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# THE EFFECT OF INFUSIONS OF GLUCOSE, ACETATE AND AMINO ACIDS ON HOURLY MILK YIELD IN FED, FASTED AND INSULIN-TREATED GOATS

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SUMMARY

1. Experiments have been carried out in lactating goats milked hourly to assess the value of this technique in studies of milk secretion.

2. On refeeding 24 hr-fasted goats there was an increase in arterial concentration and mammary uptake of volatile fatty acids within an hour, but little increase in hourly milk and lactose yield until the mammary uptake of glucose had also increased (after 2–3 hr).

3. Intravascular infusions of acetate had no effect on milk secretion in 24 hr-fasted goats but glucose infusions increased milk yield by $62 \pm 5\%$ and lactose yield by $87 \pm 12\%$ within 3 hr, with no effect on fat secretion. The addition of acetate or acetate plus amino acids had no more effect than glucose alone.

4. The yield of milk and lactose could be reduced within an hour by insulin (2 u./kg I.V.) and this was prevented or reversed by injecting glucose. In one goat, where in spite of a fall in blood sugar, mammary arteriovenous difference and blood flow did not fall, there was little or no fall in milk yield.

5. In fasted or insulin treated goats an increase in milk and lactose secretion could be obtained within an hour by infusing glucose into the artery of one gland autotransplanted to the neck, which responded before the control gland *in situ*, thus showing that the effect of glucose is directly on the mammary tissue.

6. In two normally fed goats with a low blood sugar, glucose infusions increased the milk or lactose yield by 30% within 3 hr.

7. It is concluded that frequent milking, using minimal doses of oxytocin, is a valid method of studying factors controlling milk secretion and that, in the lactating goat, the availability of glucose to the mammary gland can be a limiting factor for maximum milk secretion.

## INTRODUCTION

In a previous paper (Linzell, 1967) it was shown that the yield and composition of milk of goats when they are milked hourly is very similar to that on twice daily milking, and that this is a practicable procedure that can be carried out for at least 12 hr, in both normal goats and in 24 hr-fasted animals where the milk yield is about halved by fasting. The present paper shows that the technique of hourly milking can be used in studies of factors influencing milk yield and composition by demonstrating that milk secretion can be reversibly raised or lowered experimentally within 1–2 hr. The results also confirm the great importance of the mammary uptake of glucose to milk secretion in the goat.

## METHODS

These were the same as in the previous paper (Linzell, 1967). In addition some of the animals had been surgically prepared for infusions into one mammary artery, by auto-transplanting one mammary gland to the neck where it was thereafter supplied by an exteriorized carotid artery and drained into one jugular vein (Linzell, 1963).

## RESULTS

In order to assess the value of the technique of hourly milking it was necessary to have methods of altering the rate of milk secretion reversibly and then to see how quickly they acted. Two well known methods of lowering milk yield, fasting and treatment with insulin, have been found suitable for the present experiments.

### *Fasting and refeeding*

Linzell (1967) showed that fasting is a simple and highly reproducible way of lowering milk secretion in the goat. After 24 hr the yield drops to $56 \pm 2{\cdot}1$ % (S.E.) and conveniently remains at $48 \pm 2{\cdot}3$ % for a further 12 hr, whether the animal is milked twice daily or hourly (Figs. 3, 4, 7). In addition, on hourly milking, fasted animals showed striking changes in milk composition, notably a fall in K and lactose concentrations and a rise in Na, Cl, citrate and total N (Fig. 2). Therefore, experiments were conducted to test the effect of infusing known milk precursors into fasted lactating goats.

A clue to the relative importance of the availability of two substrates (glucose and acetate) to the mammary gland was obtained in experiments where the rate of rise of milk secretion on feeding fasted goats was followed (Fig. 1). It will be seen that within an hour of feeding there was an increase in the arterial concentration and mammary arteriovenous difference of

acetate but that no substantial increase in milk yield occurred until, after 3 hr, the mammary glucose uptake rose owing to an increase in blood flow. Thereafter the rate of rise of blood glucose, mammary blood flow and milk

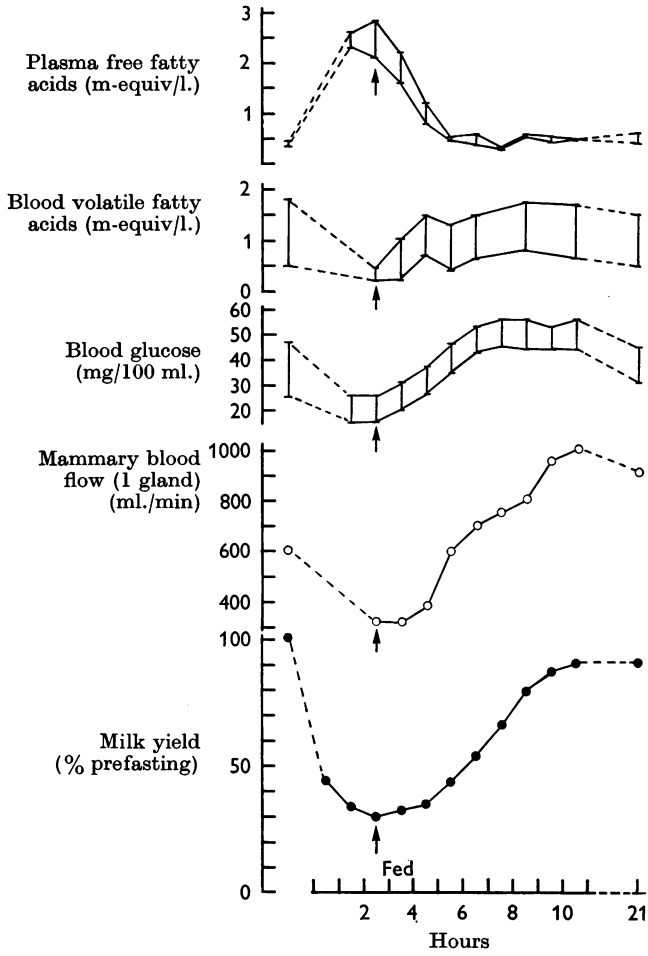


Fig. 1. The effect of feeding a goat fasted for 26 hr. At the arrow the goat was fed *ad libitum* and consumed 0·62 kg of hay and 1·5 kg of a standard pelleted cereal ration in 8 hr. Blood and plasma analyses show arterial (above) and mammary venous (below) values. The first point on each graph was made at the beginning of the fast.

yield were remarkably similar, thus suggesting that the availability of glucose was of more importance to milk secretion than that of acetate. Moreover, although milk composition reverted towards normal in all respects on refeeding, a most striking change was the rise in lactose con-

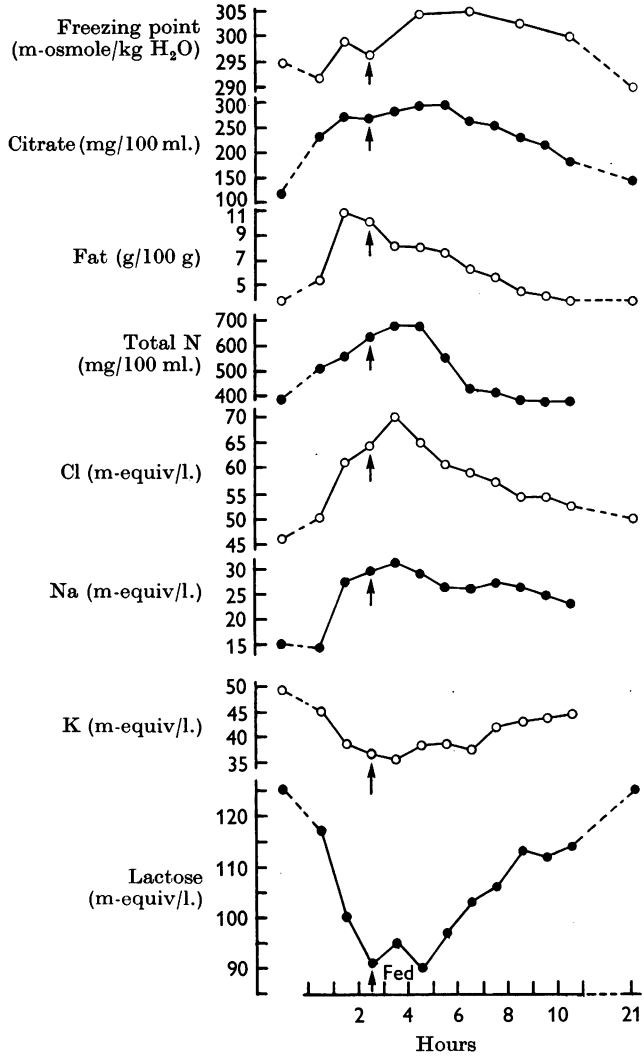


Fig. 2. Same experiment as Fig. 1 showing milk composition. The first point is for the total milk secreted 24 hr before fasting.

centration, and this ran parallel to the mammary glucose uptake (arterio-venous difference × blood flow).

*Effect of infusing milk precursors*

*Fasted goats.* This was tested in twenty-four experiments. The fall in blood concentration and mammary uptake is greatest for acetate (Linzell, 1967 and Fig. 1), but the infusion of acetate in two experiments in amounts

sufficient to restore the blood level had no effect on the yield of milk or on lactose concentration (Fig. 3). The hourly yield of fat did rise but this was no more than was seen in control experiments (Fig. 4). However, glucose infusions significantly increased the yields of total milk by $62 \pm 5\%$ and

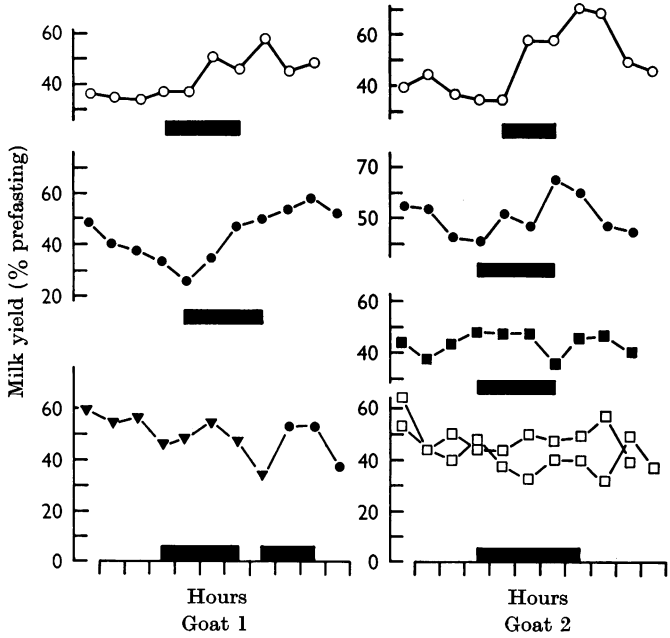


Fig. 3. Comparison of the effects on hourly milk yield of infusing different substrates intravenously into fasted goats. Milk yield expressed as a percentage of mean yield on twice daily milking 7 days before each experiment. The first point is for the overnight yield. □ Saline control; ■ Na acetate; ● glucose; ○ glucose + acetate; ▼ glucose + acetate + amino acids.

lactose by $87 \pm 12\%$ ($P = 0{\cdot}001$) but had no significant effect on the yield of fat ($P = 0{\cdot}2$–$0{\cdot}1$) (Figs. 3, 4). The addition of acetate or acetate plus amino acids (in the proportions removed by the glands of lactating fed goats, Mepham & Linzell, 1966) to the glucose had no more effect than glucose alone (Figs. 3, 4). When the infusion of glucose was made directly into the artery of one gland (autotransplanted to the neck and supplied by an exteriorized carotid) this gland responded before the control gland *in situ*, which received the glucose that escaped uptake by the infused gland and was diluted with the total blood volume (Fig. 5). However, it was very difficult to find a dose of glucose that raised the yield of the transplanted gland alone when the intra-arterial infusion was continued for more than 1 hr. The threshold was about 0·2 mg/kg body weight/min but a dose of 0·4 mg/kg/min could cause a rise in the injected gland within 1 hr and the other gland within 2 hr. With 2 mg/kg/min both glands

responded together because the arterial blood level was raised quickly by this dose. Fed lactating goats utilize glucose at about 3·6 mg/kg/min (Annison & Linzell, 1964).

It seems unlikely that the raised level of plasma free fatty acids (FFA) inhibits milk secretion in fasted goats because the milk yield increased in response to glucose in spite of the raised level of FFA (Fig. 5).

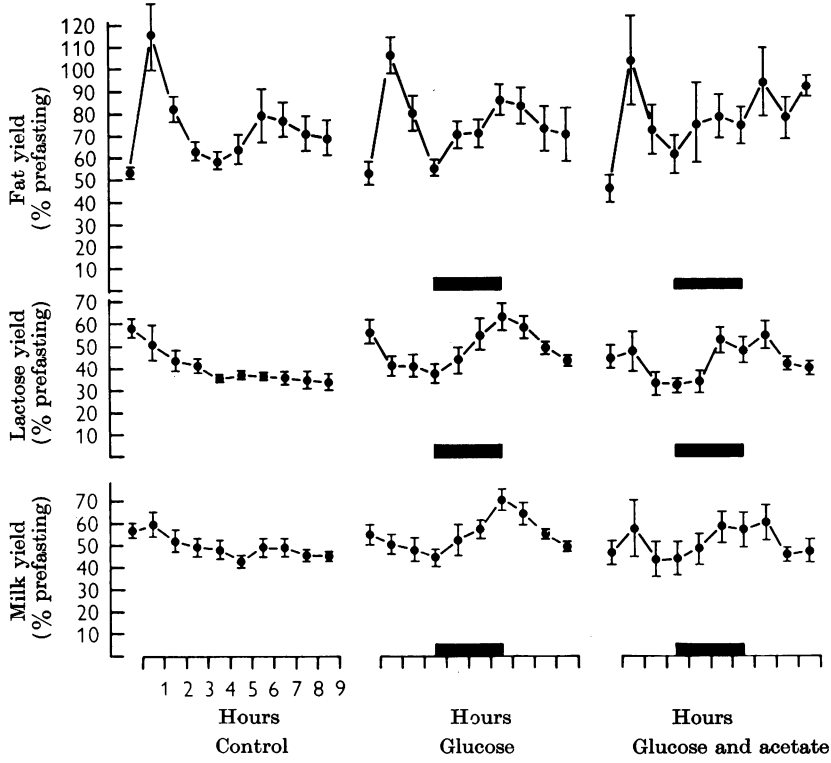


Fig. 4. Comparison of the effects on the hourly yields of milk, lactose and fat of intravenous infusions of glucose and glucose plus acetate in fasted goats. Hourly yields calculated as a percentage of that on twice daily milking before fasting. Mean ± S.E.

*Effect of insulin*

Insulin causes a fall in milk yield and milk lactose concentration in the cow (Gowen & Tobey, 1932) and in the goat (Sopeña, 1944) and Kronfeld, Mayer, Robertson & Raggi (1963) first showed that this could be prevented by an I.V. infusion of glucose. This is clearly a suitable experiment to repeat on goats milked hourly, to assess the rate of response of milk secretion to the availability of glucose. Single I.V. injections of insulin (1·5–2·0 u./kg) lowered blood sugar to 20 ± 1·7 (S.E.) mg/100 ml. within 2 hr in five goats, and the fall in milk yield could be promptly reversed by

infusions of glucose, particularly if this was made into the mammary artery (Fig. 6), thus confirming that the main action of insulin on milk secretion in the ruminant is in reducing mammary glucose uptake. However the

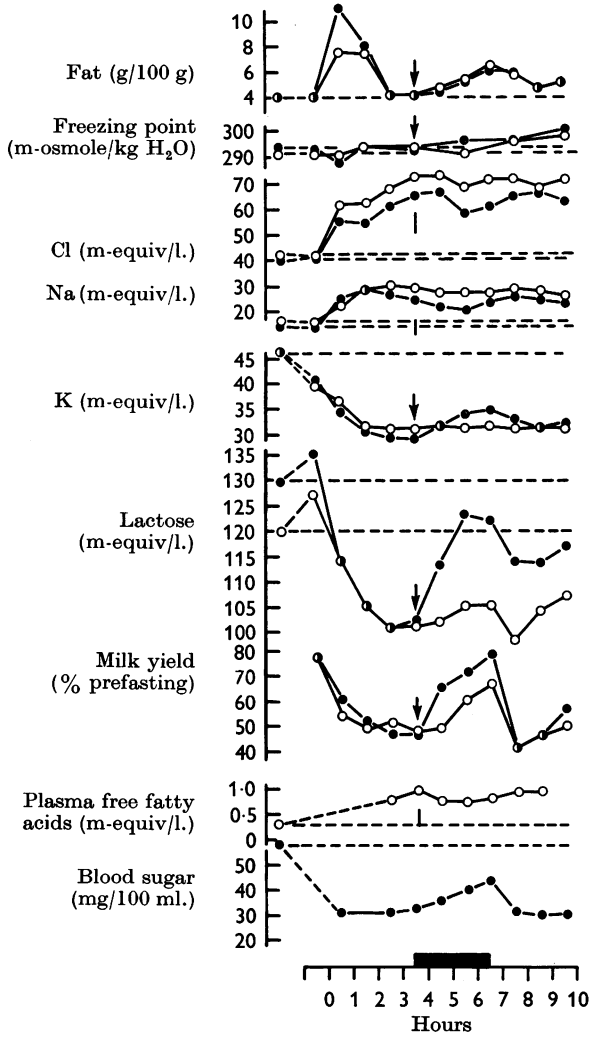


Fig. 5. Effect of infusing glucose (2 %, 1 ml./min) into the artery of an autotransplanted mammary gland (●) of a fasted goat. Control gland *in situ* (○). Graphs plotted as in Fig. 1. The first point in each graph is the prefasting value, and hour zero the milk secreted overnight.

present experiments show that the mechanism may be due to vasoconstriction, because in two experiments mammary glucose arteriovenous difference was measured and found not to fall. In a goat where both

mammary arteriovenous difference and blood flow were measured neither fell after an injection of insulin and neither did the milk yield in this experiment, although there was a delayed fall in milk lactose concentration

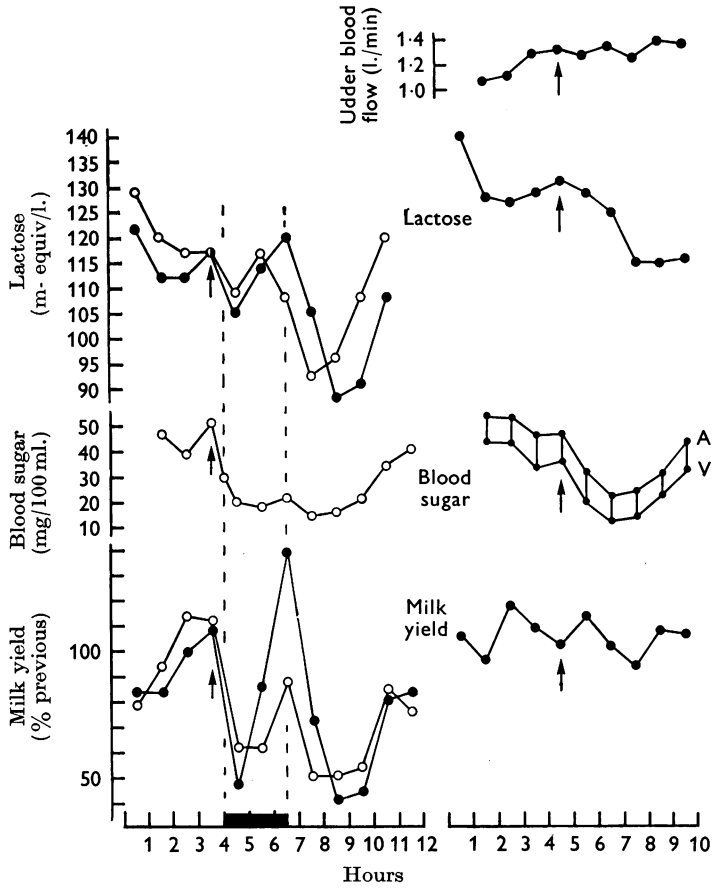


Fig. 6. Effect of single doses of insulin on hourly milk yield in two goats. At arrow insulin 2 u./kg injected I.V. In the goat on the left glucose (10%) was infused (1 ml./min) into the artery of one mammary gland autotransplanted to the neck, ●. Control gland *in situ*, ○.

(Fig. 6). A further point of interest is that the infusion of glucose at 1–1·5 mg/kg/min into insulin treated goats was not sufficient to prevent the fall in blood sugar yet did completely or partially (Fig. 6, control gland) prevent the fall in milk yield.

*Glucose infusions in fed goats*

In normally fed goats blood glucose concentration can be as low as 29 mg/100 ml., and Linzell (1960) found in one goat that in the range 40–65 mg/100 ml. mammary arteriovenous difference was related to the arterial level. Therefore infusions of glucose were given to two goats, being

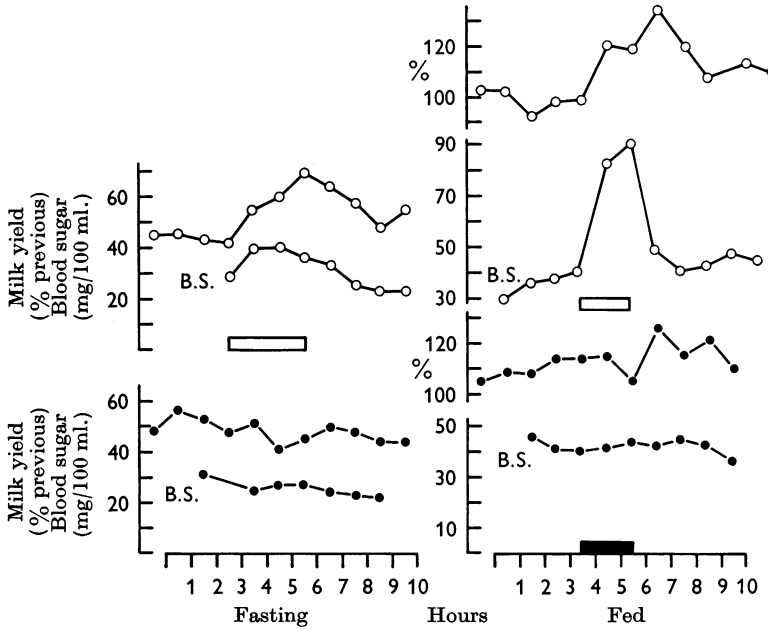


Fig. 7. Comparison of hourly milk yield (above) and blood sugar concentration (below) on four occasions in one goat. Bottom left, fasted 24 hr, no treatment. Top left, fasted, glucose infused intravenously (10 %, 1 ml./min). Bottom right, fed, no further treatment. Top right, fed and glucose infused.

milked hourly, where the blood glucose level was 29 and 34 mg/100 ml.; in one animal there was a 30 % rise in the concentration of milk lactose and in the other a similar rise in milk yield with no change in lactose concentration (Fig. 7).

## DISCUSSION

Having found that the rate of milk secretion in goats milked hourly is very similar to that on conventional twice daily milking in both fed and fasted animals with a lowered milk yield, the aim of the present work was to see if and how quickly changes in milk secretion could be induced experimentally. The evidence may be most readily assessed in the accompanying figures, where variations from hour to hour, experiment to

experiment and animal to animal are shown. It is clear, that although milk secretion is a continuous process and the great storage capacity of mammary glands means that emptying need not be frequent, nevertheless, significant changes in milk yield and composition can occur within an hour. The conclusion seems justified that very frequent milking, using exogenous oxytocin, can be a valid method of studying milk secretion, providing it is realized that too vigorous milking and excessively large doses of oxytocin can cause important changes in milk composition (Linzell, 1967).

The present results emphasize the importance of glucose for milk secretion. Glucose is essential for secretion in the isolated perfused gland (Hardwick, Linzell & Price, 1961) and in the present work there was a close parallel between changes in milk and lactose secretion and mammary glucose uptake. It also confirms the finding of Petersen & Boyd (1937) and Fisher & Elliot (1966) for the cow and Sopeña (1944) for the goat that glucose infusions can cause a rise in milk lactose, and also shows that milk yield can be raised in this way, when blood sugar is low. Very little glucose is absorbed from the gastro-intestinal tract in ruminants, so that factors controlling gluconeogenesis, and the relative uptake by the mammary glands and other tissues are likely to determine variations in the rate of milk secretion. Radloff, Schultz & Hoekstra (1966) found that blood sugar fell more on fasting in lactating than in non-lactating goats, which is probably related to the finding of Annison & Linzell (1964) that the udder of lactating goats takes up 60–85 % of the glucose entering the circulation. Previous studies have shown that the mammary arteriovenous difference of glucose was linearly related to the arterial level in cows (Graham, Jones & Kay, 1936) and in goats (Linzell, 1960), but these observations were made on normally fed animals. The present studies extend our knowledge by showing that at low levels of arterial glucose concentration the mammary arteriovenous difference can be maintained (Figs. 1, 6). This suggests that, at low arterial levels, glucose uptake will be determined by mammary blood flow.

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