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## Fat absorption by small babies fed two filled milk formulae

In common with many others caring for small infants we employ artificial milk formulae when supplies of expressed breast milk run short and in 1972-73 used both Cow and Gate V (C&G V, Cow and Gate Ltd) and SMA Ready-to-feed (SMA, Wyeth Bros. Ltd.) formulae, since the manufacturers' literature suggested that each was a satisfactory breast milk substitute. The present study was prompted by the observation that the babies appeared to fare better on one of the two artificial formulae. A prospective study of fat balance showed that consistently more steatorrhoea occurred in infants fed C&G V formula. Some implications of these findings for postnatal development are discussed.

### Patients and methods

Fat balance studies were performed on 8 infants, 4 of whom were fed SMA and then C&G V, and 4 fed in the reverse order. All the infants were of low birthweight (Table I) and were nursed for this reason in the Special Care Baby Unit. They were fed throughout their stay by gavage or bottle, with SMA or with C&G V supplied in prepacked liquid form. According to the manufacturers' specifications the total protein, fat, carbohydrate, and mineral contents of the two preparations are similar. After at least 3 days on the first milk, stools were collected between carmine markers over a 72-hour period. The infant was then changed to the other milk and after 3 or more days a further 72-hour stool collection was made. Faecal fat was measured by the method of van der Kamer, ten Bokkel Huinink, and Weijers (1949) using the modification described by Varley (1967) and excretion was expressed as a percentage of the fat ingested. Gas liquid chromatography was performed as described by Matthys, Christophe, and Verdonk (1972) on faecal fat extracts prepared for total fat analysis.

### Results and discussion

The infants varied in gestational age from 30 to 37 weeks and in birthweight from 1.16 to 2.11 kg (Table I). The degree of steatorrhoea varied greatly but was greater when the infants were fed C&G V in 7 out of 8 cases. The mean ( $\pm$ SEM) fat excretion expressed as a percentage of the intake on C&G V was  $28.1 \pm 3.9$  and higher than the value of  $10.5 \pm 2.3$  when the same infants were fed SMA ( $P < 0.01$ ).

Gas-liquid chromatography was performed on three pairs of faecal extracts. The fatty acids detected were C14:0, C16:0, C18:0, and C18:1. The percentage of stool fat that each of these comprised is shown alongside the fatty acid composition of the two milks in Table II. No conclusions can be drawn from such limited observations other than that in 2 infants C16:0 formed a larger fraction of stool fat when they were fed C&G V. Despite a higher percentage of C18:1 excreted by these infants when fed SMA, the absolute amount of C18:1 lost in the stools on either milk did not differ.

Variation in fat absorption by infants fed different milks is well documented (Southgate *et al.*, 1969; Fomon *et al.*, 1970; Williams *et al.*, 1970), but the milks used in this study are described in the manufacturers' literature as substitutes for human breast milk and specifications are given which led us to anticipate that they should be interchangeable. For these reasons they were chosen as suitable alternatives to expressed breast milk for infants of low birthweight.

Steatorrhoea was more likely to be under- than overestimated because of the possibility of incomplete stool collection, but there is no reason to expect that this occurred more with one formula than the other. Likewise care was taken to stop the application of cream to sore buttocks during the period of stool collection as this could exaggerate the estimate of faecal fat content. When C&G V formula was given by gavage a tendency for the lipid to separate out and smear the bottle and tube was noted. This did not appear to occur with SMA and might have resulted in an underestimate of the degree of steatorrhoea in those infants fed C&G V. Though this study has not proven why infants fed C&G V have more steatorrhoea than those fed SMA, a suggestion can be made from knowledge of the fatty acid composition of the lipid in the two milks. Palmitic acid (C16:0) constitutes 31.7% of the fatty acid content of C&G V formula but only 14.8% of SMA. SMA has higher concentrations of shorter chain saturated fatty acids, linoleic (C18:2) and other unsaturated fatty acids (Table II).

TABLE I  
Fat balance studies on infants fed with SMA and C & G V formulae

Birthweight (kg)	Gestational age (w)	Post-natal age (d)	First milk*	72-hour fat balance					
				C&G V			SMA		
				Ingested (g)	Excreted (g)	% Excreted	Ingested (g)	Excreted (g)	% Excreted
1.16	30	32	C&G V	15.0	7.2	47.7	21.4	3.7	17.3
1.25	30	32	C&G V	16.5	5.0	30.3	23.3	4.9	21.0
1.68	32	29	C&G V	34.0	14.1	41.6	40.6	1.9	4.7
1.72	34	22	SMA	37.5	6.9	18.4	41.2	1.9	4.6
1.78	34	12	SMA	39.6	9.9	25.0	38.8	4.8	12.4
1.80	37	7	SMA	37.8	5.1	13.5	40.7	5.5	13.5
1.98	36	12	SMA	37.5	10.8	28.8	35.0	2.1	6.0
2.11	34	7	C&G V	32.4	6.3	19.4	45.3	2.0	4.5

\*First milk indicates the order in which the fat balances were performed. Full details given in Methods.

TABLE II  
Percentage fatty acid composition of C & G V and SMA milk formulae and of faecal fat of 3 infants fed each milk

	Milk		Faecal fat					
	C&G V	SMA	1.72 kg infant		1.78 kg infant		2.11 kg infant	
			C&G V	SMA	C&G V	SMA	C&G V	SMA
C10:0	0.5	1.2	—	—	—	—	—	—
C12:0	8.8	12.3	—	—	—	—	—	—
C14:0	3.8	5.5	4.0	6.0	3.0	12.0	5.0	6.0
C16:0	31.7	14.8	68.0	42.0	72.0	40.0	34.0	35.0
C18:0	6.1	9.1	15.0	16.0	10.0	16.0	26.0	28.0
Others	0.4	3.1	—	—	—	—	—	—
C18:1	31.5	28.1	13.0	35.0	15.0	32.0	35.0	31.0
C18:2	15.0	22.0	—	—	—	—	—	—
Others	2.2	3.9	—	—	—	—	—	—

Holt *et al.* (1935) and Tidwell *et al.* (1935) reported that fatty acid absorption by newborn infants increases with the degree of unsaturation and decreases with longer chain length. This seems to explain the differences we observed in the steatorrhoea of infants fed both milks. A logical extension of this argument would be the analysis of stool fatty acid composition. But this has limitations because of bacterial metabolism of fatty acids in the gut (Gompertz and Sammons, 1963; Watson, 1965) and for this reason we did not continue with the gas-liquid chromatography studies. In 2 of the 3 infants there was an excess of C16:0 in the stools after C&G V formula, a finding which agrees with the proposed explanation for their greater steatorrhoea. The use of the extract for total fat analysis for chromatographic studies is probably the reason why only 4 of the fatty acids were detected.

Points which merit further investigation are the variation within an infant of the degree of steator-

rhoea, and the effect of the differences between the milks on calcium balance. The maximum steatorrhoea measured was 47.7%, corresponding to 23% of the calories ingested. Such a degree of steatorrhoea, if chronic, might result in a poorer rate of weight gain than expected from the number of calories ingested. There is ample evidence of a direct association between the degree of fat and calcium loss in the stools (Southgate *et al.*, 1969; Williams *et al.*, 1970), and the possibility exists that the infants fed C&G V formula may absorb less calcium than those fed SMA.

### Summary

In 3-day fat balances, 7 of 8 infants had appreciably more steatorrhoea when they were fed Cow and Gate V formula than when they were fed SMA. The mean fat excretion ( $\pm$ SEM) expressed as a percentage of the amount ingested on Cow and Gate V was  $28.1 \pm 3.9$  compared with

10.5 ± 2.3 on SMA. Gas-liquid chromatography of the faecal fat in 2 of 3 infants showed that C16:0 was responsible for most of the excess fatty acid when they were fed Cow and Gate V formula.

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## Urinary 3'5' cyclic AMP

### Diagnostic test in pseudohypoparathyroidism

Pseudohypoparathyroidism is characterized by end-organ resistance to parathyroid hormone (PTH). There is evidence that this unresponsiveness is located in the renal cortex and involves failure of the hormone to activate adenylate cyclase, the enzyme which forms adenosine 3'5'-cyclic phosphate (cyclic AMP). In normal subjects

infusion of PTH leads to a dose-dependent increase in urinary cyclic AMP (Chase, Melson, and Aurbach, 1969; Kaminsky *et al.*, 1970; Greenberg, Karabell, and Saade, 1972). In patients with pseudohypoparathyroidism, infusion of the hormone fails to alter urinary levels of the cyclic nucleotide (Chase *et al.*, 1969; Greenberg *et al.*, 1972). It has been suggested (Chase *et al.*, 1969) that measurement of urinary cyclic AMP in response to infusion of PTH may be a sensitive index for establishing the diagnosis of this disease. The present report describes 2 children diagnosed as having pseudohypoparathyroidism in whom urinary cyclic AMP levels failed to rise after infusion of PTH.

### Case reports

**Case 1.** A white male, aged 2 years 9 months, was admitted to Vancouver Children's Hospital for assessment of obesity, subcutaneous calcifications, and delay in behavioural development. He had been previously examined (at age 14 months) for delayed behavioural development and at that time was found to have multiple subcutaneous nodules in the scalp; x-rays showed plaques of calcification in the scalp, right flank, shoulder, and dorsum of the left foot; serum calcium and phosphorus were normal. When seen by us (at 33 months) he had a history of polydipsia, bed-wetting, polyphagia, screaming attacks, and increased subcutaneous calcifications. His height was 88.2 cm, which placed him on the 3rd centile; his weight was 15.4 kg, falling between the 75th and 90th centiles. Multiple subcutaneous calcified lesions on the right shoulder, right occiput, and back of legs were noted. No central nervous system abnormality was noted other than mild mental retardation and hypotonia. His hands were short and chubby but there was no evidence of shortened metacarpals. Gesell assessment placed him at behavioural level of about 2 years. The serum calcium level was 7.6 mg/100 ml, serum phosphorus 6.4 mg/100 ml, and serum magnesium 2.0 mg/100 ml.

**Case 2.** A 9-year-old Caucasian female was admitted to hospital for reassessment of pseudohypoparathyroidism and behavioural problems. Subcutaneous calcifications had been present since birth; the diagnosis of pseudohypoparathyroidism had been made on the basis of low serum calcium (7.1 mg/100 ml) and raised serum phosphorus (7.5 mg/100 ml) as well as shortened metacarpals. When examined by us (at age 9 years) she exhibited emotional instability and had learning problems. Her height was 128.5 cm (25th centile) and her weight 40.9 kg (97th centile). The significant clinical findings included multiple subcutaneous calcifications and shortening of the 3rd, 4th, and 5th metacarpals bilaterally. Serum calcium was 10.4 mg/100 ml and phosphorus 5 mg/100 ml while she was on a dosage of 50 000 units of vitamin D daily. The metyrapone test for assessment of pituitary-adrenal axis was normal.