

Energy balance, nitrogen balance, and growth in preterm infants fed expressed breast milk, a premature infant formula, and two low-solute adapted formulae

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SUMMARY Energy balance, nitrogen balance, and growth studies were done in 37 preterm infants (20 of very low birthweight) who were fed on expressed breast milk or on one of 3 formulae each of different composition, including a special premature formula and a highly adapted 'humanised' formula. The variability of breast milk composition was such that it would have been difficult to predict the infants' protein and energy intakes under normal nursing conditions. All measured parameters of nutritional performance were best in infants fed on the 'premature' formula and were reflected in greater weight gain, linear growth, and head growth. The nitrogen balance data suggest that the highly adapted formula, which had a protein content comparable with that of mature human milk, contained too little protein for small preterm infants.

Although much has been written and spoken about the feeding of preterm infants, there is no agreement on what is best. Current opinion probably favours breast milk¹⁻⁴ but this is not supported by strong evidence that it is better than, or even as good as, specially adapted cows' milk formulae as a source of nutrients for the very immature. The arguments for using human milk are based on work on its immunological and anti-infective properties,^{5,6} on the prevention of necrotising enterocolitis,⁷ on the greater biological suitability of its proteins,² on improved fat absorption,⁸ and on psychological and emotional factors. The available data do not make a convincing case because no long-term differences in outcome favouring breast milk have been demonstrated. Possibly even the reverse is true, if the preliminary finding⁹ can be confirmed, that the development of very small infants fed banked human breast milk is less satisfactory than that of similar infants fed a premature formula. In the short term there may be nutritional problems with human milk. Its composition is variable,^{10,11} and it may be deficient in energy, protein, minerals, and trace elements.¹²⁻¹⁶ Such deficiencies can on occasion limit growth and prevent the infant from thriving.^{9,14} The studies described here were designed to investigate energy and nitrogen balance, the aspects of nutrition most obviously connected with growth, in preterm

infants fed with human milk and cows' milk-based formulae. The formulae selected were a modern low-solute adapted milk with a low protein content, a more traditional infant formula with higher protein content, and a special 'premature' formula.

Patients and methods

Infants. Details of the 37 infants studied are given in Table 1. Gestation was confirmed by Dubowitz's method¹⁷ if in doubt, but most had early ultrasound dating. All infants were well at the time that they were studied. None had significant malformations. Twenty were of very low birthweight (<1500 g). Twenty-one were small for gestational age, defined as having a birthweight <10th centile for gestational age using Gairdner's charts.¹⁸ This reflects the practice of the obstetric unit, which acts as a referral centre for complicated pregnancies. In most cases the fetal growth retardation was the result of pre-eclampsia, essential hypertension, or placental abruption. Seven infants were studied more than once. To compare the different feeds, infants were matched for birthweight, gestation, and age at time of study (see page 901). Measurements were made during a total of 71 weeks, on average 2 weeks per baby. Informed parental consent was obtained and the studies were approved by the hospital's ethical committee.

Table 1 Details of infants studied

Gender	Birthweight (g)	Gestation (weeks)	Age at study (days)	Mean weight at study (g)
F	890	26	53	1370
F	1000*	33	24	1110
F	1040	28	34, 43	1590, 1830
F	1040*	32	17	1340
M	1050*	32	20, 33	1520, 2090
F	1110	29	20	1920
F	1120*	30	20	1280
F	1160*	32	17	1210
F	1160*	33	17	1260
M	1190*	32	7, 25	1190, 1630
M	1200*	32	21	1530
F	1210	31	24, 38, 56	1320, 1600, 1850
F	1220*	33	13, 28	1270, 1590
F	1260*	32	28	1560
F	1260	28	16	1360
F	1280*	34	8	1360
F	1340	31	12	1310
F	1380*	34	15	1740
F	1480*	35	11	1760
M	1540*	34	15, 24	1820, 2160
M	1540*	34	11	1670
M	1540*	35	13	1870
F	1540*	34	13	1540
F	1600	31	15	1780
F	1630*	35	5	1650
F	1650	34	27	1930
M	1680	33	6	1705
F	1700*	36	14	1920
M	1700	32	17	1960
F	1700	32	13	1780
F	1780	30	25	1870
M	1790	32	17, 24	1950, 2160
M	1860*	35	7	2020
F	2300	32	8	2170
M	2000*	35	5	1980
F	1460	31	17	1530
M	1720	32	25	1850
				1665 ± 290
1436 ± 317		32.3 ± 2.2	20 ± 11	

* < 10th weight centile.¹⁸

Feeding and study design. Most infants of very low birthweight had an initial period of partial or total parenteral feeding. Thereafter they were fed intra-gastrically, either continuously or by hourly gavage at the start, later working up to 3-hourly gavage. A few of the larger infants were studied after they had achieved partial or full bottle feeding but tube feeding was used throughout the balances in most of them. Enteral feeding was begun either with expressed

breast milk (EBM) or with the low protein formula (Osterfeed, see page 900), depending on the availability of breast milk and the mother's wishes. Thereafter selection of the feed for study was determined solely by the need to match the groups of infants for birthweight, gestation, and postnatal age. The study feed was begun 1-2 weeks after the infant had been established on full enteral feeding, and was receiving an intake of at least 180 ml/kg daily. Data on matching of the infants are shown in Tables 2 and 3. Random allocation was not considered feasible because of the fairly small numbers of suitable infants and the effects of gestational age and birthweight on postnatal digestive function and growth,^{19, 20} which make matching mandatory unless

Table 3 Details of matching for gestation and postnatal age in all infants studied

	Pre-Aptamil	Osterfeed	EBM	Milumil
Gestation (weeks)	34	34	34	
Postnatal age (days)	15	15	11	
Gestation (weeks)	28	26	28	
Postnatal age (days)	48	51	43	
Gestation (weeks)	32	33	32	32
Postnatal age (days)	25	28	28	22
Gestation (weeks)	35	35	36	53
Postnatal age (days)	5	7	12	10
Gestation (weeks)	32	33	33	31
Postnatal age (days)	20	18	24	13
Gestation (weeks)	32	32	31	32
Postnatal age (days)	17	13	15	25
Gestation (weeks)	32	32	30	31
Postnatal age (days)	17	17	20	25
Gestation (weeks)	33	32	34	
Postnatal age (days)	7	7	8	
Gestation (weeks)		32	32	
Postnatal age (days)		32	27	
Gestation (weeks)	35	35		
Postnatal age (days)	11	13		
Gestation (weeks)	34	24		
Postnatal age (days)	34	27		

Table 2 Matching for gestational age, birthweight, and age at time of study in the 4 groups of infants

	Number of infants	Birthweight (g) ± SD	Gestation (weeks) - SD	< 10th centile	Age at study (days) ± SD
Pre-Aptamil	10	1337 ± 265	32.8 ± 1.9	8	19.4 ± 10.1
Osterfeed	10	1381 ± 299	32.6 ± 2.6	8	19.3 ± 13.8
Pre-Aptamil	9	1267 ± 276	32.3 ± 1.8	7	21.3 ± 11.1
EBM	9	1304 ± 252	32.3 ± 2.3	7	19.4 ± 8.4
EBM	8	1328 ± 313	32.1 ± 2.7	6	19.1 ± 15.2
Osterfeed	8	1318 ± 266	32.4 ± 2.5	6	19.3 ± 8.9
Milumil	5	1536 ± 306	32.2 ± 1.6	3	19.0 ± 8.4

unrealistically large numbers are studied. We elected not to use a crossover design, which would have increased the numbers, because of difficulties in ensuring that the design was balanced and because of the necessarily shortened period during which an infant could be studied on any one feed.

Composition of feeds. Infants were fed on pasteurised* EBM (generally the mother's own but occasionally supplemented by banked EBM), Osterfeed (Farley Health Products, Plymouth), Milumil (Milupa Ltd, Hillingdon), or Pre-Aptamil (Milupa Ltd). Osterfeed is a cows' milk-based, low-solute, highly adapted infant formula. It is recommended for the formula feeding of term infants but is also used for feeding preterm infants in neonatal units in the UK. Milumil is a more 'traditional' cows' milk-based infant formula with higher protein and mineral content than Osterfeed, although the composition meets the ESPGAN criteria for formula feeds for neonates.²¹ Pre-Aptamil is a special premature formula adapted to meet the theoretical requirements for increased protein, energy, and minerals.²² Details of the composition of the formulae are given in Table 4. All were given as ready-to-feed liquid preparations. The total energy content of the formulae was determined by ballistic bomb calorimetry.²³ Their nitrogen content was analysed by the Kjeldahl technique using a semiautomated method. The breast milk was analysed for total energy and nitrogen during each balance. The energy content of the breast milk ranged from 49 to 76 (mean 64 ± 8) kcal/100 ml and its nitrogen content from 173 to 390 (mean 276 ± 76) mg/100 ml.

Balances. Energy and nitrogen balances were performed during 3 days between carmine markers,

* 30 minutes at 65°C.

Table 4 Composition of the formulae (per 100 ml) fed to the infants

	Osterfeed	Milumil	Pre-Aptamil
Energy (kcal)	68	68	76
Protein (g)	1.45	1.85	2.1
Protein energy (% of total)	9	11	11
Whey:casein ratio	61:39	20:80	55:45
Carbohydrate (g)	6.96*	8.4†	8.7*
Fat (g)	3.8‡	3.1‡	3.6§
Total minerals (g)	0.19	0.29	0.3
Sodium (mg)	19	27	38.5
Potassium (mg)	57	86	94.0
Calcium (mg)	36	71	67.0
Phosphorus (mg)	31	55	47.0
Magnesium (mg)	5	7	7.8
Osmolality (mOsmol/kg)	283	342	374

*Lactose.

†Lactose 6%, maltodextrin 1.3%, amylase 1.1%.

‡Cows' milk fat and vegetable oils.

§Cows' milk fat and vegetable oils, no MCT.

and were done between 4 and 10 days after the start of the study feed. Intakes were weighed. Small vomits were collected on weighed absorbent pads for later analysis and subtraction from the intake. No infant with clinically significant vomiting was studied. Excreta were collected in preweighed disposable napkins (Redinaps, Robinsons of Chesterfield, Wheat Bridge, Chesterfield, Derbyshire) and acrylic napkin liners (Boots Co Ltd, Nottingham). Special care was taken to ensure that the napkins fitted closely round the waist and thighs to prevent leakage. The liners retain the stool and allow the urine to pass through into the absorbent napkin. Although this does not give complete separation of faeces and urine, such separation is not essential for input/output balances. However the isolation of the faeces by this method is good²⁴ and the results obtained for faecal and urinary nitrogen are very similar to those found in other studies on preterm infants in which urine was collected separately.^{25, 26} At each napkin change, all stool was carefully removed from the buttocks and placed with the liner in a sealed polyethylene bag, as was the napkin containing urine. Each was promptly frozen at -20°C in a freezer kept in the unit. Stools were subsequently weighed, with subtraction for the weight of the liner, and freeze-dried. After thorough homogenisation they were analysed for energy by ballistic bomb calorimetry, in quadruplicate or quintuplicate, and for nitrogen by the Kjeldahl technique in duplicate.

Urine volume was calculated from the weight of the napkins, which were then separated from their plastic backing and pulped in a bucket containing a known volume of water (allowed for in the calculations). After thorough mashing, the homogenate was filtered through a large vacuum funnel and aliquots were freeze-dried for bomb calorimetry and the Kjeldahl nitrogen analysis. Water blanks were used to ensure that no nitrogen was recoverable from unsoiled napkins. Vomit pads were treated in the same way as the urine, and their calculated energy and nitrogen content was subtracted from the intake for the day. Digestible energy was defined as dietary energy minus faecal energy. Fat absorption coefficient was defined as dietary fat—faecal fat/faecal fat $\times 100$. Nitrogen retention was defined as dietary N minus urine and faecal N.

Growth measurements. All infants were weighed daily to the nearest 10g increment on a well-calibrated beam balance (Marsden Weighing Machines, London). Weight gains were expressed as g/kg a day, where the denominator was the mean body weight over the measurement period. The following twice weekly measurements were also made: (1) Crown-to-heel

length, to the next succeeding mm on a horizontal stadiometer.²⁷ (2) Upper arm length, to the next succeeding mm, measuring from the shoulder to the flexed elbow with a caliper.²⁸ (3) Occipito-frontal head circumference, to the next succeeding mm using a paper tape trimmed to exact zero. (4) Mid-upper arm circumference, using paper tape in the same way as for head circumference and taking particular care not to compress the tissues. (5) Biceps, triceps, and subscapular skinfolds,²⁹ using a Harpenden caliper (British Indicators Limited), the readings being taken when the jaws had ceased contracting on the fold. (6) Upper arm fat area³⁰ was calculated from mid-upper arm circumference, biceps, and triceps skinfold using the formula: fat area = arm area minus lean area, where: lean area = $\frac{1}{4\pi}$ [arm circumference - $\frac{\pi}{2}$ (triceps + biceps skinfold)]².

Metabolic monitoring. Weekly measurements of urea, electrolytes, and acid base status were made and urine specific gravity was monitored.

Analysis of results. Data on energy and nitrogen balance in preterm infants are likely to be skewed because of the effects of the varying degree of immaturity. However the study design ensured adequate pair matching between infants fed on Pre-Aptamil and those fed on Osterfeed and EBM (Tables 2 and 3). The results for these 3 feeds were therefore compared using Student's *t* test. Fewer

infants were studied on Milumil because this formula was not particularly well tolerated by preterm infants. However, the mean gestation and age at study in this group did not differ from the other groups, so the results of Milumil feeding were compared with the others in the same way. Because standards for intrauterine growth in weight, length, and head circumference are available¹⁸⁻³¹ the postnatal increments in these measurements in our infants were compared as a percentage of the 50th centile of an intrauterine standard during the same postconceptional age period. These results are expressed as coefficients of weight, length, and head growth. Growth rates the same as the intrauterine standard are expressed as unity, and greater or lesser rates as positive or negative percentages of the standard rate.

Results

Table 5 shows the results of intake, outputs, balances, and the growth measurements made during the study periods in the 4 groups of infants, and Table 6 gives the comparisons which reached statistical significance. There was no significant difference in the volumes of feed per kg given daily to the infants in each group, hence energy intake was higher in the group fed Pre-Aptamil than in the other groups, since Pre-Aptamil has a higher energy density.

There was rather poor fat absorption on Milumil but energy digestibility and retentions were similar

Table 5 Intake, output, balance, and growth data in the 4 groups of infants (mean \pm SD)

	EBM (11 infants)	Pre-Aptamil (10 infants)	Osterfeed (11 infants)	Milumil (5 infants)
Volume intake (ml/kg a day)	205 \pm 7	201 \pm 7	210 \pm 6	208 \pm 7
Energy intake (kcal/24 h)	210 \pm 53	253 \pm 51	231 \pm 40	256 \pm 52
Energy intake (kcal/kg a day)	136 \pm 17	151 \pm 12	145 \pm 14	143 \pm 12
Urine output (ml /kg a day)	131 \pm 19	118 \pm 18	132 \pm 21	114 \pm 15
Stool weight (g/24 h)	13.2 \pm 8.0	17.1 \pm 9.7	17.6 \pm 7.6	32.1 \pm 9.1
Stool energy (kcal/24 h)	48 \pm 24	48 \pm 30	51 \pm 25	84 \pm 21
Digestible energy (%)	76 \pm 16	81 \pm 11.5	77 \pm 12	66 \pm 10.7
Metabolisable energy (kcal/kg a day)	105 \pm 24	122 \pm 11	113 \pm 16	105 \pm 10
Fat intake (g/24 h)	*	11.8 \pm 2.2	12.1 \pm 2.3	10.9 \pm 2.2
Faecal fat (g/24 h)	4.2 \pm 1.6	3.1 \pm 2.4	3.5 \pm 2.4	5.9 \pm 2.0
Fat absorption coefficient (%)	*	74 \pm 19	70 \pm 21	45 \pm 19
Nitrogen intake (mg/kg a day)	552 \pm 156	613 \pm 58	399 \pm 42	586 \pm 55
Faecal nitrogen (mg/kg a day)	84 \pm 38	22 \pm 19	94 \pm 40	78 \pm 26
Urinary nitrogen (mg/kg a day)	206 \pm 70	230 \pm 57	121 \pm 27	228 \pm 70
Nitrogen retention (mg/kg a day)	262 \pm 100	322 \pm 67	185 \pm 50	280 \pm 39
Weight gain (g/kg a day)	15.6 \pm 5.4	21.5 \pm 5.2	15.3 \pm 4.9	13.7 \pm 5.1
Weight gain coefficient (%)	-18 \pm 25.7	10.9 \pm 26.1	-13.2 \pm 39.8	
Length gain (mm/week)	8.4 \pm 2.5	14.0 \pm 6.6	8.6 \pm 3.7	8.4 \pm 3.1
Length gain coefficient (%)	-16.2 \pm 24.7	45.2 \pm 66	-14.7 \pm 44.3	
Head circumference gain (mm/week)	9.3 \pm 3.6	11.3 \pm 2.8	9.1 \pm 2.1	7.3 \pm 1.6
Head circumference gain coefficient (%)	27.9 \pm 29.4	76.3 \pm 45.9	40.5 \pm 34.9	
Upper arm length (mm/week)	0.22 \pm 0.04	0.26 \pm 0.14	0.21 \pm 0.07	0.19 \pm 0.06
Arm circumference (mm/week)	0.31 \pm 0.23	0.57 \pm 0.28	0.38 \pm 0.17	0.33 \pm 0.21
Biceps skinfold (mm/week)	0.23 \pm 0.24	0.51 \pm 0.60	0.26 \pm 0.20	0.20 \pm 0.22
Triceps skinfold (mm/week)	0.23 \pm 0.14	0.64 \pm 0.38	0.35 \pm 0.20	0.26 \pm 0.18
Subscapular skinfold (mm/week)	0.20 \pm 0.25	0.42 \pm 0.39	0.44 \pm 0.22	0.28 \pm 0.27
Arm fat area (mm ² /week)	12.3 \pm 5.0	23.8 \pm 12.7	16.0 \pm 5.3	13.2 \pm 6.1

* Not measured.

in the infants on the other 3 feeds. Fat intake was not measured in the EBM group but it is worth noting that faecal fat was no lower in this group than in the others. Nitrogen intakes were fairly high on EBM, reflecting the higher N content of preterm mothers' milk.³² Nitrogen absorption from EBM was however no better than that of the other milks. The milk with the highest N content (Pre-Aptamil) gave the best N absorption and retention. Absorption of N from Osterfeed was comparable with that of EBM and Milumil, but N retention was significantly lower on this formula despite lower urine N losses. Thus the N content of this formula may not be sufficient for small preterm infants. In all the growth measurements except one (subscapular skinfold thickness) infants showed greatest increments on Pre-Aptamil. This trend reached statistical significance in many of the comparisons (Table 6). The improved nitrogen retention, linear growth, and head growth show that the infants were not simply depositing fat. Growth of infants on EBM was comparable with that of the group on Osterfeed. Blood urea was higher in infants on Pre-Aptamil and Milumil than on Osterfeed ($P < 0.05$), but not EBM. There were no significant differences in electrolytes or acid-base status (Table 7).

Table 6 Significant differences in nutritional and growth data in the groups of infants on the different feeds

Measurement compared	Comparison groups	t	P <
Energy intake (kcal/kg)	Pre-Aptamil > EBM	2.2	0.05
Stool weight	Milumil > Pre-Aptamil	2.7	0.05
Faecal energy	Milumil > Pre-Aptamil	2.7	0.05
	Milumil > Osterfeed	2.8	0.05
	Milumil > EBM	3.1	0.01
Digestible energy	Pre-Aptamil > Milumil	2.3	0.05
Energy balance	Pre-Aptamil > Milumil	2.7	0.05
Faecal fat	Milumil > Pre-Aptamil	2.6	0.05
	Osterfeed > Milumil	2.3	0.05
Fat absorption coefficient	Pre-Aptamil > Milumil	2.6	0.05
Nitrogen intake (mg/kg)	Pre-Aptamil > Osterfeed	8.9	0.001
Faecal nitrogen	Osterfeed > Pre-Aptamil	4.9	0.001
	EBM > Pre-Aptamil	4.3	0.001
Urinary nitrogen	Pre-Aptamil > Osterfeed	5.2	0.001
	EBM > Osterfeed	3.2	0.01
Retention of nitrogen	EBM > Osterfeed	2.2	0.05
	Pre-Aptamil > Osterfeed	4.9	0.001
	Milumil > Osterfeed	4.6	0.001
Weight gain (g/kg)	Pre-Aptamil > EBM	2.5	0.05
	Pre-Aptamil > Osterfeed	3.0	0.01
	Pre-Aptamil > Milumil	2.6	0.05
Weight gain coefficient	Pre-Aptamil > EBM	2.5	0.05
Length gain (mm/week)	Pre-Aptamil > EBM	2.5	0.05
	Pre-Aptamil > Osterfeed	2.5	0.05
	Pre-Aptamil > EBM	2.8	0.01
Length gain coefficient	Pre-Aptamil > Osterfeed	2.6	0.05
Head growth (mm/week)	Pre-Aptamil > Osterfeed	2.2	0.05
	Pre-Aptamil > Milumil	2.7	0.05
	Pre-Aptamil > EBM	2.8	0.01
Head growth coefficient	Pre-Aptamil > Osterfeed	2.1	0.05
Arm circumference	Pre-Aptamil > Osterfeed	2.1	0.05
	Pre-Aptamil > EBM	2.2	0.05
Triceps skinfold	Pre-Aptamil > Osterfeed	2.1	0.05
Arm fat area	Pre-Aptamil > EBM	2.4	0.05

Table 7 Metabolic blood measurements on the various feeds

	EBM	Pre-Aptamil	Osterfeed	Milumil
Blood urea (mmol/l)	2.9 ± 2.8	5.3 ± 2.3	2.3 ± 2.1	5.1 ± 3.4
Capillary blood pH	7.33	7.30	7.32	7.29
Base excess (mmol/l)	-2.3	-4.0	-2.1	-4.2
Plasma sodium (mmol/l)	131	137	134	135

To assess the effect of weight, postconceptional age, and postnatal age on energy and nitrogen balance, correlation coefficients were calculated for all infants. These were as follows:

	r	
Weight versus digestible energy	+0.09	NS
Weight versus N digestibility	+0.01	NS
Weight versus N retention	+0.09	NS
Postconceptional age versus digestible energy	+0.35	<0.05
Postconceptional age versus N digestibility	-0.06	NS
Postconceptional age versus N retention	+0.11	NS
Postnatal age versus digestible energy	+0.25	NS
Postnatal age versus digestibility	+0.19	NS
Postnatal age versus N retention	+0.14	NS

Digestible energy was not correlated with nitrogen retention ($r = -0.13$).

Discussion

Study design and methods. The aim of the study was to make nutritional comparisons of preterm infants fed with breast milk and formulae. Most existing studies are unsatisfactory in this respect because the infants are not comparable (owing to variations in postconceptional and postnatal age at the time of study) or because the study periods are too short. The importance of this is shown in our measurements where, even though good matching was achieved between the groups, there was considerable variation in the results depending on whether they were compared as absolute values or as coefficients of standard growth during the same postconceptional time period. It is important that the problems of obtaining adequate comparison groups are recognised when interpreting the results of such studies. Crossover designs resolve some of the problems but new ones emerge—such as changing digestive function and growth potential due to maturation—which may cause even greater difficulties if adequate periods of growth are to be studied.

General aspects of the balance results. Although the main purpose of the study was to compare feeds, some general comments on the energy and N balances can be made. Fourteen of the infants weighed <1500 g at the time of the study. Data on very low weight infants are scarce and are particularly valuable. However, our values for energy digestibility and N retention were little different from those of the larger infants (74.3 compared with 77.4% and 246 compared with 255 mg N/kg a day respectively). Thus weight alone is not of great significance in infants >1000 g and was not found to be correlated with energy and nitrogen absorption. More data are needed on infants <1000 g. Surprisingly we were unable to demonstrate any important effect of postconceptional and postnatal age on nitrogen retention, although there was a significant improvement in energy digestibility with increasing post-conceptional age.

If energy intake is low nitrogen retention is impaired because protein is used for energy. We could not show that improved energy balance resulted in greater N retention in our infants, indicating that at the time of the studies energy balance was not a limiting factor in the utilisation of protein for growth.

Comparison of feeds. Some specific points about the performance of the feeds are worth making. Breast milk varied greatly in composition. This makes it difficult to monitor energy and protein intakes in clinical practice, and is a problem that we and others have raised before.^{9 10} The fairly high N content did not reflect an equivalently high content of utilisable protein, since urine N losses were nearly twice as great as in the infants fed Osterfeed, whose protein content approximates mature human milk, and the proportion of N retained was about the same (~47%). It was notable also that energy digestibility was no better on human milk than on the formulae (with the exception of Milumil), and faecal fat excretion was similar. Although the digestibility of human milk fat is generally considered to be better than that of formulae, the properties of human milk may not entirely overcome the physiological handicaps of the very immature in relation to fat absorption, and heating also impairs the digestion of human milk fat.²⁶ It may also impair N absorption or biological value since recent work in very immature infants has shown better N retentions on unheated human milk than we found.³³ Infants fed human milk in our studies tended to grow the slowest.

Milumil, a formula designed for term infants, was unsuitable for the preterm despite its higher protein content. N retention was good but fat digestion poor. This may be due to its high saturated fat content

(53.5%). A comparison with Osterfeed, also designed for term infants, is interesting. Fat absorption from Osterfeed was significantly better, but N absorption and retention were worse. Osterfeed has a 60:40 whey-casein ratio, compared with 20:80 in Milumil, and this whey-predominant protein, similar to human milk, is said to improve its digestibility.³⁴ It does not appear to do so. The better fat absorption from Osterfeed is probably related to its high unsaturated fat content (61%) and fairly low content of C16 and C18 in the α positions on the triglyceride molecule.³⁵

The infants grew fastest on Pre-Aptamil. This formula, providing a modest increase in energy density and a higher protein content, gave the best results on all the measured nutritional parameters. The variability of these measures is such that it is difficult to show significant differences without large numbers. Nevertheless the main differences between Pre-Aptamil and the other milks appeared to be in protein rather than energy nutrition, and the increase in linear growth on this formula is worth comment. It is possible that other nutrients may have contributed to the increased growth, for example sodium, and we cannot be certain which were the most important factors. It is often stated that growth should not be considered the only (or even the main) criterion of feed performance, and it cannot be denied that survival is the first priority. However, with modern neonatal care the type of feeding has not been shown to influence survival. From a purely nutritional viewpoint good growth should be the main criterion of success, and there seems no reason not to aim for the best possible rate, at least until this has been shown to be undesirable. There is certainly no justification in using intrauterine growth rate as the standard to aim for, since postnatal growth is qualitatively quite different.³⁶ Neither is there any justification for saying that the slower growth of preterm infants on EBM is more desirable than the faster growth of infants on specially adapted formulae. If such growth were principally in fatness, and fat accretion rates may certainly be higher,³⁷ there would be legitimate concern about later obesity, but there is no evidence that formula-fed preterm infants become unduly fat later,³⁸ and our data show that linear measurements and head growth are improved with the use of a suitable formula.

We believe that it is reasonable to aim for maximum growth in preterm infants, since this is likely to be limited only by genetic potential so long as the necessary substrates are provided. It may be easier to achieve this on a formula than on breast milk. Atkinson *et al.*³³ have demonstrated marginally better growth and improved nutritional balances in infants on mother's own milk than in those on

banked milk, but we regard the variability of mother's own milk as a major disadvantage in day-to-day care of small infants. There are immunological and emotional arguments in favour of breast milk but we see the nutritional aspects of feeding as more important.

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