THE EFFECT OF MILK FAT AND SUNFLOWER-SEED OIL ON THE DIARRHOEA, THE NITROGEN, THE FAT AND MINERAL BALANCE, AND THE RATE OF RECOVERY, OF KWASHIORKOR PATIENTS

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It is widely believed that patients suffering from kwashiorkor tolerate milk fat poorly and a skimmed-milk diet is therefore often prescribed.¹ It is now known, however, that for laboratory animals fat is not merely a concentrated source of energy, but also an essential nutrient,² and the same is probably true of human infants.³

The results obtained in a recent study by Gillman *et al.*,⁴ with uniformly-labelled ¹⁴C glucose, 2-¹⁴C pyruvate and 1-¹⁴C acetate suggest that kwashiorkor patients, and even normal young infants, are unable to synthesize cholesterol or fatty acids readily from glucose or pyruvate, but do so easily from acetate. These authors stated 'that the normal infant (at least until the age of 3 years) cannot easily synthesize fat from carbohydrate, and that gluconeogenesis from non-carbohydrate sources is sluggish'. They concluded that 'the evidence seemed more than suggestive that the normal infant was dependent not only on dietary protein,

but also on adequate amounts of dietary fat and carbohydrate'.

Although most workers appear to favour skimmed milk for the treatment of kwashiorkor, it has been shown by Dean and Skinner⁵ that kwashiorkor patients tolerate vegetable oils well, while Goméz *et al.*⁶ regard whole milk as the dietary treatment of choice. To our knowledge, no controlled study has been carried out to establish whether diets containing fat or vegetable oil are superior to the usual skimmed-milk diets in the treatment of kwashiorkor. Such an investigation was therefore undertaken at the Pretoria General Hospital.

MATERIALS AND METHODS

The investigations were carried out during the period November 1960 to December 1961 on 120 Bantu infants with kwashiorkor, all of whom exhibited the characteristic signs of the disease.⁷ Patients with active tuberculosis were excluded from the series.

The patients were divided at random into 4 groups of 30. Each group received one of the following diets for a period of 3 weeks from the day after admission to hospital:

- A. Dried whole milk: Spray-dried whole milk, 15 G. per kg. body weight per day.
- B. Acidified dried whole milk: Acidified spray-dried whole milk, 15 G. per kg. body weight per day. The dried milk contained 0.5% lactic acid.
- C. Dried skimmed milk with added sunflower-seed oil: Spraydried skimmed milk, 11 G. and sunflower-seed oil 4 G. per kg. body weight per day. In order to facilitate suspension, 2 G. of gelatine was added to the entire daily feed.
- 2 G. of gelatine was added to the entire daily feed.
 D. Dried skimmed milk with added carbohydrate: Spraydried skimmed milk 11 G., cane sugar 7.5 G. and corn starch 1 G. per kg. body weight per day.

The dry ingredients of the 4 diets were mixed with water, the prescribed amount for each patient being 150 ml. per kg. body weight per day. All 4 diets provided about 4 G. of protein and about 75 calories per kg. body weight per day. As no adjustments in the intake of the diets were made during the course of the experiment, the intake per kg. body weight of both protein and calories usually increased somewhat after loss of oedema, and consequently loss of weight, had occurred.

Therapeutic regimen. During the first 12-18 hours all patients received frequent small feeds of skimmed milk alternated with Hartmann's solution containing 5% of dextrose. The experimental diets were introduced on the day after admission. The feeds were usually given at 4-hour intervals, but in the presence of severe anorexia or vomiting small feeds were given hourly or 2-hourly. Where necessary patients were fed by means of an indwelling polyethylene intragastric tube. All patients received 5 ml. of a multivitamin syrup daily. In view of the prevalence of infection, 125 mg. of tetracycline was given 6-hourly to all patients during the first 5 days in hospital. Intravenous therapy with electrolyte solutions and/or plasma and blood was instituted when indicated.

Examination of stools. All diapers were examined and the character of the stools recorded by a member of the nursing staff. After examination the diapers were deposited in a container at the bedside and in the morning, before their removal, inspected and the number of soiled diapers noted by one of the authors. Although it was possible to get a fair impression of the effect of the 4 diets on the diarrhoea, this method has obvious limitations,⁸ and wetstool weights were therefore recorded for those patients on whom balance studies were carried out.

Metabolic Studies

Balance studies were carried out on 40 male patients, 10 from each dietary group. All the balances were commenced within 6 days after admission and repeated $2\frac{1}{2}$ - 3 weeks after admission. For the purpose of this report the results obtained during the first balance periods only will be discussed.

Nitrogen, fat and phosphorus balance studies were carried out on all 40 patients, while calcium, magnesium, potassium and sodium balances were performed on 5 - 7 patients in each dietary group.

In all cases separate collections of urine and faeces were made by means of a metabolic bed over a 3-day period. Carmine was used to mark the faeces. Sweat collections were not attempted. Urine was collected under toluene, the 24-hour specimens being combined and stored in a deep freeze until analysis was possible. Stools passed in each 12-hour period were combined and also stored in a deep freeze. Before being analysed the pooled stools were mixed in a high-speed electric blender and suitable samples taken.

Food intake was measured by weighing the feeding bottles before and after feeds. Samples were taken daily and stored in a deep freeze until analysed. If vomiting occurred the balance study on the patient was abandoned.

Analytical Methods

The dry matter of the faeces was determined by evaporating 50 ml. aliquots in weighed silicon basins on a boiling waterbath until dry. The basins were then placed in an air oven at $100 - 150^{\circ}$ C. overnight (about 16 hours) and weighed after cooling to room temperature in vacuum desiccators.

The ash content of the faeces was determined by placing the basins containing the dry faecal matter in a muffle furnace. The temperature was increased to about 100° C., kept at this level for 10 minutes, and then increased very slowly to about 400° C. After 30 minutes the temperature was increased to $550 - 600^{\circ}$ C., this temperature being maintained for at least 3 hours, or until a white ash had been obtained. The basins were then cooled to room temperature in vacuum desiccators, weighed, and the ash content calculated. The ash contents of the urine and milk samples were determined in the same way by using 50 ml eliquete of urine and 20 G of the milk feede

by using 50 ml. aliquots of urine and 20 G. of the milk feeds. The ash was dissolved by adding 2 ml. of concentrated hydrochloric acid to the ash in the basin. The residue left after evaporation was dissolved in hot dilute hydrochloric acid and the solutions were transferred quantitatively to volumetric flasks and diluted to volume with double distilled water.

The potassium and sodium contents of the solution were determined by means of a Zeiss flame photometer, essentially according to the methods described in the A.O.A.C.,⁹ lithium being used as an interval standard. The classical oxalatepermanganate method⁹ was used for the determination of calcium, and magnesium was determined by means of a titanyellow colorimetric method.¹⁰ Phosphorus in the food, stools and urine was determined by the colorimetric method of Boltz and Mellon¹¹ after wet-ashing with sulphuric and perchloric acid.

Nitrogen in the food, stools and urine was determined by the usual Kjeldahl method,⁹ a selenium mixture being used as catalyst. The fat content of the food and stools was estimated according to an acid hydrolysis method.¹² The serum proteins were determined by the method of Robinson and Hogden.¹³

RESULTS

The results obtained are set out in Tables I - XIII. In all the statistical tests a probability level of 5% was regarded as being significant.

Mortality rate. Sixteen patients (12%) died (Table I). Most of the deaths occurred within the first few days after admission and apparently were unrelated to the type of diet given, a fact that can be deduced in most cases from the particulars given in Table I. Unfortunately, permission for autopsy was granted in only 7 cases.

The effect of the diets on weight change. In Table II are shown the mean daily changes in body weight that occurred in the 4 groups during the first, second and third weeks after admission. No significant differences were found between the 4 groups of patients in respect of any of the 3 periods, when these values were compared by means of the Kruskal-Wallis one-way analysis of TABLE I. SUMMARY OF CLINICAL AND AUTOPSY FINDINGS IN THE 16 PATIENTS WHO DIED

Dietary group	Days from admission to death	Oedema	Dermatosis	Other clinical and autopsy findings
A	2	++	++	Died suddenly. PM: Fatty liver; acute bronchitis and confluent bronchopneu- monia; maranthic thrombosis of some cortical veins.
A	7 8 hrs.	+++ +++	+++ nil	Very advanced case; convulsions. No PM. Admitted in collapsed state; extensive necrosis of buttocks and vulva. No PM.
A	4	+++	+++	Sudden death; completely anorexic. PM: Fat- ty liver; bronchopneumonia and fibrinous pleuritis; maranthic thrombosis of some cortical veins.
в	12	+++	+++	Bronchopneumonia; high fluctuating tem- perature; convulsions and coma. No PM.
B	33	‡‡	++ ++	Severe necrosis of skin in sacral area. No PM. Convulsions and coma. PM: Fatty liver; tuberculous bronchopneumonia; meningo- encephalitis.
в	9	+	++	Very apathetic; bronchopneumonia, probably tuberculosis. No PM.
с	7	+	+	Stomatitis; liver 10 cm. enlarged; ? herpes simplex hepatitis. No PM.
С	16 hrs.	+	nil	Bronchopneumonia; very apathetic; liver 5 cm. enlarged. No PM.
с	2	+++	+++	Sudden death while apparently responding well to treatment. PM: Fatty liver; atrophy of pancreatic acini; pulmonary congestion.
С	1	++	+++	Advanced case; became comatose soon after admission. No PM.
D	12	+	+	Bronchopneumonia; high temperature; con- vulsions. No PM.
D	4	+	nil	High fluctuating temperature. PM: Fatty liver; atrophy of pancreatic acini; chronic peribronchiolitis; advanced fatty changes of proximal tubules of kidneys.
D	2	++	++	Bronchopneumonia. PM: Fatty liver; bron- chopneumonia and multiple lung abscesses.
D	13	+	+	Classified a mild case on admission, but poor response to treatment. PM: Fatty liver; pancreatic atrophy; acute pyelone- phritis; pulmonary artery thrombosis with septic infarction.

Throughout the tables, A, B, C and D represent the diets shown on page 22.

variance.¹⁴ As judged by the same statistical test the number of days taken by the 4 groups of patients to reach their lowest weight (Table III), which presumably reflects

 TABLE II. MEAN DAILY CHANGE IN WEIGHT IN G./DAY DURING THE EXPERIMENTAL PERIOD

 TABLE III. DAYS TAKEN FOR ATTAINMENT OF LOWEST WEIGHT

TABLE IV. DAYS TAKEN FOR DISAPPEARANCE OF OEDEMA

	1	II.		III.	IV.	
Diet	1st week*	2nd week*	3rd week*	No. of days*	No. of days*	
A	-29.8+75.20	-17.7+37.75	9.0 + 22.16	11.8+6.39		
B	-39.4+68.55	-20.0+57.56	9.6+20.83	10.2 ± 5.39	8.8±4.46	
č	-65.5+91.63	-7.3+43.43	6.0 + 24.03	10.0 ± 5.35	9.6±4.30	
Ď	-56.3±69.25	5.6±40.79	$15 \cdot 2 \pm 17 \cdot 93$	8·4±4·49	8.8±4.77	
					1	

*Mean ±S.D.

the efficacy of the diets in causing the dispersal of oedema fluid, also did not differ significantly. In addition, as can be seen from Table IV, the average time taken for the disappearance of overt oedema was very similar in the 4 groups.

The influence of the diets on the diarrhoea. The 4 groups were compared with respect to number of stools passed daily during the first, the second and the third week after admission. No significant differences could be demonstrated for any of the 3-week periods with the Chi-square test. However, on comparing the 4 groups with regard to the number of *formed* stools averaged per day for each of the 3-week periods by means of the same test, significant differences were found for the first week (P<0.1%), the second week (P<1%) and third week (P<1%). The various groups were therefore paired and the binomial test¹⁴ was applied. Because of the multiple testing involved, a probability level of less than 0.8% corresponds to a significant difference at the 5% level in these comparisons. It was found that in most instances significant differences existed, at least in the first week, between both the dried skimmed milk + carbohydrate group and the dried skimmed milk + sunflower-seed oil group on the one hand and the other 2 groups of patients who received milk fat on the other hand. For instance, the average number of formed stools passed daily in the first week by the group of patients who received acidified dried whole milk was significantly different from the number passed by the dried skimmed milk + carbohydrate group (P < 0.1%), and also from the average number passed daily by the dried skimmed milk + sunflower-seed oil group (P < 0.1%). Similar differences existed between the dried whole milk group and the dried skimmed milk + carbohydrate group (P < 0.1%), and between the former group and the dried skimmed milk + sunflower-seed oil group (P < 0.1%). On the other hand no significant differences were found between the 2 groups which received formulae containing milk fat, or between the 2 groups which received skimmed milk + carbohydrate and skimmed milk + sunflower-seed oil. It was therefore concluded that the formulae containing milk fat were far more conducive to the production of formed stools than the other two formulae.

The mean daily wet weights, dry weights and mineral contents of the faeces of the patients on whom balance studies were carried out are shown in Table V. The most

TABLE V. WET WEIGHT, DRY WEIGHT AND ASH CONTENT OF FAECES OF TEN PATIENTS IN EACH GROUP

Diet				
		Wet weight*	Dry weight*	Ash content
A		 173+113.4	15.7 ± 4.25	3 . 27 + 0 . 921
B		 143 ± 90.3	13.1 ± 5.15	2.76+0.887
C		 172 ± 153.5	16.5 ± 11.03	3.16+0.605
BCD	••	 264 ± 200.7	13.4 ± 6.47	2·83±0·671
		Durin	g second collection	period
A B C		 94±88·5	11.9+8.06	2.40+0.958
B		 $63 \pm 29 \cdot 3$	11·6±4·35	3.04 ± 1.220
C		 $65 + 46 \cdot 5$	11.0 + 3.67	2.73+0.518
D		 104 ± 77.4	10-4±3-87	$3 \cdot 26 + 1 \cdot 180$

*In G. per day (mean ±S.D.)

noteworthy finding was the high wet-weight values obtained in all 4 groups. The mean value of 264 G. per day obtained in the skimmed milk + carbohydrate group was much higher than the mean values obtained in the other 3 groups, but the values obtained for the 4 groups of patients did not prove to be significantly different during either the first or second collection periods when the Kruskal-Wallis one-way analysis of variance¹⁴ was applied. The dry weights and mineral contents of the stools also did not differ significantly in the 4 groups of patients during either the first or the second collection periods (Table V).

Serum albumin. No significant differences were found between the 4 groups when the initial serum-albumin values, and also the increases that occurred during the experimental period, were compared by means of the Kruskal-Wallis test. It is evident from Table VI that the average values were in fact almost identical.

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TABLE VI. INCREASE IN SERUM ALBUMIN CONCENTRATION DURING TREATMENT

Die			On admission*	After 1 week*	After 2 weeks*	After 3 weeks*
A			1.9 ± 0.42	2.6 ± 0.53	3.5 ± 0.57	3.8 ± 0.41
B			1·9±0·62	2·7±0·72	3.6±0.46	$3 \cdot 8 \pm 0 \cdot 36$
C			1.9 ± 0.52	2.6 ± 0.70	3.5 ± 0.49	3.9 ± 0.46
D			1.9 ± 0.46	2.8 ± 0.71	3.5±0.51	3.5 ± 0.48
*Me	an ±	S.D.				

Results of Balance Studies

The results obtained during the balance studies are set out in Tables VII - XIII. The following statistical comparisons were made for each variable (intake, retention, percentage, retention, and percentage absorption) measured in the experiment:

(1) Comparisons of all 4 groups of patients with respect to each of the findings by means of the Kruskal-Wallis one-way analysis of variance.14

(2) Comparison of pairs of groups by means of the U test of Wilcoxon, Mann and Whitney14 with respect to findings for which the first test demonstrated significant differences.

Nitrogen balance results (Table VII). Although the apparent absorption of nitrogen was slightly below normal, high retention values were obtained in all 4 groups of patients. The retention values, whether expressed in mg.

TABLE VII. NITROGEN BALANCE RESULTS (MG./KG./DAY)

Diet			Age in months*	Weight in kg.*	Intake*	Urinary excr.*
A			22.7+10.65	7.4+1.57	564+67.38	$202 + 37 \cdot 19$
B			20.4+ 4.17	8.1+1.12	513 ± 60.40	$149 + 47 \cdot 54$
č	22		20.4+ 7.42	8.2+1.12	596+51.70	202 + 51.70
Ď			23.0 ± 8.25	8·5±1·85	$526\pm45\cdot36$	$162 \pm 64 \cdot 19$
			Faecal excr.*	Retention*	Retention %*†	Absorption %**
A			$104 \pm 34 \cdot 10$	$258 \pm 22 \cdot 16$	46 ± 8.79	82+6.74
B			70 ± 20.03	294 ± 40.40	57 ± 9.28	86±3.66
č			90 ± 14.04	304 ± 46.82	51 ± 7.93	85 ± 2.57
D	100	100	$95 \pm 32 \cdot 15$	269 ± 58.06	$51\pm14\cdot14$	82±7.67

Ten balances from each group A, B, C and D. *Mean \pm S.D. †Retention (or absorption) as percentage of intake.

per kg. body weight per day or as a percentage of nitrogen intake, did not differ significantly. Moreover, no significant differences were found between the values for apparent absorption expressed as a percentage of the intake. The nitrogen intake in the skimmed milk + sunflower-seed oil group (average 596 mg./kg. body weight per day) was, however, significantly different (P<0.2%) from the intake in the acidified whole milk group (average 513 mg./kg. body weight per day).

Fat balance results (Table VIII). Absorption of fat was impaired but did not differ significantly in the patients in

TABLE VIII, FAT BALANCE RESULTS (G./KG./DAY)

Diet		No. of balances	Intake*	Faecal excr.*	Absorption*†
A	 	10	4.02 ± 0.510	0.90 ± 0.424	78±13.86
B	 	10	3 - 23 + 1 - 040	0.65 ± 0.282	80 + 8.54
C	125	10	3.50+1.240	0.51+0.346	85+16.49
D	 	10	0.11 ± 0.036	0.11 ± 0.091	

•Mean \pm S.D. †Absorption as percentage of intake.

the 2 groups that received milk fat and in the group that received sunflower-seed oil. On the very low intakes of fats that occurred in the skimmed milk + carbohydrate group, balances were often negative.

Calcium balance results (Table IX). Although the average retention of calcium, whether expressed in mg. per

TABLE IX. CALCIUM BALANCE RESULTS (MG./KG./DAY)

Diet A	Intake* 134.3+21.14	Urinary excretion 2·3+1·06	Faecal excretion 111.4+31.30	Reten- tion* 20.6+22.25	<i>Reten-</i> <i>tion</i> *† 15+19-80
B	117.1 ± 9.78	2.1 ± 0.94	89.6±23.96	25.4 ± 16.80	22 ± 9.70
C D	$133 \cdot 1 \pm 10 \cdot 61$ $123 \cdot 1 \pm 10 \cdot 18$	2.6 ± 1.30 1.7 ± 0.42	$96 \cdot 1 \pm 19 \cdot 45$ 81 $\cdot 0 \pm 19 \cdot 79$	34.4 ± 10.80 40.4 ± 18.81	26 ± 9.27 33 ± 15.21

Five balances from each group A, B, C and D. *Mean \pm S.D. †Retention as percentage of †Retention as percentage of intake.

kg. body weight per day or as a percentage of the intake, was much higher in the skimmed milk + carbohydrate group that any of the other groups (particularly the whole milk group), the differences between the groups were not found to be statistically significant. Urinary excretion of calcium was extremely low in all 4 groups.

Phosphorus balance results (Table X). The differences in intake, retention and absorption values were not significant.

TABLE X. PHOSPHORUS BALANCE RESULTS (MG./KG./DAY)

Diet		No. of balances	Intake*	Urinary excretion*	Faecal excretion*
A	 	10	105.6+13.6	21.8 + 8.93	54.2+27.12
B	 	10	99·4+ 8·71	$13 \cdot 1 + 23 \cdot 32$	44.0 ± 17.01
B C	 	10	104.4+10.31	$13 \cdot 1 + 8 \cdot 69$	65 . 3 + 39 . 66
D	 	10	96·3± 8·81	12·9± 6·01	47.6 ± 19.05
			Retention*	Retention*†	Absorption*†
A	 	10	29.6+15.2	28 + 15.99	$49 + 20 \cdot 27$
B	 	10	42.3+18.05	43 + 17.73	56+16-64
С	 	10	26.0+32.85	$25 + 29 \cdot 38$	$37 + 32 \cdot 34$
D	 	10	35·8±17·24	37 ± 15.79	51±21.88

*Mean \pm S.D. †Retention (or absorption) as percentage of intake.

The urinary excretion of phosphorus was very low in all the groups, the retention values therefore being high despite large faecal losses.

Magnesium balance results (Table XI). The mean faecal excretion of magnesium was considerably higher in the

TABLE XI. MAGNESIUM BALANCE RESULTS (mEq./KG./DAY)

Diet	Intake* 1.14+0.176	Urincry excretion* 0.04+0.024	Faecal excretion* 1.12+0.472	Retention* -0.02+0.318	Reten- tion•†
B	1.00+0.137	0.04 ± 0.024 0.05 ± 0.039	0.76 ± 0.381	-0.02 ± 0.318 0.19+0.291	19+27.4
С	1.09 ± 0.149	0.11 ± 0.097	0·74±0·162	0.24 ± 0.136	23 ± 16.0
D	1.12 ± 0.176	0.04 ± 0.003	0.75 ± 0.277	0.33 ± 0.269	29 ± 21 3

Seven balances from each group A, B and D; and 6 balances from Group C. *Mean \pm S.D. †Retention as percentage of intake.

dried whole-milk group than in the other groups. When tested statistically, however, the values for absorption in this group were not found significantly different from the values obtained in the other groups. Of note was the very low urinary excretion in the patients of all 4 groups.

Absorption of potassium and sodium (Tables XII and XIII). Apparent absorption of potassium and sodium was reduced in most of the patients studied. The differences between the 4 groups were not significant, although, as can be seen from Table XIII, the mean faecal loss of sodium was exceptionally high in the skimmed milk + carbohydrate group, resulting in a mean apparent absorption of only 51%.

DISCUSSION

The 4 diets appeared to be tolerated equally well and no evidence of any harmful effects resulting from the presence of milk fat was obtained during the investigation. The belief that kwashiorkor patients tolerate milk fat poorly^{1, 15} was therefore not confirmed by our findings. The observation that vegetable oil is tolerated well5, 16 was corroborated

TABLE XII. FAECAL POTASSIUM LOSS (mEq./KG./DAY)

Di	et	No. of patients	Intake*	Faecal excretion*	Absorption*†
A		 5	4.03 ± 1.147	1.09 ± 0.722	73 ± 30.1
B		 5	$5 \cdot 12 + 0 \cdot 940$	1.82 ± 0.981	$64 + 27 \cdot 9$
C		 5	5.16+1.215	1.14 ± 0.525	78 ± 7.3
D		 5	4·80±1·048	1.14 ± 0.775	76±15-9

*Mean \pm S.D. †Absorption as percentage of intake.

TABLE XIII. FAECAL SODIUM LOSS (mEq./KG./DAY)

Di	et	No. of studies	Intake*	Faecal excretion*	Absorption*†
A		 5	$2 \cdot 20 \pm 0 \cdot 285$	0.50 ± 0.327	77 ± 20.2
B		 5	1.79 ± 0.365	0.41 ± 0.377	77±13.6
C		 5	1.93 ± 0.312	0.23 ± 0.126	88 ± 4.84
D		 5	2.09 ± 0.529	1.03 ± 0.637	51±26.0

*Mean \pm S.D. †Absorption as percentage of intake.

by our results but, since no evidence emerged that sunflower-seed oil was superior to milk fat in this respect, the view that vegetable oils are tolerated far better than animal fats by kwashiorkor patients^{1, 17} was not supported. The low total mortality rate of 12% probably reflects the effectiveness of all 4 diets used in the present series.

The mean daily weight loss during the initial period and the subsequent rate of gain did not differ significantly in the patients of the 4 groups. This finding is of interest because it has been suggested that the presence of increasing amounts of linoleic acid in the diets of infants, up to an optimum of 4% of the total calories, results in a more rapid weight gain than that which occurs in infants on isocaloric low-fat feeds.¹⁸ Such an effect was not apparent in the patients of the skimmed milk + sunflowerseed oil group who probably received at least 25% of their calories from linoleic acid. No demonstrable 'sparing' effect on caloric utilization was therefore evident in this group.

Diarrhoea is often troublesome in kwashiorkor and, when severe, may cause an impairment in the absorption of nitrogen,^{8, 19} electrolytes,¹⁹ and possibly other nutrients. It was found that the 2 diets containing milk fat were more conducive to the production of formed stools than the other 2 diets, a finding that differs from that of Trowell,¹⁷ who stated that whole milk and its products provoke severe diarrhoea.

The mean daily wet-stool weights recorded during the first balance periods were very high, especially in the patients of the skimmed milk + carbohydrate group, who excreted an average of 264 G. per day. This value, however, did not differ significantly from the values obtained in the other groups. This may possibly be due to the very marked day-to-day variation in the wet weights of the stools recorded in all 4 groups. We ourselves gained the impression that diarrhoea was least effectively controlled in the patients who received the skimmed milk + carbohydrate diet.

Although the diarrhoea-provoking properties of highcarbohydrate diets in infants, believed to be the result of fermentation, have been questioned,²⁰ there seems to be little doubt that a high intake of sugars (especially lactose but also sucrose) provokes diarrhoea in kwashiorkor patients.¹⁵ It has recently been shown that the congenital absence of sugar-splitting enzymes causes diarrhoea and increases the faecal excretion of lactic acid and other organic acids.²¹ It is known that the activity of many enzyme systems is decreased in kwashiorkor, and these may well include the sugar-splitting enzymes.

The skin lesions described by Hansen *et al.*³ in infants on a deficient linoleic-acid intake resemble somewhat those seen in kwashiorkor. In all our patients the consumption not only of protein, but also of fat, was probably very low before admission. No conspicuous differences in the rate of healing of the skin lesions were observed, but the accurate assessment of day-to-day skin changes is extremely difficult, and inconspicuous differences could easily have been overlooked.

No evidence was obtained that protein metabolism was influenced by the presence or absence of milk fat or sunflower-seed oil in the diets. Regeneration of the serum proteins, and apparent absorption and retention of nitrogen, were very similar in the 4 groups. These results are in agreement with those of Scrimshaw *et al.*,²² whose preliminary results seemed to indicate that retention of nitrogen was not affected appreciably by the presence or absence of fats in the diets of convalescent kwashiorkor patients. Similar observations were also made during balance studies on 2 pairs of normal young adults receiving alternately high- and low-fat isonitrogenous diets.²³ In spite of some impairment in the absorption of nitrogen in all 4 groups, retention of nitrogen was very high, a well-known finding in acute kwashiorkor.^{24, 25}

Some degree of steatorrhoea is often present in kwashiorkor.^{24, 26, 27} Normally, children retain about 97% of the dietary fat ingested.²⁸ Impaired absorption of fat therefore occurred in the patients of all 3 groups who received fat or oil. However, considerable quantities of milk fat or sunflower-seed oil were nevertheless absorbed. The steatorrhoea tended to reduce rather than to aggravate the diarrhoea, as judged by the number of formed stools passed. The fact that the low fat intakes of patients in the skimmed milk + carbohydrate group were often productive of negative balances supports the view that some of the faecal fat in kwashiorkor patients is of endogenous origin.²⁶ It seems well established that in normal infants dietary fat is virtually all absorbed, and that lipids are excreted through the wall of the large intestine.²

It is noteworthy that the average amount of calcium retained by the skimmed milk + carbohydrate group was about twice the corresponding value obtained in the whole-milk group. Although the difference was not statistically significant, the possibility is not excluded that calcium was nevertheless absorbed more efficiently by the patients in the former group. It is not unlikely that, as a result of the very low fat content of the diet, less calcium was lost in the form of insoluble soaps. It is moreover well established, at least in the rat, that the presence of certain carbohydrates in the diet, including lactose and sucrose, enhances the absorption of calcium.²⁹

On the whole, calcium was absorbed and retained very efficiently by most of the patients in all 4 groups. In this respect our patients seemed to resemble those of Holemans and Lambrechts,³⁰ who found that in Congolese children on very low intakes the values for absorption and retention of calcium and phosphorus were comparable with those in apparently healthy children in the same area.

No striking differences in absorption and retention of phosphorus were observed between the four groups. Considerable impairment in the absorption of phosphorus was present in all 4 groups, since healthy children on a mixed diet absorb about 70% of their intake,28 whereas in our cases the average values varied from 37 to 56%. In Jamaica, Waterlow and Wills³¹ found a slight impairment of absorption in malnourished infants during the first few days in hospital only. Urinary excretion of phosphorus was very low both in their patients and in ours, a finding which suggests a possible deficiency of phosphorus in the acute stage of kwashiorkor.

Urinary excretion of magnesium was very low in all the patients, a finding in agreement with that of Montgomery 32, 33 in Jamaica and probably indicative of a magnesium deficiency. Faecal excretion of magnesium was high in most of the patients of all 4 groups, often resulting in low or negative balances. The mean faecal excretion of magnesium was considerably higher in the whole-milk group than in the other groups. The possibility of an excessive loss in the form of magnesium soap arises, although, as with calcium, the differences between the 4 groups were not statistically significant.

Healthy children absorb about 87% of dietary potassium and 98% of dietary sodium.28 Gross impairment in the absorption of both these electrolytes was present in most of the patients in all 4 groups. Absorption of sodium was particularly poor in the patients in the skimmed milk + carbohydrate group, who absorbed on the average only 51% of their intake. Although the difference between this value and those obtained in the other groups was also not statistically significant, it is nevertheless possible that the excessive loss of sodium in this group bears some relationship to the high wet-weight of the stools.

The question arises whether the use of whole milk or of skimmed milk supplemented with vegetable oils should be recommended in all cases of kwashiorkor during the acute stage. As regards the effect on the diarrhoea alone, the use of such formulae appears to be advantageous, but there is no evidence that these diets reduced the mortality rate or increased the speed of recovery. It should be taken into account, however, that this investigation was carried out in a metabolic ward where proper nursing care and supervision were available. Severe diarrhoea, for instance, was detected early and loss of water and electrolytes was promptly remedied. Adequate medical and nursing care are seldom available in the technically underdeveloped countries, and it is conceivable that differences in response to treatment might be demonstrated if investigations similar to ours were carried out in a general children's ward.

SUMMARY

An investigation is described of the therapeutic effect of dried whole milk, acidified dried whole milk, dried skimmed milk with added sunflower-seed oil, and dried skimmed milk with added carbohydrate, on 120 Bantu infants suffering from kwashiorkor.

As judged by mortality rates, the rate of disappearance of oedema, changes in weight, and rise in serum-albumin concentration, the 4 diets appeared to be equally effective.

Control of diarrhoea, as assessed by the daily number of formed stools, was more readily effected by the 2 diets containing milk fat. Differences in the mean daily wetstool weights determined for 10 patients in each of the 4 groups suggested a greater loss of water in the stools of the patients who received skimmed milk with added carbohydrate than in those of the other groups, although the difference was not statistically significant. The mean daily dry-weight values of the faeces and the values for mineral excretion were also not significantly different in the 4 groups.

Balance studies carried out on 40 patients failed to reveal statistically significant differences between the 4 groups in respect of apparent absorption and retention of nitrogen, calcium, phosphorus and magnesium. The fatbalance results obtained in some of the patients of the 3 groups who received fat or oil also did not differ significantly, absorption being impaired in the patients in all 3 groups.

The characteristically high retention of nitrogen that occurs in kwashiorkor was evident in all 4 groups, in spite of some impairment of nitrogen absorption. Urinary excretion of magnesium and phosphorus was low in all the patients, probably indicating a deficiency of these minerals in the acute stage of kwashiorkor. Marked impairment in the absorption of potassium and sodium occurred in most of the patients studied, but the differences between the 4 groups were not significant.

It is concluded that the diets containing milk fat or sunflower-seed oil had no adverse effects and were very well tolerated. On the other hand there was no evidence that these diets were in any way specially beneficial, except that the diarrhoea appeared to be more effectively controlled.

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