'Added lactose' and 'added sucrose' cow's milk formulae in nutrition of low birthweight babies

AUDREY S. FOSBROOKE and BRIAN A. WHARTON*

Mothers' Hospital, Clapton, and Institute of Child Health, London

Fosbrooke, A. S., and Wharton, B. A. (1975). *Archives of Disease in Childhood*, 50, 409. 'Added lactose' and 'added sucrose' cow's milk formulae in nutrition of low birthweight babies. During the manufacture of dried milks for infant feeding the composition of cow's milk may be modified by the addition of extra carbohydrate powder to lower the relative proportions of protein and minerals, and in practice various carbohydrates are used in a largely empirical manner. In other circumstances it is known that the quality of dietary carbohydrate affects intestinal tolerance, deposition of body fat (in rats), and concentrations of plasma lipids (in man). Therefore, in this study the effects of feeding newborn infants on added lactose formula and added sucrose formula have been investigated. 29 low birthweight babies were observed throughout the first 3 months of life. The added carbohydrate achieved a satisfactory composition in terms of mineral and protein concentration of the reconstituted milk, but the 'added lactose' group experienced more diarrhoea and a greater degree of metabolic acidosis during the first week of life.

The added lactose group was slightly fatter and the plasma triglyceride concentration slightly higher than in the 'added sucrose' group. Despite teleological evidence in favour of lactose, we found no objective contraindication to the addition of sucrose to cow's milk in the manufacture of infant feeding formulae. Both milks contained only small quantities of linoleic acid and the polyunsaturated fatty acid content of the plasma and adipose tissue lipids fell to low levels, but no clinical evidence of 'essential fatty acid deficiency' was found.

During the manufacture of infant feeding formulae the composition of cow's milk may be modified by the addition of extra carbohydrate powder in order to achieve lower relative proportions of protein and minerals. Lactose is most commonly chosen, but maltodextrins and sucrose are also used. In the U.K. Cow and Gate Baby Milk 1, V formula, Premium, Ostermilk No. 1, SMA, S26, and Similac all have lactose added during manufacture, while Ostermilk Complete has maltodextrins added. In Europe maltodextrins and sucrose, as well as lactose, are commonly added (Widdowson, 1973). Factors governing the choice of carbohydrate have been recently reviewed (Wharton and Fosbrooke, 1975); lactose has teleological support but other sugars may be considered on the grounds of avoiding transient

lactose intolerance, the use of alternative gut transport systems, cost of the final products, etc. In rats, added lactose formulae result in leaner, though well grown, animals when compared to the effects of sucrose formulae (Tomarelli, Hartz, and Bernhart, 1960), while the occurrence of 'sucrose-induced hypertriglyceridaemia' in adult humans (Macdonald, 1965; Szanto and Yudkin, 1969) might be considered an argument against the use of added sucrose infant formulae.

This investigation was planned to study the effect of added lactose and added sucrose cow's milk formulae on the growth and fat metabolism of newborn human babies.

Patients and methods

Patients. Table I gives details of the patients studied. Low birthweight babies, weighing 1.5–2.1 kg at birth, admitted to the Special Care Baby Unit of the Mothers Hospital, Clapton, entered the study if their

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*Present address: Infant Development Unit and Sorrento Maternity Hospital, Birmingham.

TABLE I
Details of babies studied

Babies	Added sucrose formula	Added lactose formula
No. starting trial	12	17
No. withdrawn in first 2 w	1	5
No. completing 3 w	11 (3 boys)	12 (4 boys)
Gestation* (completed weeks)		
Mean $\pm$ SD	35.5 $\pm$ 2.8	35.3 $\pm$ 3.2
Range	(30–40)	(31–40)
Birthweight		
Mean $\pm$ SD	1.80 $\pm$ 0.19	1.88 $\pm$ 0.19
Range	(1.52–2.01)	(1.54–2.07)
Weight for gestation†		
10–50 centile	6 (55%)	7 (58%)
<10	5	5
No. leaving trial between 3 w and 3 m‡	4	4
No. completing 3 m in trial	7 (3 boys)	8 (1 boy)
Gestation (completed weeks)		
Mean $\pm$ SD	34.6 $\pm$ 3.2	33.8 $\pm$ 2.5
Range	(30–40)	(31–40)
Birthweight (kg)		
Mean $\pm$ SD	1.79 $\pm$ 0.21	1.81 $\pm$ 0.21
Range	(1.52–2.01)	(1.54–2.07)
Weight for gestation		
10–50 centile	4 (57%)	6 (75%)
<10	3	2

*Determined by maternal dates, and methods described by Dubowitz, Dubowitz, and Goldberg (1970).

†From date of British perinatal mortality survey (Butler and Alberman, 1969).

‡3 failed to return; 1 did not fast adequately; 4 received other food (usually cereals) as well as the trial milks.

mother was unable or unwilling to provide breast milk for them, and if she had given her informed consent to the investigation. Low birthweight babies were chosen for study firstly because their enforced stay in hospital allowed us to control their diet accurately; and secondly, it seemed probable that any differences in the effect of the two formulae would be more apparent in small babies. Of the babies entering the trial, a number were subsequently withdrawn for clinical reasons (see Results), and the remainder completed a minimum of 21 days on one or other of the two formulae before they were discharged home with a supply of the milk to continue until the age of 3 months. During the 21-day–3-month period, 8 babies were lost to follow-up. Table I shows that the babies receiving the added lactose and added sucrose formulae were similar in birthweight and gestational age. Both groups included two Indian babies and the rest were European. Anthropometric and biochemical results are given for the 23 babies who completed 21 days and the 15 who completed the full 3 months on the trial milks alone, while receiving no other food. 2 other babies completed the full 3 months but their results were subsequently excluded: one with cystic fibrosis and the other with peripheral pulmonary stenosis who had had normal serum calcium levels at diagnosis (5 m) and at 7 days, but possibly had had a period of undiagnosed hypercalcaemia.

Formulae and feeding regimens. The formulae were manufactured and supplied by Glaxo Laboratories. They consisted of dried cow's milk with added vitamins and iron, and either added lactose or added sucrose. The formulae were reconstituted in the Special Care Baby Unit on the morning of the day the feed was to be consumed, as a 17% w/v solution in water at 60° C.

Table II shows the composition of the reconstituted formulae; the composition of human milk and unmodified cow's milk is shown for comparison. In the added lactose formula all the carbohydrate was lactose, while in the added sucrose formula about three-fifths of the carbohydrate was sucrose and two-fifths lactose. The quantity of carbohydrate was the same in both milks and they were identical in all other respects. The fat content by our own gravimetric analysis was 3.5 g/100 ml, confirming the manufacturers information.

The added sucrose formula was given to the first 13 babies entering the trial, and the added lactose formula to the next 22 babies. The first feeds were given within 4 hours of birth to babies nursed initially at the optimum environmental temperature (Hey, 1971), subsequently aiming to maintain rectal temperature at 36.5–37.5° C. Indwelling polyvinyl intragastric tubes were used as necessary. Appropriate weight-for-dates babies (weight 10–90th centile for gestation, data of Butler and Alberman, 1969) received 40 ml/kg birthweight during the first 24 hours of life, the volume increasing by 20 ml/kg

TABLE II

Constituents of added lactose and added sucrose formulae compared to human milk and unmodified cow's milk

Nutrient	Contents/100 ml as fed (and /100 kcal)			
	Added lactose formula*	Added sucrose formula*	Human milk†	Unmodified cow's milk†
Carbohydrate (g)				
Lactose in milk	4.5 (5.6)	4.5 (5.6)	7.0 (10.4)	4.8 (7.3)
Added lactose	6.1 (7.6)			
Added sucrose		6.1 (7.6)		
Total	10.6 (13.2)	10.6 (13.2)		
% of energy	53%	53%	42%	29%
Protein (g)		2.1 (2.6)	1.2 (1.8)	3.3 (5.0)
% of energy		10%	7%	20%
Energy (kJ)		335	280	276
(kcal)		80	67	66
Fat				
Total		3.3 (5.0)	3.8 (5.7)	3.7 (5.6)
% of energy		37%	51%	51%
Fatty acid (g/100 g total)				As for added carbohydrate formulae
C12:0	4.5		6.0	
C14:0	12.1		9.0	
C16:0	30.4		28.3	
C16:1	2.3		3.0	
C18:0	17.2		8.0	
C18:1	32.3		37.3	
C18:2	1.2		8.4	
Minerals				
Iron (mg)	1.1 (1.3)		0.15 (.22)	0.10 (.15)
Calcium (mg)	69 (85)		33 (49)	125 (189)
Phosphorus (mg)	57 (70)		15 (22)	96 (145)
Sodium (mg)	30 (35)		15 (22)	58 (88)
(mEq)	1.3 (1.6)		0.65 (1.0)	2.5 (3.8)
Potassium (mg)	89 (110)		55 (82)	138 (209)
(mEq)	2.3 (3.0)		1.4 (2.1)	3.5 (5.2)
Renal solute load‡ (mOsm)		14.0 (17.5)	7.9 (11.8)	22.1 (3.3)

*Information from manufacturer; fat and fatty acids by our analysis.

†Macy and Kelly (1961).

‡Calculated by method of Ziegler and Fomon (1971).

each day, reaching 200 ml by the 9th day. Small-for-dates babies (weight < 10th centile) received 60 ml/kg birthweight on the first day, increasing by 30 ml/kg each day, reaching 200 ml by the 6th day. Thereafter, the volume remained at 200 ml/kg per day until day 21, after which the mothers were advised to give approximately 200 ml/kg per day according to appetite. For volume calculations, birthweight was used until this had been regained and then the volume was recalculated after each twice-weekly weighing. If plasma bilirubin concentration exceeded 10 mg/100 ml, extra sterile water (30% of the above volume) was given until the bilirubin level had fallen to <10 mg/100 ml for 24 h. Plasma bilirubin did not exceed 15 mg/100 ml in any child and phototherapy was not given.

Methods of assessment and analysis. Anthropometry was performed at birth, at 21 days, and at 3 months (weight: Salter spring balance; length: infant

measuring board; head circumference: steel tape; skin-fold thickness over biceps, triceps, and subscapular regions using calipers with 3 mm diameter heads).

Plasma lipids were estimated in cord blood and then at 21 days and 3 months after an 8-hour fast (cholesterol: Fosbrooke and Pringle, 1970; triglyceride and fatty acid composition of cholesterol ester and triglyceride: Fosbrooke and Tamir, 1968). Adipose tissue biopsies using a No. 1 needle were usually obtained at the same time and the fatty acid composition of the triglyceride determined (Fosbrooke and Tamir, 1968). Other biochemical estimations were performed at intervals by conventional methods.

Cross-sectional comparison, i.e. between the added lactose and added sucrose groups at one point in time have been tested for statistical significance with the Mann Whitney U test; while for sequential comparisons, i.e. results in the same groups at different points in time, the paired 't' test has been used.

Results

Clinical. One of the 12 children starting the added sucrose formula and 5 of the 17 starting the added lactose formula were withdrawn because of diarrhoea: 3 of the children receiving the added lactose had reducing substances in the stools of 1% or more, and 2 of these had marked metabolic acidosis.

Anthropometry. The Fig. shows the changes in anthropometry of the two groups of children who completed 21 days and 3 months on the trial. At birth the groups were similar in size, but the added lactose babies had significantly thicker skinfolds at 21 days and 3 months than the added sucrose babies. The added lactose babies were a little heavier and slightly longer at 21 days and 3 months, but these differences were not statistically significant.

FIG.—Changes in head circumference, length, weight, and skinfold thickness (biceps + triceps + subscapular) in the two groups of babies. ● ■ Added sucrose, 11 babies at birth and 21 days, 7 at 3 months; △ □ added lactose, 12 babies at birth and 21 days, 8 at 3 months. Total skinfold thickness (mm) at 21 days in the added lactose group (mean $5.7 \pm \text{SD } 1.3$) was significantly greater ($P < 0.02$) than in the added sucrose group (4.8 ± 1); and at 3 months the total skinfold thickness in the added lactose group (10.9 ± 2.6) was significantly greater ($P < 0.03$) than in the added sucrose group (8.7 ± 2.2), using the Mann Whitney U test.

Plasma and adipose tissue lipids. Table III shows the plasma lipid concentrations. In general triglyceride concentration was low at birth (though the mean value for triglyceride for the 11 babies at birth who were in the added sucrose group was raised by two babies with unusually high values), and rose throughout the 3 months. At 3 months the triglyceride concentration was significantly higher in the added lactose group than in the added sucrose group.

Plasma cholesterol concentration increased markedly from birth to 3 weeks and thereafter remained unchanged at 3 months. There was no difference between the 2 groups in cholesterol concentrations.

Table IV shows the fatty acid composition of plasma and adipose tissue lipids. The values were similar in the added lactose and added sucrose group throughout the trial. Sequential changes in both groups during the 3 months occurred mainly in the proportions of the unsaturated fatty acids. For example, (i) C18:2 in adipose tissue remained low throughout; in plasma triglyceride the value fell by 3 weeks and was at the same level at 3 months; in plasma cholesterol ester the value fell at 3 weeks but at 3 months the level had returned towards that present at birth. (ii) C20:4 in cholesterol ester fell to a very low level at 3 weeks and remained low at 3 months. (iii) C16:1—in plasma triglyceride and cholesterol ester the level rose at 3 weeks and then fell by 3 months. (iv) C18:1—in plasma triglyceride and cholesterol ester the level increased at 3 weeks, and in adipose tissue the level rose throughout the 3 months.

Other findings. Table V shows the results of the other biochemical determinations in the two groups. The babies receiving the added lactose formula had slightly lower serum albumin levels at 7 and 21 days and experienced a greater degree of metabolic acidosis during the first week of life.

Follow-up. 16 of the 23 babies completing 21 days in the trial were seen at the corrected age of 10–22 months. Table VI shows the assessment of these children. The added sucrose group (at a mean corrected age of 22 months) had a slightly higher centile distribution for weight, length, and skinfolds than the added lactose group (at a mean corrected age of 13 months), but these differences were not significant. The development quotient was similar and within normal limits in the two groups. Physical examination was normal: no flexural skin lesions were observed.

Replies were received from the family doctor or health visitor concerning 5 other children in the

TABLE III

Plasma lipid concentration in two groups of babies

Plasma lipid and groups of babies	Plasma concentrations at various ages (mean $\pm$ SEM)					
	Birth		3 w		3 m	
	No. of babies	mg/100 ml	No. of babies	mg/100 ml	No. of babies	mg/100 ml
Triglyceride						
(a) In babies completing 3 w on trial						
Added sucrose group	11	54 $\pm$ 12.7	(11)	56 $\pm$ 7.8		
Added lactose group	10	39 $\pm$ 6.6	(10)	71 $\pm$ 11.4		
						$P < 0.05$
(b) In babies completing 3 m on trial						
Added sucrose group	7	29 $\pm$ 4.5	(7)	45 $\pm$ 6.1	7	68 $\pm$ 13.2*
Added lactose group	8	36 $\pm$ 7.8	(8)	63 $\pm$ 11.3	8	92 $\pm$ 4.6†
						$P < 0.05$
Cholesterol						
(a) In babies completing 3 w on trial						
Added sucrose group	11	100 $\pm$ 12.4	(11)	174 $\pm$ 10.0		
Added lactose group	10	93 $\pm$ 5.1	(10)	161 $\pm$ 7.3		
						$P < 0.001$
(b) In babies completing 3 m on trial						
Added sucrose group	7	89 $\pm$ 8.7	(7)	173 $\pm$ 12.1	7	160 $\pm$ 10.2
Added lactose group	8	96 $\pm$ 5.7	(8)	169 $\pm$ 6.7	8	159 $\pm$ 12.4
						$P < 0.001$

P represents significance of difference between means using paired 't' test; values > 0.10 not shown.*Mean significantly greater than at birth (paired 't' test, $P < 0.02$).†Mean significantly greater than at birth (paired 't' test, $P < 0.001$), and significantly greater than in added sucrose group (Mann Whitney U test, $P < 0.01$).

trial, all of whom were apparently thriving. The remaining 2 children were completely lost to follow-up because the family had moved house.

Discussion

The addition of carbohydrate to cow's milk in these two experimental formulae successfully reduced the concentration of protein and minerals and also the resulting renal solute load to levels nearer those in human milk, particularly when they were expressed in relation to the energy content. This reduction was reflected in the 'satisfactory' plasma calcium levels found on day 7.

Differences in first week. The added lactose milk was associated with two problems in the early days of life. First, diarrhoea sufficiently severe to require alteration of diet and withdrawal from the trial was more common. Work *in vitro* suggests that the gut of the term baby at birth may not be able to hydrolyse more than 8 g lactose/kg body weight per day (compared to the 6 g/kg received by the small-for-dates babies on the added lactose diet during day 1, rising to 21.2 g/kg per day by day 6). Furthermore, the transient developmental lactase deficiency occurring in many preterm babies would result in a great susceptibility to diarrhoea (Auric-

chio, Rubino, and Mürset, 1965). Nevertheless, 8 of the 12 babies completing 21 days on the added lactose diet were born at 36 weeks' gestation or less; it seems that a number of preterm babies can handle much larger quantities of lactose without diarrhoea than *in vitro* studies suggest. The added sucrose diet was tolerated well by all except one baby, presumably because the amount of lactose received (9 g/kg per day by day 6 in small-for-dates babies and by day 9 in those appropriate-for-weight) did not exceed the hydrolytic capacity of the available lactase, while jejunal sucrase (present from the 6th month of gestation) was sufficient to handle the added sucrose (12.2 g/kg per day by day 6 in small-for-dates babies, and by day 9 in those appropriate-for-weight).

A second difference observed during the first week was the greater degree of metabolic acidosis in the added lactose group. After the first week the acid-base balance was similar in both groups. Possibly this difference was due to the absorption of organic acids formed by fermentation in the colon of lactose which had not been hydrolysed in the small bowel. However, there are other possible explanations, e.g. lactose may enhance calcium retention in the bones (Gerstley, Cohn and Lawrence, 1945) leading to a flux of hydrogen ions from the bones to the blood. Whatever the explanation, the degree of acidosis did not require

TABLE IV
Fatty acid composition of plasma and adipose tissue lipids in two groups of babies

Fatty acid and groups of babies	Fatty acid composition at various ages* (g/100 g total fatty acid, mean $\pm$ SEM)									
	Plasma triglyceride			Plasma cholesterol ester			Adipose tissue triglyceride			
	Birth	2 w	3 m	Birth	3 w	3 m	Birth	3 w	3 m	
Added sucrose group (no.)	11	11	7	11	11	7	4	8	7	
Added lactose group (no.)	10	10	8	10	10	8	9	10	8	
Fatty acids (values for sucrose group first line)*										
C14:0	4 $\pm$ 0.6 3 $\pm$ 0.6	4 $\pm$ 0.1 4 $\pm$ 0.5 P < 0.01	5 $\pm$ 0.8 6 $\pm$ 0.4	3 $\pm$ 0.5 3 $\pm$ 0.4	3 $\pm$ 0.2 3 $\pm$ 0.2	3 $\pm$ 0.2 3 $\pm$ 0.2	5 $\pm$ 0.5 4 $\pm$ 0.3	7 $\pm$ 0.2 6 $\pm$ 0.4	8 $\pm$ 0.4 6 $\pm$ 0.2	
C16:0	32 $\pm$ 1.0 32 $\pm$ 1.3	30 $\pm$ 1.5 31 $\pm$ 1.2	34 $\pm$ 0.4 34 $\pm$ 0.4	22 $\pm$ 1.2 21 $\pm$ 0.9 P < 0.01	17 $\pm$ 0.4 17 $\pm$ 0.6	16 $\pm$ 0.5 17 $\pm$ 1.0	43 $\pm$ 0.8 P < 0.02 44 $\pm$ 0.7 P < 0.01	39 $\pm$ 0.8 39 $\pm$ 1.1	37 $\pm$ 0.9 36 $\pm$ 1.0	
C16:1	8 $\pm$ 0.7 P < 0.05 10 $\pm$ 0.8	11 $\pm$ 1.0 12 $\pm$ 1.4	9 $\pm$ 0.4 8 $\pm$ 0.7	12 $\pm$ 1.6 13 $\pm$ 0.8 P < 0.01	20 $\pm$ 1.3 21 $\pm$ 2.4 P < 0.05	14 $\pm$ 1.5 14 $\pm$ 1.5	14 $\pm$ 0.5 15 $\pm$ 0.7	14 $\pm$ 1.6 15 $\pm$ 0.5	12 $\pm$ 0.4 13 $\pm$ 0.5	
C18:0	6 $\pm$ 0.5 6 $\pm$ 0.5	5 $\pm$ 0.3 5 $\pm$ 0.7	5 $\pm$ 0.8 6 $\pm$ 0.4	3 $\pm$ 0.4 4 $\pm$ 0.4	3 $\pm$ 0.2 3 $\pm$ 0.3	3 $\pm$ 0.3 3 $\pm$ 0.3	5 $\pm$ 0.8 4 $\pm$ 0.3	4 $\pm$ 0.5 4 $\pm$ 0.3	5 $\pm$ 0.4 4 $\pm$ 0.2	
C18:1	44 $\pm$ 1.4 P < 0.01 43 $\pm$ 1.6	50 $\pm$ 1.1 P < 0.05 47 $\pm$ 1.1	46 $\pm$ 0.8 45 $\pm$ 1.1	34 $\pm$ 2.1 P < 0.001 38 $\pm$ 1.7 P < 0.001	50 $\pm$ 0.7 49 $\pm$ 1.3	51 $\pm$ 0.8 48 $\pm$ 1.4	29 $\pm$ 0.8 30 $\pm$ 0.5 P < 0.001	33 $\pm$ 1.4 35 $\pm$ 0.7 P < 0.002	36 $\pm$ 0.9 39 $\pm$ 0.9	
C18:2	7 $\pm$ 1.5 P < 0.001 6 $\pm$ 0.7 P < 0.001	< 1 $\pm$ 0.2 1 $\pm$ 0.5	1 $\pm$ 0.3 2 $\pm$ 0.7	17 $\pm$ 3.5 P < 0.01 13 $\pm$ 1.9 P < 0.02	5 $\pm$ 0.2 P < 0.001 7 $\pm$ 0.6 P < 0.001	12 $\pm$ 1.1 13 $\pm$ 1.1	3 $\pm$ 0.2 2 $\pm$ 0.2	2 $\pm$ 0.5 2 $\pm$ 0.4	2 $\pm$ 0.7 < 1 $\pm$ 0.1	
C20:4				9 $\pm$ 1.5 P < 0.001 9 $\pm$ 1.3 P < 0.001	1 $\pm$ 0.3 2 $\pm$ 0.3	2 $\pm$ 0.4 2 $\pm$ 0.4				

P, significance of difference between means using paired 't' test; values > 0.10 not shown.

* Values quoted only for those fatty acids exceeding 1%.

† Mean significantly greater than at birth (paired 't' test, P < 0.001).

TABLE V

Concentration of various substances in blood of babies receiving added sucrose and added lactose formulae

Blood constituents (mean $\pm$ SEM)	Formulae		Significance of difference between means (P)*
	Added sucrose	Added lactose	
Haemoglobin (g/dl)			
7 d	15.4 $\pm$ 0.5	17.3 $\pm$ 0.8	
14 d	14.6 $\pm$ 0.9	16.3 $\pm$ 0.8	
21 d	12.0 $\pm$ 0.5	13.2 $\pm$ 0.6	
3 m	10.7 $\pm$ 0.7	10.8 $\pm$ 0.4	
Serum iron (μ g/100 ml) at 3 m	80 $\pm$ 6	71 $\pm$ 4	
Serum albumin (g/100 ml)			
7 d	3.9 $\pm$ 0.1	3.4 $\pm$ 0.1	<0.05
14 d	3.5 $\pm$ 0.1	3.3 $\pm$ 0.1	
21 d	3.9 $\pm$ 0.1	3.5 $\pm$ 0.1	<0.05
3 m	4.4 $\pm$ 0.2	4.3 $\pm$ 0.1	
Acid-base balance (Pco ₂) (mmHg)			
2 d	41 $\pm$ 4	44 $\pm$ 3	
7 d	39 $\pm$ 2	40 $\pm$ 1	
14 d	37 $\pm$ 2	41 $\pm$ 1	
21 d	36 $\pm$ 2	36 $\pm$ 1	
Base excess			
2 d	1.4 $\pm$ 1.2	-1.4 $\pm$ 1.1	$\approx$ 0.08
7 d	-2.6 $\pm$ 1.3	-7.2 $\pm$ 1.1	<0.05
14 d	-8.1 $\pm$ 1.8	-6.3 $\pm$ 1.7	
21 d	-5.8 $\pm$ 1.9	-5.2 $\pm$ 1.9	
Day 7			
Calcium (mg/100 ml)	8.4 $\pm$ 0.3	9.0 $\pm$ 0.4	
No. of children with calcium <7mg/100 ml	Nil	1	
Phosphorus (mg/100 ml)	7.8 $\pm$ 0.4	7.7 $\pm$ 0.7	
Alkaline phosphatase (IU/l)	156 $\pm$ 21	158 $\pm$ 20	
Magnesium (mEq/l)	2.0 $\pm$ 0.1	2.0 $\pm$ 0.1	
Blood glucose (mg/100 ml) before feed on day 2	46 $\pm$ 6.5	46 $\pm$ 4	

*Mann Whitney U test. Significance of differences between other means, $P > 0.10$.

treatment, nor was there any suggestion of an increased weight loss in the added lactose group as has been described in acidosis associated with high protein intakes (Kildeburg and Winters, 1972).

Anthropometry. Anthropometric findings were unlike what might have been predicted from observations made in rats in that the added lactose group were not leaner—they were, in fact, a little fatter. Lactose-fed rats ate less and had less body fat (8% cf 14%) than rats receiving glucose, sucrose, or maltodextrins, and this difference in body composition was still apparent if the intake of the glucose-fed rats was kept down to that of the lactose-fed ones (Tomarelli *et al.*, 1960). They concluded, however, that this difference in fat deposition in the rats was related more to intestinal events than to changes in intermediary metabolism, since glucose/galactose mixtures did not mimic the effects of lactose, and increasing proportions of

dietary lactose were associated with smaller proportions of body fat, increased size of the caecum, and transient diarrhoea. Perhaps if the added lactose milk had been continued in the babies who developed diarrhoea they would have gained less weight and have been less fat, i.e. shown the same response to lactose as that observed in rats.

Plasma and adipose tissue lipids. In adult men high sucrose diets (e.g. up to 500 g/day) may result in an increased concentration of plasma lipids (Macdonald, 1965; Szanto and Yudkin, 1969), although it is uncertain whether this is a specific effect of sucrose or that of a high carbohydrate diet (Mann *et al.*, 1973; Anderson *et al.*, 1963). In this study the added sucrose milk did not result in higher cholesterol, nor triglyceride; in fact plasma triglyceride was significantly higher in the added lactose group.

There are few values for plasma triglyceride

TABLE VI
Assessment of two groups of babies at 10-22 months' corrected age

	Added sucrose (no. = 8)	Added lactose (no. = 8)
Corrected age at follow-up (mean and range)	20 m (18-22)	13 m (10-18)
No. of children within centile bands for age		
Weight*		
90-50	2	-
50-10	3	6
<10	3	2
Length*		
>90	1	-
90-50	3	1
50-10	3	6
<10	1	1
Head circumference*		
>90	-	1
90-50	2	2
50-10	3	5
<10	3	-
Triceps skinfold†		
>90	-	-
50-90	4	2
10-50	3	3
<10	1	3
Subscapular skinfold†		
>90	1	1
50-90	4	3
10-50	3	4
<10	-	-
Developmental quotient‡ (mean and range)		
Motor	104 (86-116)	109 (100-120)
Social	92 (86-100)	109 (91-130)
Hearing and speech	94 (68-116)	100 (71-120)
Eye and hand	100 (88-109)	100 (85-116)
Total	98 (87-109)	104 (86-120)

*According to data summarized by Gairdner and Pearson (1971).
†According to Tanner and Whitehouse (1962), but note that published standards are for Harpenden calipers (not used by us) on a small number of children.

‡According to Birmingham Children's Hospital Development Chart (Wood, 1970).

concentration during infancy because of the difficulty in fasting babies having frequent feeds. We used an 8-hour fast, as in the study of Tamir *et al.* (1972) in which infants aged 4-11 months were given 5 days of high carbohydrate diets. They found that feeding both sucrose and glucose to give 73% total calories (in place of the 39% calories supplied by glucose in the basal diet) resulted in similar, marked increases in plasma triglyceride. Our diets provided about 53% of energy as lactose and/or sucrose, and the mean value for plasma triglyceride in our 3-month babies was intermediate between their values for the baseline and high carbohydrate diets in their differently organized but relevant study. The values for triglyceride concentration reported by Olegard and Svennerholm

(1970) are much higher, but their blood samples were collected after only 4 hours' fast at which time fat from the previous feed contributes to the triglyceride level.

We do not know why the added lactose diet resulted in higher serum triglyceride levels. Nestel, Carroll, and Havenstein (1970) and Reaven *et al.* (1967) have emphasized the association between triglyceride concentration and plasma insulin levels in adults on high carbohydrate diets. We did not measure insulin, but in the absence of the relevant data we have speculated whether the lactose might have stimulated more insulin secretion than the sucrose, thus favouring more fatty acid synthesis and storage in adipose tissue (Maruhama and Macdonald, 1973). It is conceivable that lactose-fed subjects might have higher insulin levels because absorption of galactose (as well as that of the glucose) results in insulin secretion (Berger *et al.*, 1973), whereas after sucrose, only the glucose moiety is insulinogenic (Cook, 1970). Whatever the exact mechanism, the use of sucrose was certainly not associated with unduly high plasma triglyceride concentrations during the 3-month study.

Clinical implications. It is evident that added carbohydrate alone, without any other action, will achieve a reduction in the mineral and protein content of cow's milk, which is of practical importance in infant nutrition. In our experience, however, the simple addition of lactose caused diarrhoea in a proportion of low birthweight babies, whereas added sucrose was not associated with any apparent embarrassment of gut function. In this small series of babies the added sucrose milk was not associated with greater fatness nor higher plasma lipids. Despite the teleological arguments in favour of lactose, we have found no objective evidence to caution the addition of sucrose rather than lactose. This addition should be quantitatively correct and, therefore, made during the process of manufacture and not by the individual mother when she is making up the milk. Since sucrose is considerably sweeter than lactose the use of sucrose formulae might result in a 'sweet tooth'. We know of no evidence of this.

Fatty acid composition of lipids. The sequential changes in the fatty acid composition of the plasma and tissue lipids were similar in both groups and so were not related to the quality of the dietary carbohydrate. Though not directly relevant to this investigation, these results are nevertheless of interest because they detail changes in the

natural biochemical and nutritional history of babies receiving a cow's milk formula and because the cow's milk used as the basis for the formulae was low in polyunsaturated fatty acids.

The milks used contained only 0.5% total calories as C18:2, and probably only a minor proportion of this C18:2 content would be the cis:cis w9 isomer, i.e. linoleic acid (Garton, 1963; Hilditch and Williams, 1964). The polyunsaturated fatty acids do have a number of important biological functions such as their role as components of membrane lipids and as precursors of prostaglandins (Alfin-Slater and Aftergood, 1968; Guarneri and Johnson, 1970). Hansen *et al.* (1962) and Holman, Caster, and Wiese (1964) concluded it was necessary to give 1.4% total calories in the form of linoleic acid to avoid 'essential fatty acid (EFA) deficiency' leading to defective skin and hair, and poor growth. We did not find any clinical evidence of EFA deficiency, in fact skin, hair, and growth were satisfactory both at 3 months and again when the children were examined at 10-22 months. The levels of the polyunsaturated fatty acids (C18:2, C20:4) in the plasma lipids fell considerably, probably reflecting the very low levels of these fatty acids in the dietary fat; and this fall was accompanied by a considerable increase in the proportion of the monoenes (C16:1, C18:1) similar to that found in rats with EFA deficiency. We did not observe the appearance of C20:3, w9, usually taken as the chemical marker of EFA deficiency in the rat (Holman, 1960), though we did not analyse the fatty acids of the phosphatidyl choline fraction which is most likely to accumulate this endogenously synthesized polyunsaturate.

The increase in C18:2 in the cholesterol ester fraction between 3 weeks and 3 months was unexpected in view of its consistently low content in the diet. However, the daily intake of milk and therefore the daily intake of C18:2 did increase during the 3 months and perhaps the extremely selective chemical process whereby C18:2 is concentrated in cholesterol ester may account for the rise. No other foods were given over this period, and we excluded the data of those babies who had received other foods (see Table I). An alternative *a priori* explanation might be endogenous synthesis of C18:2, but there is no evidence for such a synthetic pathway.

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- Correspondence to Dr. B. A. Wharton, Infant Development Unit, Queen Elizabeth Medical Centre, Edgbaston, Birmingham B15 2TG.