LOW MILK FAT SYNDROME

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Summary

Milk fat production in well-fed cows may fall sharply if the proportion of roughage in the diet is too low, or if the roughage is finely ground. Although mainly associated with the feeding of high levels of starch-rich concentrates, the low milk fat syndrome may occur in herds grazing lush green feeds without adequate supplementary roughage.

The primary cause of the syndrome is increased production of propionate in the rumen, which enhances gluconeogenesis. The raised glucose supply stimulates insulin secretion, which leads to increased utilisation of acetate for adipose tissue synthesis and accounts for the reduction in blood acetate concentration. Circulating triacylglycerol concentrations may also fall, and extraction rates by the mammary of triacylglycerol gland decline significantly. The reduced supply of acetate, and lowered uptakes of triacylglycerol by the mammary gland largely accounts for the fall in milk fat production, since the two substrates are the major precursors of milk fat.

I. INTRODUCTION

Milk fat production in well-fed cows may fall sharply if the ratio of digestible carbohydrate to roughage in the ration is high (Van Soest and Allen 1959; Storry and Sutton 1969), or if the roughage in the ration is finely ground (Powell 1939). Oils rich in polyunsaturated fatty acids may also depress milk fat levels, but responses to all types of diet are influenced by level and frequency of feeding, stage of lactation, level of milk production and condition of the animal (see Davis and Brown 1970).

The recognition in the 1950's of the major role of acetate in both bovine mammary gland metabolism (McClymont 1951) and in milk fat synthesis (see Annison 1983) led to the view that decreased acetate supply is the primary factor in the low milk fat 'syndrome. Indeed, several reports of reduced ruminal acetate concentrations in affected animals gave support to this hypothesis (see Van Soest 1963). More comprehensive studies, however, revealed that ruminal acetate levels in low roughage fed animals were often unchanged but the ratio of acetate to propionate (C_2/C_3 ratio) was found to be closely related to milk fat concentrations (see Armstrong and Prescott 1971).

The view that increased propionate production, and not decreased acetate supply, is responsible for the low milk fat syndrome was first put forward by McClymont and Vallance (1962), who showed that the intravenous infusion of glucose into lactating cows reduces milk fat output. These workers suggested that the enhanced gluconeogenesis which accompanies increased ruminal propionate production on low roughage diets suppresses the mobilisation of fat from adipose tissue and results in the lowered availability of plasma triacylglycerides for milk fat synthesis.

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Comprehensive metabolic studies in cows which had responded to high starch:low roughage diets by producing milk of low fat content confirmed the key role of propionate in the low milk fat syndrome (Annison et al. 1974). Low C_2/C_3 ratios were attributable to increased propionate production. Gluconeogenesis was increased, and the higher levels of circulating glucose were associated with significant falls in the concentrations of acetate and 3-hydroxybutyrate.

The most convincing explanation of the adverse effects of raised glucose supply on milk fat levels is that increased circulating levels of glucose stimulates insulin secretion.' This, in turn, promotes lipogenesis from acetate in adipose tissue, and suppresses triacylglycerol mobilisation from adipose tissue. The end results are lowered blood levels of the two major precursors of milk fat, acetate and triacylglycerol. In the absence of increases in either mammary blood flow, or the avidity of the mammary gland for these substrates, milk fat synthesis falls (Annison et al. 1974).

An alternative explanation of the aetiology of the low milk fat syndrome is that diets which enhance ruminal propionate production may reduce vitamin B_{12} synthesis, and lead to the accumulation of methylmalonyl CoA in the liver (Frobish and Davis 1977). Methylmalonyl CoA is known to inhibit fatty acid synthesis.

In this review aetiology of the low milk fat syndrome is discussed in relation to current knowledge of milk fat synthesis.

II. MILK FAT SYNTHESIS IN RUMINANTS

The precursors of milk fat are extracted from blood by the lactating mammary gland. Quantitative data have been obtained by combining arteriovenous (AV) difference measurements with isotope dilution (see Annison 1983).

All of the short and medium chain length fatty acids (C_4-C_{14}) and part of the palmitate which appears in milk fat triacylglycerols are synthesised de novo in the mammary gland from acetate and 3-hydroxybutyrate. The remainder of the palmitate, and all of the stearate, oleate, linoleate and longer chain fatty acids are transferred intact into the mammary gland from circulating triacylglycerols, which are hydrolysed in the mammary gland capillary bed (see Annison 1983). Carbon balance data for the production of milk fat in the goat, cow and sheep are shown in Table 1.

Table 1. Carbon balance(%) for the production of milk fat in fed lactating ruminants (King et al., 1985)

Substrate	Goats	Cows	Sheep
Acetate	16.1[a]	25.0[b]	25
3-Hydroxybutyrate	14.4[a]	11.8[b]	13
Plasma FFA	-	-	4
Triacylglycerol	61.8	49.6	60
Total	92.3	86.4	102

[a] Corrected for oxidation (Annison and Linzell 1964; Annison 1970).
[b] Data from Palmquist et al. (1969).

High starch:low roughage diets may result in reduced ruminal biohydrogenation and increased levels of trans fatty acids. The suggestion that these fatty acid isomers may cause derangement of lipoprotein metabolism and contribute to the low milk fat syndrome (see Davis and Brown 1970) has not been ruled out by studies showing that labelled cis and trans isomers of octadecenoate are incorporated into milk fat at similar rates (Bickerstaffe et al. 1972). Lipoprotein triacylglycerols rich in trans fatty acids, or other partial hydrogenation products may have structural configurations that reduce their susceptibility to lipoprotein lipase in mammary tissue capillaries. The 50% fall in the extraction rate (A-V/A x 100) of circulating triacylglycerol observed in animals producing milk of low fat content (Annison et al. 1974) is consistent with this hypothesis.

III. QUANTITATIVE STUDIES ON GLUCOSE AND VOLATILE FATTY ACID METABOLISM IN COWS PRODUCING MILK OF LOW FAT CONTENT

The low milk fat syndrome was induced in two Friesian cows by changing the concentrate:hay ratio in their diets from 5:3 to 17:2. Milk fat content declined from 3.0 and 2.3 to 2.3 and 1.5 g/100 g respectively. Changes in glucose, acetate and long chain fatty acid metabolism in the mammary gland, and in the whole animal were examined by AV difference and isotope dilution procedures (Annison et al. 1974).

(a) Rumen VFA metabolism

On transfer to the low roughage diet, the ratio of acetate plus butyrate to propionate in rumen contents changed from a mean ratio of 2.8 to 1.4, without a significant change in acetate concentration. Butyrate concentrations fell from a mean level of 21 mmol/l to 10 mmol/l.

(b) Mammary gland metabolism

Arterial blood concentrations of glucose increased, acetate and 3-hydroxybutyrate levels decreased and triacylglycerol was unchanged. The proportion of triacylglycerol taken up from arterial blood by the mammary gland fell by about 50%, and this factor, coupled with the reduced availability of acetate and 3-hydroxybutyrate, accounted for the reduction in milk fat production.

(c) Glucose metabolism

The mean entry rate of glucose into the circulation rose by 31% and the mean contribution of glucose to total body CO_2 production increased from 5 to 11% when the low roughage diet was fed.

(d) Acetate metabolism

Arterial blood acetate concentrations fell from a mean value of 8.1 mg/100 m l to 4.1 mg/100 ml when the animals were fed the low roughage ration, reflecting a decrease of 55% in the mean acetate entry rate. The corresponding reduction in the contribution of acetate to total CO_2 production was 55%.

The large fall in acetate entry rate was unexpected in view of relatively unchanged rumen acetate concentrations. A partial explanation was

afforded by the three-fold fall in endogenous acetate production by the mammary gland, if other tissues responded in the same way.

(e) Long chain fatty acid metabolism

In the one cow studied, clear evidence was obtained of reduced ruminal biohydrogenation when the animal was fed low roughage:high concentrate rations. Total unsaturated fatty acids in arterial triacylglycerols increased from 37% on the high roughage diet to 55% on the low roughage diet. Corresponding values for the proportion of trans-isomers in the octadecenoate fraction of arterial triacylglycerols increased from 22 to 56% respectively.

IV. SIGNIFICANCE OF THE ACETATE:PROPIONATE RATIO IN THE RUMEN

Armstrong and Prescott (1971) collated data from thirteen experiments on lactating cows in which ruminal volatile fatty acid (VFA) concentrations were correlated with milk fat concentrations. Although a range of diets was fed, acetate:propionate ratios below 3.0 were invariably associated with milk fat depression, which increased as the ratio decreased. The elegant energy balance studies of W.P. Flatt, summarised by Annison and Armstrong (1970), clearly show that adipose tissue is deposited at the expense of milk fat as the acetate:propionate ratio falls (Table 2).

Table 2. Data relating to the mean energy balances of cows eating rations containing 40, 60 or 80% concentrates

Concentrate content of diet (%)	C_2/C_3 ratio	Body tissue gain (+) or loss (-) (g)	Yield of milk fat	Change in body fat (g/24 hr)	Net change in fat yielded
40	3.2	-1275	714[a]	-138[b]	576[a,b]
60	2.3	- 575	627	- 62	565
80	1.7	+1323	489	+144	633

[a] Yield of milk x fat content.
[b] Assuming all body tissue energy to be fat of calorific value 9.21 k cal/kg.

V. EFFECTS OF INSULIN STATUS ON MILK FAT PRODUCTION

McClymont and Vallance (1962) showed that the intravenous infusion of glucose into lactating cows reduced milk fat concentrations. The authors hypothesis to account for this finding was that increased insulin secretion suppressed the release from adipose tissue of free fatty acids, the precursors of circulating triacylglycerols. This study was remarkably perceptive, since recent findings at that time that acetate, and not glucose, is the major source of milk fatty acid carbon dominated thinking on milk fat synthesis (see Annison 1983).

Support for the view that increased insulin secretion is a major factor in the low fat syndrome was provided by the finding that the intravenous infusion of glucose or insulin stimulated the activity of lipoprotein lipase in adipose tissue (Rao et al. 1973), but not in mammary tissue (Benson et al. 1972).

A recent study by Laarveldt and Chaplin (1985) in which mixtures of insulin and glucose were intravenously infused into lactating cows failed to demonstrate any effects on milk fat synthesis. The 2 hour period over which insulin was administered, however, may have been too short to effect measurable changes in lipid metabolism.

D. Leenanuruksa and G.H. McDowell (personal communication) have studied the effects of glucose and insulin on milk fat production in lactating ewes treated with alloxan to eliminate insulin secretion. The ewes were given insulin intravenously at rates sufficient to maintain a mild hyperglycemia. Milk yield was unaffected, but milk fat levels rose significantly, in contrast with the'situation in intact lactating cows, where the intravenous infusion of glucose to raise blood levels resulted in a sharp fall in milk fat concentration (McClymont and Vallance 1962).

Evidence that the main role of insulin the aetiology of the low milk fat syndrome is the diversion of acetate into adipose tissue was obtained in experiments in which glucose and acetate were infused into lactating ewes (Hough 1982). Glucose, or glucose and acetate were infused intravenously for 4 d at rates equivalent to 37.5% and 50% respectively of calculated irreversible loss rates. As expected from earlier work, glucose infusions lowered milk fat levels, but when acetate was infused with glucose, milk fat levels were substantially restored (Table 3).

Table 3. Effects of intravenous infusions of glucose and acetate on milk yields and milk fat levels in 5 ewes (mean values for final 2 d of each treatment, with saline controls)

	Infusion			
	Saline	Glucose	Glucose plus Acetate	Saline
Milk yield (g/d)	1181$_a$	1105$_b$	1169$_c$	1076$_a$
Milk fat (%)	6.4^a	5.0^b	5.8^c	6.8^a

a,b,c Values with different superscripts differ significantly ($P < 0.05$).

VI. VITAMIN B_{12} AND THE LOW MILK FAT SYNDROME

Frobish and Davis (1977) proposed that a contributory factor in the aetiology of the low milk fat syndrome was impaired propionate metabolism stemming from high levels of propionate production and decreased vitamin B_{12} synthesis in the rumen. Propionate is metabolised in the liver to methylmalonyl CoA, which is in turn converted to succinyl CoA. The latter conversion requires the enzyme methylmalonyl CoA isomerase and a coenzyme form of vitamin B_{12} as cofactor. High grain:low roughage diets may reduce vitamin B_{12} production (Walker and Elliott 1972), and in B_{12} deficiency the intermediate methylmalonate accumulates. Methylmalonate has been shown to inhibit fatty acid synthesis from acetyl CoA and malonyl CoA (Cardinale et al. 1970).

Experimental evidence that vitamin B_{12} deficiency may contribute to reduced milk fat production is equivocal. Frobish and Davis (1977) found

that 3 out of 7 cows fed a high grain:low roughage ration responded to injections of hydroxocobalamin by increasing milk fat production. Later work by Elliott et al. (1979) and Groom et al. (1981) failed to confirm these findings.

VII. PREVENTION OF LOW MILK FAT SYNDROME

McClymont (1951) discussed the relationships between the type and quantity of roughage and the fat content of the milk of grazing cows. In NSW, low milk fat levels occurred in dairy herds grazing young, green herbage without access to long roughage, The occurrence of the syndrome in cows grazing young green oats (fibre content 5-7%) had long been recognised. Experience in NSW suggests that when herbage is the sole feed, the minimum roughage content should be about 20% to avoid milk fat depression. Roughage chopped to less than 1 cm is ineffective in preventing milk fat depression, so it is important to feed supplementary roughage in long form.

When concentrates are fed, the ideal ratio of concentrates to roughage is about 60:40 (Kay 1969). This feeding system, in addition to maintaining normal milk fat levels, ensures maximum fertility, Increased calving intervals have been reported at higher proportions of concentrates (Kay 1969). Where there is limited grazing and 'intakes of starch rich concentrates are high, a minimum of 5 kg hay/d, or the equivalent, is recommended in order to avoid milk fat depression.

VIII. DISCUSSION

There is overwhelming evidence that the key factor in the aetiology of the low milk fat syndrome is a rumen fermentation which gives rise to a C_2/C_3 of below 3.0 (Armstrong and Prescott 1971). Although there is strong indirect evidence that a changed insulin status stemming from enhanced gluconeogenesis reduces the availability to the mammary gland of acetate and triacylglycerol, the main precursors of milk fat, direct evidence of the role of insulin has not yet been reported.

In most instances, reduced acetate supply to the mammary gland is the major factor causing milk fat depression (Pethick and Lindsay 1982). Engvall (1980) has shown that forty three field cases of cows producing milk of low fat content, the milk fatty acids showing significant reduction were those synthesised from acetate and D(-)3-hydroxybutyrate. In fed animals, 3-hydroxybutyrate is derived mainly from ruminal butyrate, and conditions in the rumen which favour propionate production often suppress butyrate formation,

The significance of the apparent reduction in endogenous acetate production in cows producing milk of reduced fat content (Annison et al. 1974) remains unclear. Pethick et al. (1981) suggested that endogenous acetate production is largely unaffected by physiological or nutritional states. King et al. (1985) have shown that endogenous acetate production by the mammary gland of the ewe increases linearly with milk yield, but data are required for other tissues in animals producing milk of low fat content.

The possible involvement of B_{12} deficiency in the low fat syndrome should always be considered in regions where cobalt deficiency is suspected.

The reduced mammary extraction rate of triacylglycerols in cows induced to produce milk of low fat content (Annison et al. 1974) merits further study. Although acetate shortage appears to be the dominant feature of the low fat syndrome, the possibility that triacylglycerols rich in partially hydrogenated fatty acids are less readily hydrolysed by lipoprotein lipase in mammary capillaries is of considerable interest,

Changes in systems of payment for milk which minimise the returns for milk fat might lead to a reassessment of priorities in dairy cow feeding. If at some future date milk of low fat content becomes acceptable to marketing authorities, the producer must take into account possible reductions in fertility that appear to be associated with low roughage rations (Kay 1969).

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