undetermined matter, probably unavailable carbohydrate derived from the matooke which formed part of their diet. In the light of previous and present findings the ratios of K/N and Mg/N retained, though higher than those found in muscle or in the whole body, cannot be taken to mean that the children were K or Mg deficient.

Different groups of investigators have measured the intake and excretion of organic and inorganic nutrients during the treatment of malnutrition in children up to the toddler stage. These measurements have been made for various reasons. Sncal (1958) for instance used this technique to investigate the effectiveness of amino acids as a source of protein for dietary supplementation. Others used balance experiments to find out if the digestion and absorption of protein from the gut was interfered with by malnutrition and, if so, to what extent (Pretorius and Smit, 1958; Holemans and Lambrechts, 1955). Cravioto (1958) and others, e.g. Clegg and Dean (1960), compared the absorption and retention of nitrogen by malnourished children from diets consisting predominantly of milk and those made of corn and beans, or peanuts. Hansen (1956), Holemans and Lambrechts (1959), and Waterlow and Wills (1960) compared the absorption and retention of nitrogen with other, mostly inorganic, nutrients, e.g. potassium and phosphorus. This technique was later applied to magnesium (Montgomery, 1961). Linder, Hansen, and Karabus (1963) and Pretorius and Wehmeyer (1964) have probably made the most comprehensive

of these investigations for they studied sodium, potassium, magnesium, calcium, and phosphorus as well as nitrogen. On the basis of work of this kind Hansen (1956) considered that there were often serious potassium deficiencies on admission, probably due to preliminary diarrhoea. These conclusions were based upon the initial retention of potassium when no nitrogen was being given and the subsequent proportions of nitrogen, potassium, and magnesium retained (Garrow, Smith, and Ward, 1968). Conclusions based upon the measurement of intakes, absorptions, and excretions, however, can be misleading unless they have been confirmed in some other way (Wallace, Weil, and Taylor, 1958; Montgomery, 1960). Halliday (1967) and others in Jamaica have done their best to do this, but the reality and the extent of the potassium and magnesium deficiencies are still not clear (Vis *et al.*, 1965; McCance, 1970). The present balance experiments were planned to be a little more comprehensive than some of the previous ones and to add some information about the 'trace' elements, copper, zinc, manganese, and chromium.

Subjects and Methods

Table I shows the ages of the 6 male children studied, their severity rating and oedema on admission; their weight at that time, and before and after studies were made; information about their serum proteins; haemo-

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TABLE I
Clinical Details of Subjects

Name	Mukwaya	Sulaimani	Sakosa	Musisi	Batte	Sonko
Age (mth.)	21	19	32	23	22	22
Severity	Moderate	Moderate	Moderate	Moderate	Moderate	Mild
Extent of oedema	++	++	++	+++	++	+
Time of experiment (days after admission) ..	11	19	18	27	13	14
Weight (kg.) on admission	6.98	7.54	10.60	8.92	9.00	8.50
Before experiment	7.62	8.06	10.63	9.24	8.14	8.06
After	7.58	8.22	11.10	9.50	8.50	8.42
Serum protein (g./100 ml.)						
On admission	4.5	3.9	4.3	4.2	3.6	4.0
During experiment	5.9	6.9	6.6	8.6	6.6	6.2
Serum albumin (g./100 ml.)						
On admission	—	1.3	1.5	1.3	1.7	2.0
During experiment	4.15	4.3	—	3.36	3.8	3.74
Hb						
On admission	7.5	7.7	7.0	4.8	9.0	8.4
During experiment	8.0	9.8	11.0	10.1	9.1	10.8
Hookworm infestation	No	Yes	No	Yes	No	No
History of loose stools	Yes	Yes	No	No	Yes	Yes

globin on admission and later; hookworm infestations and stools.

All the children received the routine milk mixture used at the unit for children with kwashiorkor, which consists of Casilan, dried skim milk, sucrose, cottonseed oil, potassium chloride, and magnesium hydroxide, and provides approximately 4 g. protein and 100 calories/kg. body weight per day (Wharton and McCance, 1968). In addition they were also given 250–600 g. cooked plantain daily, according to appetite. A vitamin supplement of 0.6 ml. Abidec (Parke Davis Ltd.) and 5 mg. folic acid were given on alternate days and a single dose of 1000 µg. B12 on admission. The children also received 12 ml. of a solution of FeSO₄ daily; this contained 9.96 mg. iron and negligible amounts of the trace elements.

Twice the quantity of the milk mixture required was prepared every 24 hours and one-half was placed in a refrigerator for analysis. A specimen of cooked plantain (matooke) was reserved in a similar way. At the end of each balance period, which always consisted of 3 days, the duplicate samples for each day were mixed and homogenized and one-tenth taken for analysis. The matooke aliquot was weighed and dried at 95–100 °C. Each meal during the experimental period was closely supervised by a member of the nursing staff and the children wore large polythene 'bibs' with bags at the bottom to minimize losses through spillage. After each meal the cups, plates, and bibs were rinsed with distilled water, and the washings, together with any plate waste, were placed in a polythene vessel in the refrigerator. At the end of each 24-hour period any unconsumed milk or plantain was also added to this container. At the end of the experiment the leavings for each day were mixed and homogenized and one-third to one-quarter taken for analysis.

The children were nursed throughout in a metabolic chair. Urine was collected by means of a plastic urine collector, strapped to the child, which drained into a polythene bottle under toluene. Each 24-hour collection of urine was placed in a refrigerator. Carmine was used as a marker for the stools which were collected in stainless steel bowls. As soon as any faeces were seen, the bowl was removed, covered with polythene sheeting, stored at –16 °C., and replaced with a clean one. At the end of the period of investigation, the urine and faeces for the three days were pooled and the faeces homogenized. Glacial acetic acid 1 ml./100 ml. urine and 10 ml./100 g. faeces was added as a preservative. One-tenth of the urine was taken for analysis. One-fifth to one-tenth of the whole of the faeces was weighed and dried at 95–100 °C. to be used for analysis.

All equipment used in the balance studies was rinsed with distilled water and air-dried in an oven before use.

Aliquot samples of milk, matooke, plate waste, urine, and faeces for each child were analysed for nitrogen by micro-Kjeldahl procedure using the catalyst and digestion procedures of Chibnall, Rees, and Williams (1943). The matooke and urine were assumed to contain no fat. Fat was estimated in the faeces, milk, and residues by a modification of Liebermann and Székely's (1898) method. Ash extracts were prepared according to the procedure of McCance, Widdowson, and Shackleton (1936). These extracts were used to determine phosphorus by the method of Fiske and Subbarow (1925), and sodium, potassium, calcium, magnesium, copper, zinc, manganese, and chromium by atomic absorption spectrophotometry (SP 90 Unicam Instrument Co. Ltd.).

Each child's food was analysed separately, but the milk contained so little manganese that an aliquot portion of each of the ash extracts was pooled and evaporated down before analysis. The mean figure,

TABLE II

Mean Intake, Absorption, Excretion, and Retention of Nitrogen, Fat, and Minerals by Six Children
(Units/kg. body weight per 24 hours)

	Intake	Urine	Faeces	Total Excretion	Absorption		Retention	
					Amount	% Intake	Amount	% Intake
Nitrogen (g.)	0.71 ± 0.09	0.38 ± 0.04	0.10 ± 0.02	0.48 ± 0.03	0.61 ± 0.08	86 ± 2.2	0.23 ± 0.09	31 ± 8.8
Fat (g.)	3.77 ± 1.42	0.0	0.19 ± 0.10	0.19 ± 0.10	3.58 ± 1.39	95 ± 2.7	3.58 ± 1.29	95 ± 2.7
Sodium (mEq)	0.87 ± 0.08	0.23 ± 0.24	0.29 ± 0.17	0.51 ± 0.31	0.59 ± 0.17	67 ± 20.2	0.36 ± 0.30	42 ± 35.3
Potassium (mEq)	9.5 ± 1.9	5.5 ± 1.4	2.7 ± 1.3	8.2 ± 1.4	6.8 ± 1.7	73 ± 12.2	1.3 ± 0.6	13 ± 4.0
Calcium (mg.)	42.3 ± 8.3	2.1 ± 3.0	20.1 ± 6.2	22.2 ± 6.1	22.1 ± 5.9	53 ± 11.1	20.0 ± 6.1	47 ± 11.3
Phosphorus (mg.)	76.0 ± 7.3	14.2 ± 9.2	33.3 ± 6.3	47.5 ± 5.7	42.7 ± 10.6	56 ± 10.3	28.5 ± 7.1	37 ± 7.3
Magnesium (mg.)	31.3 ± 7.6	3.4 ± 1.4	21.5 ± 4.7	24.9 ± 5.1	9.8 ± 4.4	31 ± 10.1	6.4 ± 4.8	19 ± 13.5
Copper (mg.)	0.11 ± 0.04	0.02 ± 0.03	0.07 ± 0.02	0.09 ± 0.03	0.04 ± 0.03	29 ± 25.1	0.02 ± 0.04	18 ± 20
Zinc (mg.)	1.38 ± 0.31	0.28 ± 0.23	0.34 ± 0.12	0.61 ± 0.22	1.05 ± 0.25	76 ± 6.4	0.79 ± 0.43	53 ± 26.8
Manganese (mg.)	0.32 ± 0.22	Trace	0.23 ± 0.21	0.28 ± 0.21	0.04 ± 0.03	15 ± 12.4	0.04 ± 0.03	15 ± 12.4
Chromium (μg.)	30.0 ± 10.0	14.0 ± 5.0	8.0 ± 2.0	21.0 ± 6.0	23.0 ± 9.0	72.0 ± 10.5	9.0 ± 6.0	24.0 ± 16.5

thus obtained, was taken to apply to all the samples of milk.

The standard solution of chromium was made up from the chromium salt $\text{Cr}_2(\text{SO}_4)_3 \cdot \text{K}_2\text{SO}_4 \cdot 24\text{H}_2\text{O}$. It has been stated (E. J. Butler, 1969, personal communication) that the state of oxidation of the chromium in the standard affects the results obtained, but this has not been substantiated.

Results

Table II shows the mean intakes, excretions, absorptions, and retentions of nitrogen, fat, sodium, potassium, calcium, phosphorus, magnesium, copper, zinc, manganese, and chromium with their respective standard deviations. The mean N balances indicated considerable N retention, and the absorption as a percentage of the intake was $86 \pm 2.2\%$. The digestion and absorption of fat was normal (Macy, 1942) and the retentions averaged 95% of the intakes. The mean intake of sodium was 0.87 ± 0.08 mEq/kg. per day which was intentionally low for therapeutic reasons (Wharton, Howells, and McCance, 1967), but the children had lost their oedema by the time the experiments were made and they retained $42 \pm 35\%$ of the intake. The diets had been fortified with potassium and magnesium to correct possible deficiencies of these elements. This partly accounts for the high intakes, but the matooke made large contributions to both. The mean amount of potassium absorbed was $73 \pm 14\%$ of the intake—very similar to the mean percentage of sodium. The mean intake of calcium was 42 ± 8.3 mg./kg. per day owing to the large amount of milk products in the food, and of this $53 \pm 11\%$ was absorbed and $47 \pm 11\%$ was retained. The mean intake of magnesium was 31.3 ± 7.6 mg./kg. per day. The mean intake of phosphorus was 76.0 ± 7.3

mg./kg. per day, and of this 14.2 ± 9.2 and 33.2 ± 6.3 mg. were found in the urine and faeces, respectively, giving mean absorptions and retentions of 56 ± 10.3 and $37 \pm 7.3\%$ of the intake, respectively, figures not far from those for calcium and magnesium. The intake of copper was 0.11 ± 0.04 mg./kg. per day. Much of this was excreted in the faeces and smaller but appreciable amounts in the urine. The mean absorption was 29% of the intake and the mean retention 18%. The intake of zinc was 1.38 ± 0.31 mg./kg. per day—over 10 times higher than that of copper in terms of weight, and of this a high percentage was absorbed and $53 \pm 27\%$ retained. The diets contained an average of 0.32 mg./kg. per day of manganese. None of this could be detected in the urine: most of it was found in the faeces, but 15% was absorbed and retained. The intake of chromium was of a much lower order of magnitude than anything else and the mean was only 30 μg./kg. per day. Of this, 72% appeared to be absorbed. The amounts excreted in the urine were too low to be measured with accuracy, but if the figure of 14 μg./kg. per day is accepted, 24% of the intake was retained.

Table III shows the contribution of the milk and the matooke to the children's intake of the N and minerals. The notable features are the large amounts of carbohydrate, potassium, and magnesium, and particularly of some of the trace elements such as copper and manganese, and to some extent zinc and chromium contributed by the matooke, in spite of the fact that its intake was less than half that of the milk.

Table IV gives the mean weight and composition of the faeces excreted by the 6 children, compared with values for healthy 4-year-old children reported by Macy (1942). There was a large standard

TABLE III

Contribution of Milk and Matooke to Children's Intake of N and Minerals

	Milk	Matooke
N (g./kg. per day)	0.72	0.10
Fat (g./kg. per day)	4.60	—
Carbohydrate (g./kg. per day)	5.5*	7.4†
Na (mEq/kg. per day)	0.96	0.02
K (mEq/kg. per day)	5.43	4.75
Ca (mg./kg. per day)	46.00	0.30
Mg. (mg./kg. per day)	21.00	14.00
P (mg./kg. per day)	69.00	16.00
Cu (mg./kg. per day)	0.06	0.07
Zn (mg./kg. per day)	1.16	0.55
Mn (mg./kg. per day)	0.06	0.26
Cr (μg./kg. per day)	24.00	12.00

*Calculated from the amounts of lactose in dried skim milk.

†Calculated from the figures of Southgate (1969).

deviation among the malnourished children, but the mean weight of their stools was more than twice that of the healthy children. This was due both to water and to dry matter but the percentage of water in them was very much the same as in those of the children studied by Macy (1942), namely 85% and 82%, respectively. In spite of this large excess of solid matter in the stools of children undergoing treatment, the weights of the measured constituents excreted daily differed little from those of the normal children except in a few respects. They contained considerably more potassium, however, and less calcium, copper, and zinc.

Discussion

In spite of the state in which these children, and others previously described, were admitted (Holemans and Lambrechts, 1955, 1959; Waterlow and Wills, 1960), there was really no evidence of any failure of intestinal function. The percentages of the intake of N and fat absorbed were approximately within normal limits and, considering the large bulk of the stools, must be reckoned remarkably high. Both were a little higher than those found by Robinson *et al.* (1957) and the absorptions of N were much the same as those of Clegg and Dean

(1960), De Maeyer and Vanderborcht (1958), Waterlow and Wills (1960), and Waterlow, Wills, and György (1960) from diets based on milk.

The amounts of potassium and particularly of magnesium added to the diets probably accounted for the percentages of the intakes absorbed being rather low, but the volume and composition of the faeces may have been partly responsible. Pretorius and Wehmeyer (1964) found 79% of the intake absorbed, Macy (1942) found 88%. The small percentages of these two elements retained, however, compared say to the percentages of sodium and calcium, do not suggest a deficiency of either at the time the measurements were made. There is some evidence that zinc deficiencies may complicate malnutrition in Shiraz and Egypt (Eminians *et al.*, 1967; Sandstead *et al.*, 1967). The conclusions have been criticized by Coble *et al.* (1966). There were no clinical signs of zinc deficiency in the 6 children studied and their home diets of plantain banana probably contained plenty. Their absorption was good. A deficiency of chromium in Jordan and possibly in Nigeria has been held to account for the low glucose tolerance in malnutrition (Majaj and Hopkins, 1966; Hopkins, Ransome-Kuti, and Majaj, 1968), but again this work has been criticized (Carter *et al.*, 1968). Chromium has been said to be very poorly absorbed, but the present work suggests that this may not always be true.

Much has been written, sometimes without much evidence, about the damaging effect of malnutrition on intestinal structure and function, but Cook and Lee (1966) considered some of the changes attributed to malnutrition to be genetic, and the work of Neame and Wiseman (1959), and Neale and Wiseman (1969) and of Kershaw, Neame, and Wiseman (1960) showed that starvation in rats enhanced the absorption of glucose and certain amino acids. They regarded this as an adaptation: it is certainly not evidence that malnutrition injures the intestine permanently as many have supposed.

The figures given in Table IV require a word of discussion. The protein ($N \times 6.25$), fat, and minerals, together with their accompanying anions, etc. accounted for between 10 and 11 g./day in the

TABLE IV

Mean Daily Weights of Faeces and of Substances in Them Excreted by Normal American Children 4 years old and Children Recently Admitted for Kwashiorkor

	Wet Weight (g.)	Solids (g.)	Water (g.)	N (g.)	Fat (g.)	Na (mg.)	K (mg.)	Ca (mg.)	P (mg.)	Mg (mg.)	Cu (mg.)	Zinc (mg.)	Mn (mg.)
Macy (1942)	84 ± 21	15 ± 3 (18%)	69 (82%)	1.07	1.6	41	311	503	311	168	1.7	10.5	2.2
This study	195 ± 68	27 ± 8 (15%)	168 (85%)	0.88	1.7	51	847	171	289	184	0.60	3.2	2.3

TABLE
Retention Ratios of K, Mg, Ca, and P to N by Normal Children
(Units/kg. body weight)

	Nitrogen		Potassium		K (mEq)/N (g.) ratio
	Intake (g.)	Retention (g.)	Intake (mEq)	Retention (mEq)	
Macy, 1942	0.52	0.037	3.56	0.15	4.00
Holemans and Lambrechts, 1955	0.88	0.48			
Hansen, 1956†	0.81	0.26	6.84	0.99	3.82
Linder <i>et al.</i> , 1963	0.72	0.24	7.10	2.30	9.60
Waterlow and Wills, 1960	0.37	0.22			
Pretorius and Wehmeyer, 1964	‡ 0.54	0.28	4.46	1.75	6.20
	§ 0.59	0.13	3.72	1.05	8.10
This study, 1969	0.71	0.23	9.40	1.30	5.60

*Holemans and Lambrechts' (1955) figures for nitrogen are those for 9 children receiving more than 0.5 g. N/kg. per 24 hours. The figures for calcium and phosphorus are for 8 children receiving a low intake of these minerals but more than 1.1 and 1.8 mEq/kg. per 24 hours, respectively. Hansen's figures for potassium are the means for 6 children during the first 14 days of treatment and those for N are the means for the same children over the smaller number of days on which their diets contained protein. The figures of Waterlow and Wills (1960) for N are the means for 17 children between days 11 and 25 of treatment (see their Table 4). The figures for

stools of both groups of children. The great difference between them lay in the large amount of undetermined solid matter in the stools of the Kampala children—17 g. as against 4 g. in the case of Macy's children. Some of this solid matter may have been lactose (Cook, 1967), but most of it must be reckoned to have been unavailable carbohydrate from the matooke which is a curious substance when eaten in bulk (Crawford, 1964) and is no doubt responsible for the voluminous stools of those who subsist largely on it. The matter is worth further investigation.

As already stated, Hansen (1956) and others have concluded from their balance experiments that malnourished children, even after a week or more of treatment, were still in a state of greater potassium, magnesium, and possibly calcium deficiency than they were of nitrogen deficiency. These conclusions were based upon the accepted K/N and Mg/N ratios of muscle and of the body respectively, and the ratios of K/N and Mg/N retained by the recovering children (Garrow *et al.*, 1968). There is, however, still some uncertainty about these findings (McCance, 1970), and Table V sets out the mean intakes and retentions of N, K, Mg, Ca, and P obtained in the present study together with those published by previous authors on similar children, and those of normal 4-year-old ones published by Macy (1942). The K (mEq)/N (g.) ratio in normal muscle is about 3 and in the whole body 2.0. The Mg (mEq)/N (g.) ratios are about 0.59 and 1.05, respectively. The Ca (mEq)/N (g.) ratio in the body is about 21.0, and the P (mEq)/N (g.) ratio in the body is about 14.4. The Ca (g.)/P (g.) ratio in bone is of the order of 2.2.

The data presented in Table V show that the intakes of N were all of the same order of magnitude which gives a satisfactory baseline. The K/N ratios retained were all over 3, including those of Macy's children.

The Mg/N ratios in the present study were 2.47, higher than the ratios for muscle or for the body, and about the same as those found by Linder, but only half those of Macy. The ratios found by Pretorius and Wehmeyer were below those in the whole body but about the same as those of muscle soon after admission, and well below both later. There was no clinical evidence of either potassium or magnesium deficiencies in the children in this study and the percentage of the intakes of these elements retained does not suggest it either. However, the high ratios were obtained, and whatever their explanation, technical or physiological, all the experiments indicate that the children were putting on flesh satisfactorily and further than this it would seem to be unwise to go at present.

The Ca/N ratios in the Kampala children were 5.1, close to those of Pretorius and Wehmeyer (1964), below those of Linder *et al.* (1963), and only one-third those of Macy (1942). The only ones below them were those of Holemans and Lambrechts (1959). If it be assumed that all the calcium retained went to form bone it may be calculated that the percentages of the P retained going to form the soft tissues were as follows: Macy (1942) 45%, Linder *et al.* (1963), Pretorius and Wehmeyer (1964) (soon after admission), and Holemans and Lambrechts (1959) 30%, Pretorius and Wehmeyer (1964) (3 weeks after admission) 20%, and this study 27%. These are satisfactory agreements and indicate that about 70%

of Recently Admitted Malnourished Children* (24 hours)

Magnesium		Mg (mEq)/N(g.) ratio	Calcium		Ca (mEq)/N (g.) ratio	Phosphorus		P (mEq)/N (g.) ratio †
Intake (mEq)	Retention (mEq)		Intake (mEq)	Retention (mEq)		Intake (mEq)	Retention (mEq)	
1·31	0·22	5·94	2·24 1·90	0·57 0·90	15·4 1·9	3·59 2·56	0·58 1·34	15·7 2·8
3·30	0·65	2·71	9·10	2·25	9·4	8·89 3·90	3·31 1·38	13·8 6·4
1·07	0·17	0·60	6·35	1·45	5·2	5·81	2·15	7·6
1·18	0·04	0·31	6·95	0·75	5·8	6·51	1·68	13·0
2·61	0·53	2·47	2·12	1·00	5·1	4·42	1·66	7·9

phosphorus are based upon 9 of the children at the same time during treatment who received a mean intake of 3·9 mEq/kg. per 24 hours (see their Table 5 and legend).

†A valence of 1·8 has been used in calculating phosphorus in terms of mEq.

‡Within 6 days from admission.

§Three weeks after admission.

of the P retained by children recuperating from wasting and malnutrition went to form soft tissue but only 55% in healthy children.

The ward routine, originally built up by the late R. F. A. Dean, to measure all the food consumed by the children accurately, coupled with the devotion of the nursing staff, made these experiments comparatively easy to perform.

REFERENCES

- Carter, J. P., Kattab, A., Abd-El-Hadi, K., Davis, J. T., El Gholmy, A., and Patwardhan, V. N. (1968). Chromium (III) in hypoglycemia and in impaired glucose utilization in kwashiorkor. *American Journal of Clinical Nutrition*, **21**, 195.
- Chibnall, A. C., Rees, M. W., and Williams, E. F. (1943). The total nitrogen content of egg albumin and other proteins. *Biochemical Journal*, **37**, 354.
- Clegg, K. M., and Dean, R. F. A. (1960). Balance studies on peanut biscuit in the treatment of kwashiorkor. *American Journal of Clinical Nutrition*, **8**, 885.
- Coble, Y. D., VanReen, R., Schulert, A. R., Koshakji, R. P., Farid, Z., and Davis, J. T. (1966). Zinc levels and blood enzyme activities in Egyptian male subjects with retarded growth and sexual development. *American Journal of Clinical Nutrition*, **19**, 415.
- Cook, G. C. (1967). Lactase activity in newborn and infant Baganda. *British Medical Journal*, **1**, 527.
- , and Lee, F. D. (1966). The jejunum after kwashiorkor. *Lancet*, **2**, 1263.
- Cravioto, J. (1958). Protein metabolism in chronic infantile malnutrition (kwashiorkor). *American Journal of Clinical Nutrition*, **6**, 495.
- Crawford, M. A. (1964). Degradation of amino-acids in the large gut of East Africans and its possible significance. *East African Medical Journal*, **41**, 228.
- De Macey, E. M., and Vanderborgh, H. (1958). A study of the nutritive value of proteins from different sources in the feeding of African children. *Journal of Nutrition*, **65**, 335.
- Eminians, J., Reinhold, J. G., Kfoury, G. A., Amirhakimi, G. H., Sharif, H., and Ziai, M. (1967). Zinc nutrition of children in Fars province of Iran. *American Journal of Clinical Nutrition*, **20**, 734.
- Fiske, C. H., and Subbarow, Y. (1925). The colorimetric determination of phosphorus. *Journal of Biological Chemistry*, **66**, 375.
- Garrow, J. S., Smith, R., and Ward, E. E. (1968). *Electrolyte Metabolism in Severe Infantile Malnutrition*. Pergamon Press, London and Oxford.
- Halliday, D. (1967). Chemical composition of the whole body and individual tissues of two Jamaican children whose death resulted primarily from malnutrition. *Clinical Science*, **33**, 365.
- Hansen, J. D. L. (1956). Electrolyte and nitrogen metabolism in kwashiorkor. *South African Journal of Laboratory and Clinical Medicine*, **2**, 206.
- Holemans, K., and Lambrechts, A. (1953). Nitrogen metabolism and fat absorption in malnutrition and in kwashiorkor. *Journal of Nutrition*, **56**, 477.
- , and — (1959). Calcium and phosphorus metabolism in malnutrition and in kwashiorkor. *Journal of Tropical Pediatrics*, **4**, 129.
- Hopkins, L. L., Jr., Ransome-Kuti, O., and Majaj, A. S. (1968). Improvement of impaired carbohydrate metabolism by chromium (III) in malnourished infants. *American Journal of Clinical Nutrition*, **21**, 203.
- Kershaw, T. G., Neame, K. D., and Wiseman, G. (1960). The effect of semistarvation on absorption by the rat small intestine *in vitro* and *in vivo*. *Journal of Physiology*, **152**, 182.
- Liebermann, L., and Székely, S. (1898). Eine neue Methode der Fettbestimmung in Futtermitteln, Fleisch, Koth, u.s.w. *Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere*, **72**, 360.
- Linder, G. C., Hansen, J. D. L., and Karabus, C. D. (1963). The metabolism of magnesium and other inorganic cations and of nitrogen in acute kwashiorkor. *Pediatrics*, **31**, 552.
- McCance, R. A. (1970). Malnutrition in the children of underdeveloped countries. In *Recent Advances in Paediatrics*, 4th ed. Ed. by D. Gairdner and D. Hull. Churchill, London.
- , Widdowson, E. M., and Shackleton, L. R. B. (1936). The nutritive value of fruits, vegetables and nuts. *Medical Research Council. Special Report Series*, **213**, 19.
- Macy, I. G. (1942). *Nutrition and Chemical Growth in Childhood*, vol. 1. C. C. Thomas, Springfield, Illinois.
- Majaj, A. S., and Hopkins, L. L. (1966). Human chromium deficiency: the response of hypoglycemia and impaired glucose utilization to chromium (III) treatment in protein calorie malnourished infants. *Journal Médical Libanais. Lebanese Medical Journal*, **19**, 177.
- Montgomery, R. D. (1960). Magnesium metabolism in infantile protein malnutrition. *Lancet*, **2**, 74.
- (1961). Magnesium balance studies in marasmic kwashiorkor. *Journal of Pediatrics*, **59**, 119.
- Neale, R. J., and Wiseman, G. (1969). Active transport by dietary-restricted small intestine. *Journal of Physiology*, **204**, 116P.
- Neame, K. D., and Wiseman, G. (1959). The effect of diet on intestinal active transport. *Journal of Physiology*, **146**, 10P.

- Pretorius, P. J., and Smit, Z. M. (1958). The effect of various skimmed milk formulae on the diarrhoea, nitrogen retention and initiation of cure in kwashiorkor. *Journal of Tropical Pediatrics*, **4**, 50.
- , and Wehmeyer, A. S. (1964). Nitrogen, fat and mineral balance studies in patients with protein malnutrition. *South African Journal of Laboratory and Clinical Medicine*, **10**, 52.
- Robinson, U., Béhar, M., Viteri, F., Arroyave, G., and Scrimshaw, N. S. (1957). Protein and fat balance studies in children recovering from kwashiorkor. *Journal of Tropical Pediatrics*, **2**, 217.
- Sandstead, H. H., Prasad, A. S., Schulert, A. R., Farid, Z., Miale, A., Bassilly, S., and Darby, W. J. (1967). Human zinc deficiency, endocrine manifestations and response to treatment. *American Journal of Clinical Nutrition*, **20**, 422.
- Sénécal, J. (1958). The treatment and prevention of kwashiorkor in French West Africa. *Annals of the New York Academy of Sciences*, **69**, 916.
- Southgate, D. A. T. (1969). Determination of carbohydrates in foods, II—Unavailable carbohydrates. *Journal of Science of Food and Agriculture*, **20**, 331.
- Vis, H., Dubois, R., Vanderborcht, H., and De Maeyer, E. (1965). Etudes des troubles électrolytiques accompagnant le kwashiorkor marastique. *Révue Française d'Etudes Cliniques et Biologiques*, **10**, 729.
- Wallace, W. M., Weil, W. B., and Taylor, A. (1958). The effect of a variable protein and mineral intake upon the body composition of the growing animal. *Ciba Foundation Colloquia on Ageing*, **4**, 116.
- Waterlow, J. C., and Wills, V. G. (1960). Balance studies in malnourished Jamaican infants. I. Absorption and retention of nitrogen and phosphorus. *British Journal of Nutrition*, **14**, 183.
- , —, and György, P. (1960). Balance studies in malnourished Jamaican infants. 2. Comparison of absorption and retention of nitrogen and phosphorus from human milk and a cow's-milk mixture. *British Journal of Nutrition*, **14**, 199.
- Wharton, B. A., Howells, G. R., and McCance, R. A. (1967). Cardiac failure in kwashiorkor. *Lancet*, **2**, 384.
- , and McCance, R. A. (1968). Kwashiorkor. In *Current Pediatric Therapy*, 3rd ed., vol. 3, p. 7. Ed. by S. S. Gellis and B. M. Kagan. Saunders, Philadelphia and London.

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