# The role of carbohydrate metabolism in the regulation of milk production

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Carbohydrate metabolism in the ruminant has several distinctive features. Within the reticulo-rumen (rumen) there is extensive degradation of soluble and insoluble carbohydrates to short-chain fatty acids (mainly acetic, propionic and butyric) and, with usual diets, only small quantities of soluble carbohydrate are available for hydrolysis and absorption in the small intestine. As a consequence, gluconeogenesis is a quantitatively more important process in the ruminant than in the non-ruminant and propionate is the major glucose precursor.

There is evidence of metabolic adaptation to the restricted glucose supply and to the provision of acetate and butyrate as major alternative energy sources. A low activity of ATP citrate lyase in ruminant mammary and other tissues limits the utilization of glucose for fatty acid synthesis. Though there is no invariable block on glucose oxidation in the mammary gland, during lactation when demands for glucose for lactose synthesis are high, there are indications that under some circumstances glucose oxidation may be restricted (Smith & Taylor, 1977). Moreover, plasma glucose concentration in the ruminant is typically lower than in the non-ruminant, although the specific reasons for this are not clear. Because of the greater diversity of the products of carbohydrate digestion in the ruminant than in the simple-stomached animal the hormonal and neural responses to the ingestion of food may be more complex (to date they are less well defined) and the interactions bettween hormone release and substrate uptake and utilization modified (Bassett, 1975).

The extent and nature of carbohydrate fermentation in the rumen also influences production of ATP and its use for microbial synthesis and the redox potential, and affects the amount of microbial protein passing to the abomasum and the degree of hydrogenation of dietary unsaturated fatty acids.

In this article, the importance of the distinctive features of carbohydrate metabolism for the processes of milk synthesis and secretion will be examined both in terms of the metabolic details of the processes themselves and within the context of milk production in the intact animal.

## *Milk synthesis and secretion*

***Lactose synthesis and secretion and milk volume.*** The major precursor of milk lactose is blood glucose; other precursors, such as lactate and glucogenic amino acids, contribute in total only about 15% (Linzell, 1974). The withdrawal of glucose from the perfusate of an isolated perfused goat mammary gland inhibits both lactose synthesis and milk secretion (Hardwick *et al.* 1961). The depression of milk secretion appears to be a consequence of the dependence of water secretion on the synthesis and secretion of lactose: on the re-introduction of glucose into the

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perfusate the first secretion is rich in protein and fat, implying a continued synthesis and secretion of these constituents until inhibition is brought about by their accumulation in the small amounts of milk contained with the alveoli. In contrast, the withdrawal from the perfusate of acetate results in a general reduction in the synthesis and secretion of all milk constituents and especially fat (see later).

In the intact lactating cow or goat, depression of plasma glucose concentration to less than 400 to 500 mg/l either by intravenous infusion of insulin (for references see Linzell, 1967; Rook & Hopwood, 1970) or intra-ruminal infusion of butyric acid (Storry & Rook, 1962*a*) depresses milk lactose synthesis and secretion, milk lactose content and milk volume, effects offset by the simultaneous intravenous infusion of glucose. There is an approximately linear relationship between milk volume and plasma glucose concentration within the range of 100 to 300 mg glucose/l blood plasma. Effects on the rates of synthesis and secretion of milk protein and fat are small and the concentrations of those constituents in the milk increases.

These observations are consistent with a direct precursor (glucose) concentration–product (lactose) yield relationship but the mechanism of transfer of glucose to the alveolar (secretory) cell and the factors controlling that transfer have yet to be described: in addition to plasma glucose concentration, there are indications that blood flow through the udder also is a factor that may limit glucose uptake particularly in situations where sympathetic activity depresses blood flow by a direct vasoconstrictor effect (e.g. stress and in some animals by a reduction in plasma glucose concentration following insulin administration (Linzell, 1967)). In both the fed and the starved ruminant, however, the plasma glucose concentration is normally within the range of 400 to 800 mg/l and effects analogous to those induced experimentally are unlikely to arise in practice. Severe experimental underfeeding of cows in late pregnancy and early lactation, however, has been shown to depress markedly plasma glucose concentration and, in a single cow, the mean value for days 2 to 14 post partum was 375 mg/l and the minimum value, 6 days after parturition, 230 mg/l (Storry & Rook, 1962*b*).

Linzell (1967) concluded that variations in plasma glucose concentration within the 'normal' range may also be associated in the goat with variations in lactose secretion and milk volume but M. Peaker (private communication) has suggested that in Linzell's experiments there may have been a confounding of the main treatment effects with those of short-interval milking since in later experiments Linzell & Peaker (1971) found a marked increase in the rate of milk secretion in otherwise untreated goats milked hourly with the aid of oxytocin. Fisher & Elliott (1966) have demonstrated in the cow small (up to 0·19 percentage units), but not statistically significant, responses in milk lactose content and significant responses in milk yield, of 7 to 10%, to intravenous infusion of glucose or of propionate (an unphysiological treatment) at rates of 11·7 MJ/d (2·8 Mcal/d) (i.e. 745 g glucose or 564 g propionate/d) over a 4 d period. Several experiments with lactating cows given intraruminal infusions of propionate (in amounts up to 1·6 kg/d) over

periods of 24 to 28 d (Rook *et al.* 1965) have failed to demonstrate any consistent immediate or longer-term effect on milk lactose content or milk volume. Intra-abomasal infusion of glucose (and propionate) (for references, see Ranawana & Kellaway, 1977*b*; Vik-Mo *et al.* 1974) has only in some instances, more particularly with the higher rates and longer periods of infusion, increased milk yield without distinctive change in lactose or protein contents. The extent to which the composition of the basal diet may be a factor in determining a response is not clear but extensive uptake of glucose (or propionate) from the hind gut, which does not occur in the normally-fed animal, may promote a modified hormonal response capable of a general stimulation of milk secretion analogous to that suggested for intra-abomasal infusions of casein (see later).

In contrast, intraruminal infusion of acetate (in amounts up to 2 kg/d) over periods of 21 to 28 d (Rook *et al.* 1965; Johnson & Kitchen, 1978) in animals past their peak in yield has consistently maintained the yields of milk, lactose, protein and fat or reduced their rates of decline. These observations suggest that under the conditions of the experiments, the supply of acetate, and not that of glucose, was limiting for milk secretion.

A possible mechanism for this effect of acetate is one related to the supply of ATP. Materials oxidized by the mammary gland include acetate, glucose, β-hydroxybutyrate and, during fasting and possibly physiological undernutrition in early lactation, the non-esterified fatty acids (Linzell, 1974). Oxidation of glucose is primarily by the pentose phosphate pathway. A low activity of pyruvate dehydrogenase in ruminant mammary gland (Reed *et al.* 1977) may restrict glucose oxidation by the tricarboxylic acid cycle, and thus increase the importance of oxidation of acetate. Succinate, which may inhibit acetate oxidation, when infused intravenously has been found to depress milk secretion in the cow (Rook *et al.* 1965) and goat (Rook & Hopwood, 1970).

There is no indication of a direct relationship between plasma acetate concentration and the rate of milk synthesis: throughout a feeding cycle, acetate concentration may vary tenfold, yet the rate of milk secretion is constant. Responses in milk secretion to acetate infusion are progressive and develop over a period of 2 to 3 weeks and it is probable the responses of the gland to acetate supply are modulated by hormonal factors or dependent on a hormonal control of secretion unrelated to the direct supply of acetate to the gland.

Though acetate infusion has delayed the usual lactational decline in yields, significant absolute increases in yield have not been achieved. There are, however, physiological limitations to the amount of acetate that may be provided. Absolute increases in yield, which similarly develop over a period of weeks, are readily achieved with improved feeding. A complex nutritional–endocrine response may be involved and experimental studies have failed to reveal differential responses in milk yield with diets of different composition designed to give a different composition of ruminal short-chain fatty acids (Anon, 1961; 1962; 1963). In the early part of lactation, prior to the peak in yield, diets which favour a 'propionate-type' of fermentation restrict the mobilization of depot fat (at that stage of

lactation, FFA may be an important energy source for the mammary gland) and may limit the development of yield (Armstrong & Prescott, 1971).

Diets deficient in protein depress milk yield and, to a lesser extent, milk protein content (for references, see Rook, 1975). The effects are much exaggerated in animals in very early lactation receiving diets deficient in energy and protein (Ørskov *et al.* 1977), as the lack of energy, but not that of protein, may in part be offset by mobilization of body reserves. There is evidence, both from the earlier feeding trials and the more recent investigations into the effects of abomasal infusion of casein or a mixture of amino acids (for references, see Schwab *et al.* 1976), that there may be separate mechanisms for the effects on yield and protein content (see later). The mechanism for milk yield may involve a hormonal (possibly growth hormone) response to the entry of protein into the abomasum (see Clark, 1975) or to the absorption of a complement of amino acids from the intestine.

*Milk fat synthesis and secretion.* The amount, composition and physical form of dietary carbohydrates, through effects on rumen fermentation, have a profound influence on milk fat content, composition and yield. The subject has been reviewed frequently in recent years and a further comprehensive review will appear shortly (Sutton, 1979). Variations in the uptake from the gut of any of the major short-chain fatty acids, acetic, propionic or butyric, or in the normally small amounts of glucose, affect milk fat synthesis. An increase in the uptake of acetate or butyrate increases the synthesis *de novo* and secretion of $C_4$-$C_{16}$ fatty acids, whereas an increased uptake of propionate or glucose depresses the secretion of mainly the longer chain ($C_{16}$, $C_{18}$) fatty acids. The detailed mechanisms for the actions of acetate and butyrate are not clear but both acetate and β-hydroxybutyrate (a major product of butyrate metabolism) are recognized precursors of the shorter-chain fatty acids. An increased uptake of propionate or glucose may depress the concentrations in blood plasma of acetate and β-hydroxybutyrate and depress slightly fatty acid synthesis *de novo* but their main action is through an insulin response which promotes an increased utilization of plasma triglycerides for depot fat formation and limits the role of the triglycerides as a source of the longer-chain fatty acids of milk fat.

As conditions within the rumen are less reducing when propionic acid production is high, a reduction in milk fat secretion may be associated with an increased content in the milk fat of the unsaturated fatty acids of the diet and of their partially hydrogenated derivatives.

*Protein synthesis and secretion.* Alteration of diets of hay and concentrates, either by change of physical form or chemical composition or the amount of food offered, in a manner that promotes an increase in the ruminal production of propionic acid relative to that of acetic acid, specifically increases milk protein content (and secretion) by up to 0·5 percentage units. Similar responses have been obtained to the intraruminal infusion of propionic acid as an addition to such diets. The improvements in milk protein content develop over a period of 2 to 3 weeks. The mechanism of the effect has yet to be established but the suggestion has been made, and some evidence presented in support (Halfpenny *et al.* 1969), that the

supply of propionate absorbed from the rumen influences the over-all degradation and synthesis of glucogenic amino acids in the liver, and that certain of the glucogenic amino acids, glutamic acid and proline in particular, may contribute to a 'glutamic-acid pool' within the mammary gland. Through that pool, the supply of these acids may influence the rate of synthesis of milk proteins. Ranawana & Kellaway (1977*b*) have demonstrated increases in the plasma concentration of proline, and also of serine and glycine, in response to intra-abomasal infusions of glucose.

Recent information (J. S. Chalmers & P. C. Thomas, unpublished results) has shown that when the diet contains a high proportion of silage, it is not only more difficult, by altering the amount or type of concentrate, to promote a fermentation that gives a high production of propionic acid but also that intraruminal infusion of propionic acid is not associated with an increase in milk protein content. It appears that for such diets, the mixture of dietary and microbial proteins reaching the small intestine is low in methionine (P. C. Thomas, D. G. Chamberlain, N. C. Kelly & M. K. Wait, unpublished results) and the supply of methionine may limit milk protein synthesis.

Diets deficient in protein can also produce a slight depression in milk protein content and it appears that the effect on milk protein content, as opposed to the more general effect on milk secretion (see earlier), may also be due to a shortage of specific essential amino acids. Non-significant increases in the plasma concentrations of several essential amino acids have been reported in response to abomasal infusions of casein in lactating goats receiving a low protein diet (Ranawana & Kellaway, 1977*a*). The first limiting amino acid for milk protein synthesis may vary with basal diet.

### *Dietary carbohydrates and the prediction of lactation performance*

Though the mechanisms whereby the products of carbohydrate digestion and metabolism influence milk secretion are not firmly established, the nature of the effects, and especially those on milk protein and fat contents, are well defined. Nevertheless, it is difficult, solely from a knowledge of the carbohydrate composition of the diet, to predict with certainty the effect on milk secretion as the composition of the products of rumen fermentation are determined not only by the composition of the substrate fermented but also by the metabolic activity of the rumen microbes. The higher the dietary content of soluble carbohydrates, the more variable is the composition of the fermentation products: with a diet of (g/kg) 240 ground hay, 560 barley and 200 flaked maize offered to sheep under strictly controlled conditions, two discrete patterns of fermentation were observed, one giving 58:15:23, the other 46:33:12, for the molar percentage of acetic, propionic and butyric acids respectively (Ishaque *et al.* 1971).

In addition, if the feeding level is to be maintained, a change in the proportion of dietary carbohydrate requires a compensatory change in the fat or protein content of the diet and the effects of those dietary constituents on the composition of ruminal short-chain fatty acids, on the provision of substrates for milk synthesis

and on the secretion of milk and milk production, are as yet less well defined.

Computer-based models have, however, been constructed to simulate the effect of nutrient intake and partition by the dairy cow on lactation performance. A recent example is a model constructed on two levels, one a control level which relates performance to genetic potential, the other an operational level defined in terms of a pool of metabolites available for productive purposes which is derived from ingested nutrients and tissue catabolism and determines the ability to achieve the control level of the programme (Bywater & Dent, 1976; Bywater, 1976). The application of this model for prediction purposes is still to be evaluated.

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