BUTYRATE INDUCED HYPERGLYCEMIA IN SHEEP

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CHAPTER I

INTRODUCTION

Previous work has shown that metabolism in the ruminant animal differs somewhat from that of the monogastric animal. For example, in monogastric animals the major end product of dietary carbohydrate digestion is glucose, whereas in the adult ruminant animal most dietary carbohydrates are fermented by ruminal microorganisms resulting in the formation of short-chain fatty acids. These major end products of microbial fermentation in the rumen are acetic, propionic, and butyric acids (3, 9, 12). Several studies have shown that these volatile fatty acids are absorbed directly from the rumen (6,26). These studies on ruminal absorption of the volatile fatty acids have shown that the blood draining the rumen is considerably higher in volatile fatty acid concentration than that of the peripheral blood. It has also been established that acetate, propionate, and butyrate serve as the major sources of energy to the ruminant animal (3,33).

Of these short-chain fatty acids, acetic and butyric are known to be ketogenic and not glycogenic. Ash, et al. (5), Kronfield (19), Phillips, et al. (32), Phillips and Black (31), and Manns and Boda (22) have all reported a hyperglycemic response to the intravenous administration of butyrate to sheep and goats, both of which are ruminants; on the other hand, butyrate administration to dogs, swine, or horses, which are "monogasters", did not produce this hyperglycemic response. Trenkle and

Kuhlemeier (42) failed to demonstrate an increase in blood glucose following the intravenous administration of butyrate to sheep. Further studies by Phillips and Black (31) have shown that the administered butyrate itself is not converted to glucose but that butyrate triggers some other mechanism to bring about glycogenolysis in the liver and hence an elevation in blood glucose. The mechanism of this hyperglycemic response to the intravenous infusion of butyrate has not been explained. Previous work using adrenalectomized sheep, has shown that the hyperglycemia following butyrate administration is not an epinephrine response (32). Phillips et al. (32) have shown that the intravenous injection of butyrate into sheep resulted in an increase in liver phosphorylase activity which was followed by a decrease in liver glycogen and an increase in plasma glucose concentration. The reports of Black et al. (7) and Annison et al. (2) indicate that pathways for direct conversion of butyrate to glucose are unlikely since studies in the intact cow and sheep, using ^{14}C-butyrate, have demonstrated that butyrate is not directly converted to glucose.

A decrease in plasma nonesterified fatty acids which coincided with the hyperglycemic response to the intravenous administration of butyrate has been reported by Phillips et al. (32). The studies of Annison et al. (2) showed an increase in blood acetate following the intravenous infusion of ^{14}C-butyrate in sheep.

The studies of Bost et al. (8) indicate that anesthetizing sheep with ether or pentobarbital results in an increase in blood glucose. The hyperglycemic effect of ether was reported to be more intense than that of pentobarbital. Furthermore, Bost et al. (8) reported that anesthetizing sheep with ether results in an increase in plasma free fatty acids,

whereas anesthetizing sheep with pentobarbital results in a decrease in the plasma free fatty acids.

Inasmuch as conflicting reports have appeared in the literature concerning the hyperglycemic response in sheep to butyrate administration, and since butyrate plays an important role in the energy metabolism in sheep, an experiment was designed to study the effects of the intravenous administration of this volatile fatty acid on blood glucose in anesthetized and unanesthetized sheep. The effects of the intravenous infusion of butyrate on the concentrations of other volatile fatty acids in blood were also incorporated into the design of the experiment.

CHAPTER II

REVIEW OF LITERATURE

Energy metabolism in the adult ruminant differs somewhat from that of the monogastric animal. For example, the major source of energy in the adult ruminant is derived from acetate, propionate, and butyrate, whereas the major source of energy in the monogastric animal is derived from glucose. In the ruminant, dietary carbohydrates are fermented by ruminal microorganisms and only small amounts of glucose are absorbed from the alimentary tract (1). Several studies have shown that the volatile fatty acids are absorbed through the rumen wall into the portal blood (6,14,26,37). The absorption of the volatile fatty acids through the rumen wall is based upon the evidence that the portal blood leaving the rumen has a higher concentration of volatile fatty acids than that found in the arterial blood which enters the rumen.

The volatile fatty acids are metabolized to some extent by the rumen wall (23,27,28). It has been demonstrated that when an equilmolar solution of volatile fatty acids are present in the rumen, the concentration of the volatile fatty acids leaving the rumen does not contain equilmolar amounts of the volatile fatty aicds (23). This is based upon the evidence that the concentration of acetic acid in the blood leaving the rumen has been shown to be present in greater concentrations than that of either propionic acid or butyric acid. Also, the concentration of propionic acid in portal blood has been shown to be present in greater

concentrations than that of butyric acid. The studies of Pennington (27, 28) have clearly demonstrated that there is a greater oxygen consumption in tissue slices of rumen epithelium when butyrate is used as the substrate compared to the oxygen consumption when acetate, propionate, or glucose is used as the substrate. The concentrations of the fatty acids found in the blood leaving the rumen are in the order: acetate > propionate > butyrate.

An interesting feature in the energy metabolism in the ruminant animal is that the newborn ruminant animal has a blood glucose concentration of approximately 100 mg./100 ml. (mg.%) of blood (24). The blood glucose level in the newborn ruminant animal is similar to that which can be found in the monogastric animal. The studies of Reid (36) show that the blood glucose in the newborn ruminant animal gradually decreases to that of the adult ruminant animal 6 to 9 weeks after birth. The blood glucose levels in the adult ruminant animal are normally about 40 to 65 mg.%, and the blood glucose level does not normally rise above these levels for the remaining life of the ruminant animal. Thus, in the newborn, the ruminant animal is similar to the non-ruminant animal in that the newborn multigastric animal has a blood glucose level which is characteristic of the monogastric animal. The blood glucose gradually decreases early in the life of the ruminant animal, whereas the blood glucose in the normal non-ruminant animal, remains unchanged. This gradual decrease in the blood glucose in the ruminant animal does not mean that the ruminant animal lives entirely in the absence of glucose. There is a change in the utilization of substrates for energy purposes, i.e., the major source of energy in the adult ruminant animal is derived from the volatile fatty acids. The studies of Goetsch (13) show that there is a

decrease in the activity of the liver glycolytic enzymes during the development of the rumen in calves. This decrease in the activity of the glycolytic enzymes can be attributed to the decrease in glucose absorption during the development of the rumen. In other words, as the rumen becomes more functional, the dietary carbohydrates are fermented in the rumen and less glucose is available to be metabolized in the liver.

Since the volatile fatty acids have been shown to have such an important role in energy metabolism in the ruminant animal, several experiments have been designed to study the utilization of these acids by ruminant tissues. The metabolism of acetate, propionate, and butyrate in sheep liver slices was studied by Leng and Annison (20). In these studies, it was demonstrated that when ^{14}C-labelled volatile fatty acids were incubated with sheep liver slices, propionate and butyrate were oxidized more readily by liver tissue than was acetate. Furthermore, it was demonstrated that ^{14}C-propionate was incorporated into glucose to a greater extent than was ^{14}C-acetate or ^{14}C-butyrate.

Annison, et al. (1) have reported that acetate is present in greater amounts in the peripheral blood than either propionate or butyrate, and that most of the propionate and butyrate are metabolized by the liver. It has been demonstrated too that the rate of oxidation of acetate by the cells is dependent upon the availability of acetate to the cells (10). In other words, the higher the concentration of acetate in the peripheral arterial blood, the greater the rate of oxidation of acetate by the cells.

Of the three short-chain fatty acids, only propionate has been shown to contribute significantly to the net synthesis of glucose. It has been well established that propionate is glucogenic in function, whereas acetate and butyrate have been shown not to contribute significantly to the

net synthesis of glucose (20). The metabolic pathway for the synthesis of glucose from propionate has been studied by several investigators (18, 20,21,27). The studies of Annison, et al. (2) have demonstrated the incorporation of ^{14}C-1-propionate and ^{14}C-2-propionate into glucose. These studies also have demonstrated that the incubation of liver slices from sheep with ^{14}C-1-propionate resulted in the labelling of glucose predominantly in C-3 and C-4. Furthermore, the incubation of liver slices from sheep with ^{14}C-2-propionate resulted in the labelling of glucose predominantly in C-1, C-2, C-5, and C-6. Annison, et al. (2) reported that the incorporation of ^{14}C-1-propionate and ^{14}C-2-propionate into glucose was found to be in agreement with the well established pathway for the conversion of propionate to glucose, which they presented in outline form; propionate is converted to succinate, an intermediate in the tricarboxylic acid cycle, before being converted to phosphoenolpyruvate, and then to glucose by reverse glycolysis. The metabolic pathway for the conversion of propionate to glucose is outlined as follows: the conversion of propionate to propionyl-CoA; the carboxylation of propionyl-CoA to methylmalonyl-CoA; the isomerization of methylmalonyl-CoA to succinyl-CoA; the conversion of succinyl-CoA to succinate; the oxidation of succinate to fumarate; the reversible hydration of fumarate to malate; the oxidation of malate to oxaloacetate; the decarboxylation of oxaloacetate to phosphoenolpyruvate; the reduction of phosphoenolpyruvate to the triosephosphate; the formation of fructose-1, 6-diphosphate; and the conversion to glucose (3).

Different pathways have been postulated for the metabolism of propionate. For example, the studies of Leng, et al. (21) have demonstrated that a substantial amount of propionate is first converted to lactate

before being converted to glucose. The studies of Pennington and Sutherland (30) and Taylor and Ramsey (41) have shown that propionate is converted to lactate in rumen epithelial tissue. They further reported that methylmalonyl-CoA could not be formed in the absence of CO_2. These studies have further substantiated the fact that a major role of propionate in the energy metabolism of the ruminant animal is gluconeogenesis.

In the ruminant animal, the metabolism of acetate and butyrate has been demonstrated to be somewhat different from that of propionate. For example, it has been well established that acetate and butyrate do not contributed significantly to the net synthesis of glucose. The studies of Leng and Annison (20) have demonstrated that the intravenous infusions of ^{14}C-acetate and ^{14}C-butyrate resulted in no net synthesis of glucose.

Acetate is metabolized only to a small extent by rumen tissue, with most of the acetate being absorbed through the rumen wall into the portal blood and passing to the liver. Leng and Annison (20) have reported that propionate and butyrate are metabolized in the liver to a greater extent than is acetate. Annison, et al. (1) have reported that the peripheral blood contains greater concentrations of acetate when compared to the concentration of either propionate or butyrate.

A major source of energy in the ruminant animal is supplied by the oxidation of acetate via the tricarboxylic acid (TCA) cycle. Acetate can be oxidized directly in the cells, and Davis, et al. (10) have reported that the oxidation of acetate is dependent upon the availability of acetate to the tissues. The oxidation of acetate via the TCA cycle is outlined by the following steps: the conversion of acetic acid to acetyl-CoA at the expense of adenosine triphosphate (ATP); the condensation of acetyl-CoA with oxaloacetate with the formation of citrate; and

the oxidation of the TCA intermediates to CO_2 and H_2O (3). Thus, two carbons are contributed to the TCA cycle by acetate, and for every turn of the cycle two carbons are eliminated as CO_2. In order for acetate to be oxidized via the TCA cycle, there must be a supply of ATP for the formation of acetyl-CoA, as well as, a supply of a four carbon dicarboxylic intermediate (oxaloacetate) to condense with acetyl-CoA to form citrate. Oxaloacetate can be supplied by propionate and glucose. Annison, et al. (2) have reported that the infusion of propionate resulted in a decrease in the concentrations of acetate in the blood. It is well established that propionate enters the TCA cycle through succinyl-CoA and thus could serve as a supply of oxaloacetate for the oxidation of acetate.

Different pathways have been postulated for the utilization of acetate in the ruminant animal. For example, several investigators have reported that acetate carbon can be incorporated into glucose as evidenced by their radioisotopic studies (2,4,20). The studies of Pennington and Pfander (29) have shown that acetate is converted to ketone bodies in the liver. Even though other metabolic pathways have been demonstrated for the utilization of acetate, these pathways are secondary to the oxidation of acetate via the tricarboxylic acid cycle.

Butyrate is metabolized to a large extent by the liver in ruminant animals (15). Much controversy exists among several investigators as to the exact mechanisms of butyrate metabolism in the liver. Several workers are in agreement that butyrate is ketogenic in function and is metabolized into ketone bodies (27,43), while others support the idea that butyrate is glycogenic in function and is oxidized via the TCA cycle (2,15,16,20).

Butyrate is metabolized to a large extent in ruminant animals by the liver. The possibility of butyrate being glucogenic in function lacks support, since butyrate does not contribute significantly to the net synthesis of glucose. The studies of Leng and Annison (20) and Annison et al. (2) have demonstrated that the incorporation of radioactive labelled butyrate does not involve a net synthesis of glucose. These studies are supported by earlier findings of Ash, et al. (5) who attempted to show the effects of short-chain fatty acids on blood glucose in sheep. They reported that the injection of carboxy-^{14}C-butyrate into insulinized sheep resulted in less than 1% of circulating glucose being derived directly from the labelled butyrate.

In ruminant animals, butyrate is believed to be metabolized to ketone bodies (acetone, acetoacetate, and β-hydroxybutyrate). This theory is supported by the studies of Pennington and Pfander (29) who found that, in vitro, butyrate was converted into ketone bodies and in particular into acetoacetate. Spahr, et al. (39) found that butyric acid was readily converted into β-hydroxybutyrate in the perfused goat rumen. Ramsey and Davis (35) and Leng and Annison (20) reported that butyrate is metabolized via the tricarboxylic acid cycle. They demonstrated close similarities in the labelling of glucose in carbons 3 and 4 obtained from ^{14}C-1-acetate, ^{14}C-1-butyrate, and ^{14}C-3-butyrate. These studies have been found to be in agreement with the metabolic pathway for the oxidation of butyrate, i.e. via the tricarboxylic acid cycle. The metabolic pathway for the oxidation of butyrate is outlined as follows: butyrate is converted by butyryl-CoA; butyryl-CoA is converted crotonyl-CoA; crotonyl-CoA is converted to β-hydroxybutyryl-CoA; β-hydroxybutyryl-CoA is converted to acetoacetyl-CoA; acetoacetyl-CoA is then converted into

acetyl-CoA which enters the TCA cycle by condensing with oxaloacetate to form citrate (3).

The possibility of butyrate being glucogenic in function has been the subject of special interest since butyrate plays an important role in the energy metabolism of the ruminant animal. In 1952, Potter (34) demonstrated that the intravenous injection of sodium butyrate relieved insulin convulsions as evidenced by the concurrent rise in blood glucose concentrations. In 1952, Jarret (17) reported an immediate increase in blood glucose following the intravenous injection of sodium butyrate into sheep. It was postulated that the increase in blood glucose was mediated through the release of epinephrine from the adrenal medulla.

In 1956, Kronfield (19) studied the effect of butyrate administration in sheep. He reported that the intravenous infusion of sodium butyrate resulted in an increase in blood glucose concentration when the initial level was low and a decrease in blood glucose level when the initial level was high. Ash, et al. (5) found that the administration of 0.25 millimoles of butyrate per kilogram of body weight into insulin treated sheep caused a rapid increase in the blood glucose concentration within a few minutes after the injection. They postulated that the increase in blood glucose was due to the release of glucose from the liver. Furthermore, they postulated that the adrenal glands were stimulated by butyrate causing the release of epinephrine which is known to stimulate the liver to release glucose.

Phillips, et al. (32) demonstrated a significant rapid increase in blood glucose concentration in insulin treated sheep a few minutes after the intravenous injection of sodium butyrate. They further demonstrated an increase in liver phosphorylase activity immediately following the

injection of sodium butyrate and a concomitant decrease in the liver glycogen content during this same time period. They further reported that the intravenous injection of sodium butyrate in adrenalectomized lambs and intact lambs produced similar results. They postulated that butyrate may either stimulate the liver directly, causing the release of glucose, or butyrate may activate some other mechanism such as glucogon release from the pancreas to cause the release of glucose from the liver.

Trenkle and Kuhlemeier (42) failed to demonstrate a hyperglycemic response to butyrate in sheep. They analyzed blood glucose samples 1 and 2 hours after the injection of butyrate and found that the blood glucose concentrations decreased following the butyrate injection. Mann, et al. (31), using a technique of direct canulation of the pancreatic vessels in vivo in adult sheep, reported that butyrate stimulated insulin release through a direct effect on the pancreas which could not be attributed to the effect of hyperglycemia or hyperketonemia. Inasmuch as there are some conflicting reports appearing in the literature on the effects of butyrate on blood glucose, it seemed apparent that additional experiments need to be done to study the intravenous effects of butyrate and to ascertain whether or not a hyperglycemic response occurs following the intravenous injection of sodium butyrate.

CHAPTER III

MATERIALS AND METHODS

Twenty mature sheep, 2-3 years of age, were used to study the effects of the intravenous injection of sodium butyrate upon blood glucose concentrations and blood levels of acetate, propionate, and butyrate. The sheep were kept in outside pens. Their diet consisted of prairie hay ad libidum and a daily feeding of a commercially prepared grain mixture. The sheep were brought indoors on the day before the experiment and were not fed on the day of the experiment. All experiments were performed in the morning.

In order to study the effects of sodium butyrate on blood glucose and blood volatile fatty acid concentrations in the anesthetized sheep, the sheep were anesthetized with sodium pentobarbitol. A 15 cm. polyethylene cannula was inserted into the jugular vein prior to the experiment in order to facilitate the administration of the sodium butyrate solution and the taking of blood samples at precise time intervals. In regards to the unanesthetized sheep, the sheep were restrained with a halter and kept in a small retaining pen, but were free to lie or stand at will. A 15 cm. polyethylene cannula was inserted into the jugular vein of the unanesthetized sheep prior to the experiment in order to minimize excitement of the animal, while administering the sodium butyrate solution, and taking blood samples from the jugular vein. Heparin was added to the cannula in both the anesthetized and unanesthetized

sheep in order to prevent blood coagulation in the cannula.

Three 12 ml. blood samples were taken at 10 min. intervals prior to the administration of the sodium butyrate solution to establish preinjection blood glucose and volatile fatty acid levels. The sodium butyrate solution, neutralized to a pH of 7.2 with NaOH, was administered to the sheep via the jugular vein cannula at the rate of 2.5 millimoles/Kg. body weight. The sodium butyrate solution was infused slowly over a five minute period and 12 ml. blood samples were drawn from the jugular vein cannula every 10 minutes for a period of 3 hours following the infusion.

Immediately upon the removal of 12 ml. of blood from the jugular vein, one milliliter of whole blood was diluted with 5 ml. of glass distilled water to hemolyze the red blood cells. This was followed by the addition of 2 ml. of 2% $Ba(OH)_2$ and 2 ml. of 2% $ZnSO_4$. The barium and zinc solutions were adjusted so that a solution of pH 7.2 resulted when equal volumes of each solution were mixed. The barium and zinc were added to precipitate the proteins of the blood. One milliliter of the protein free filtrate was then used to determine blood glucose concentrations according to the methods of Nelson (25) and Somogyi (38). Also, immediately following the removal of 12 ml. of blood from the jugular vein, 10 ml. of whole blood were diluted with 50 ml. of glass distilled water to hemolyze the red blood cells, followed by the addition of 20 ml. of 2% $Ba(OH)_2$ and 20 ml. of 2% $ZnSO_4$. Again, the equal volumes of $Ba(OH)_2$ and $ZnSO_4$ were added to precipitate the protein from the whole blood. The protein free filtrate was then adjusted to a pH of 9.0 with 10% NaOH in order to form the sodium salts of the volatile fatty acids. The filtrates were concentrated to a volume less than 2 ml. in a water bath and frozen until ready for analysis by gas chromatography.

Before gas chromatographic analysis of the prepared samples, each sample was acidified with 10% phosphoric acid and the volume adjusted to 2.0 ml. with glass distilled water. The acetic, propionic, and butyric acids were separated on a 62 inch stainless steel column (1/8" diameter) packed with chromosorb W (60/80 mesh) coated with carbowax 4000 containing 20% terephtalic acid[1]. A Perkin-Elmer model 900 Gas Chromatograph[2] equipped with a hydrogen flame ionization detector was used for gas chromatographic analysis of the volatile acids. Helium was used as the carrier gas. The oven temperature was isothermally maintained at 280° C. The areas formed on the gas chromatograph recordings by the acetic, propionic, and butyric acid peaks were determined by triangulation. The concentrations of the three volatile fatty acids were determined by comparing the areas formed from the injection of 1 µl. of a standard solution containing acetic acid (100 mg./ml. H_2O), propionic acid (100 mg./100 ml. H_2O), and butyric acid (100 mg./100 ml. H_2O).

Statistical analysis was made on the blood glucose concentrations and the blood levels of acetate, propionate, and butyrate in both the anesthetized and unanesthetized sheep. The statistical analysis tests used were the F-test, the Duncan's new multiple range test, and the t-test as presented in Steel and Torie (40). The t-test was used for comparisons between anesthetized and unanesthetized groups, and the F-test and Duncan's new multiple range tests were used for comparisons within each group.

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[1]Applied Science Laboratories, Inc., State College, Pennsylvania.

[2]Perkin-Elmer Corporation, Norwalk, Connecticut.

CHAPTER IV

RESULTS

The objective of this study was to measure the blood glucose concentrations in anesthetized and unanesthetized sheep following the intravenous infusion of sodium butyrate. A second objective was to measure the blood acetate, propionate, and butyrate concentrations in anesthetized and unanesthetized sheep following the intravenous injection of sodium butyrate.

Blood Glucose

The changes in blood glucose concentrations in anesthetized and unanesthetized sheep following the intravenous injection of sodium butyrate are shown in Figure 1. Each point on the graph represents the mean of 10 replications.

There was an increase in blood glucose concentrations in both the anesthetized and unanesthetized sheep following the intravenous injection of sodium butyrate. The post-injection increase in blood glucose concentration in the unanesthetized sheep was greater than that of the anesthetized sheep. There was a very highly significant difference ($p < 0.001$) in blood glucose levels between the anesthetized and unanesthetized sheep at 30 minutes following the intravenous sodium butyrate injection. The blood glucose increased from a mean of 70 mg.% to a mean of 153 mg.% in the unanesthetized sheep and from 69 mg.% to 116 mg.% in the

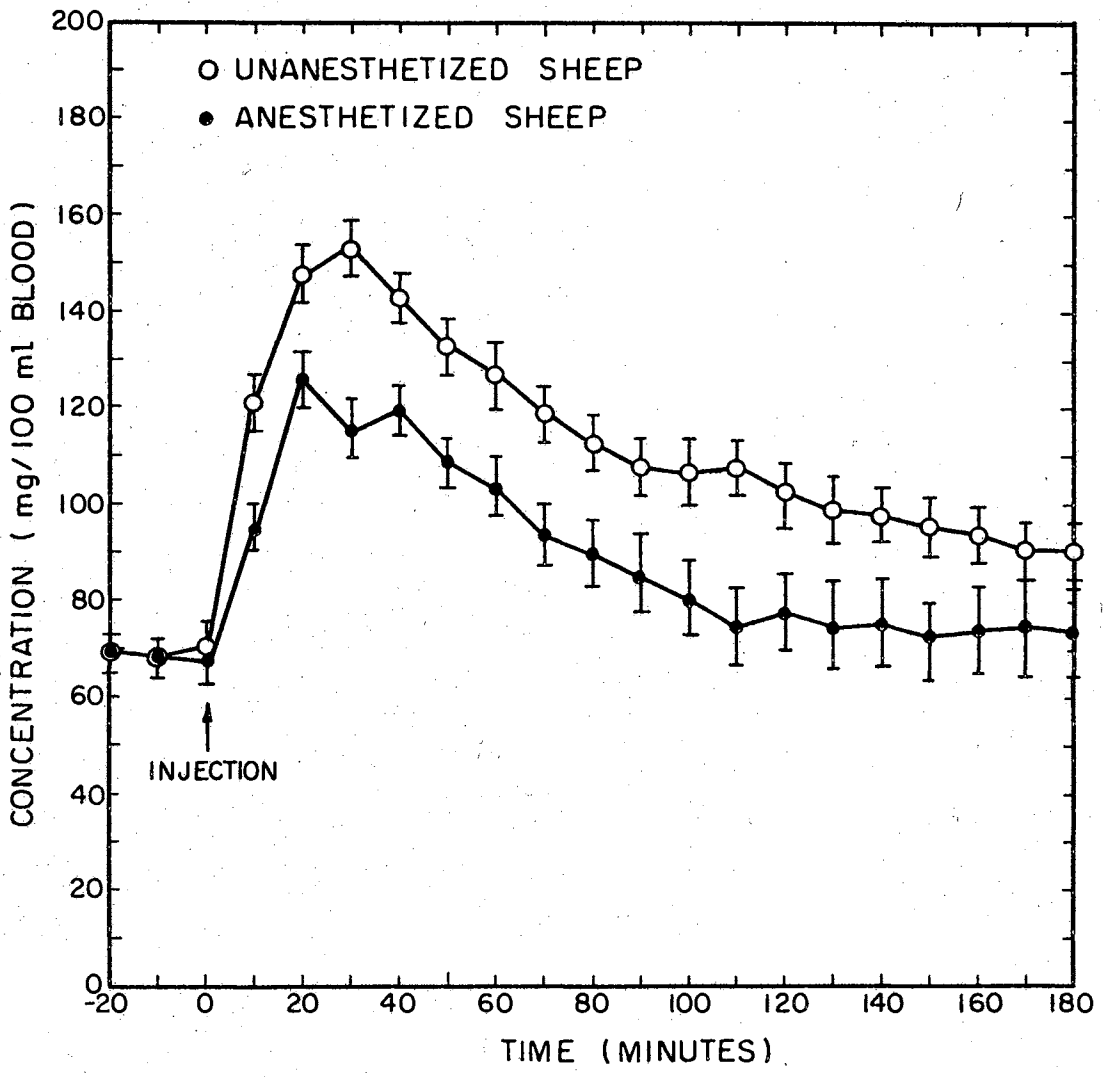

Figure 1. The Average Changes in Blood Glucose Concentrations in the Anesthetized and the Unanesthetized Sheep Before and Following the Injection of Sodium Butyrate (2.5 mMoles/Kg.) at Zero Time

anesthetized sheep 30 minutes after the butyrate administration. Also, there was a highly significant difference in blood glucose ($p < 0.01$) between the anesthetized and unanesthetized sheep at 10, 40, 70, and 110 minutes following the butyrate injection, and a significant difference ($p < 0.05$) at 20, 50, 60, 100, 120, and 150 minutes following the butyrate injection.

The average blood glucose concentration prior to the administration of sodium butyrate was 68.6 mg.% for the anesthetized sheep and 68.9 mg.% for the unanesthetized sheep. In anesthetized sheep, there was a highly significant increase ($p < 0.01$) in blood glucose concentration at 20, 30, 40, 50, and 60 minutes following the butyrate injection, and a significant increase ($p < 0.05$) at 10 and 70 minutes following the butyrate injection. The intravenous injection of sodium butyrate to unanesthetized sheep also resulted in an increase in blood glucose shortly after the butyrate administration. There was a highly significant increase in blood glucose concentration ($p < 0.01$) at all time intervals between 10 and 150 minutes following the butyrate injection, and a significant increase ($p < 0.05$) in blood glucose at 160, 170, and 180 minutes following the administration of butyrate to the unanesthetized sheep. Table 1 summarizes the average blood glucose concentrations obtained at the various time intervals for the anesthetized and unanesthetized sheep throughout this experiment.

Blood Volatile Fatty Acids

Table II and Figures 2 and 3 summarize the changes in the blood levels (mg.%) of acetate, propionate, and butyrate following the intravenous infusion of sodium butyrate in anesthetized and unanesthetized

TABLE I

THE AVERAGE BLOOD GLUCOSE CONCENTRATION CHANGES IN ANESTHETIZED AND UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INJECTION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME[1]

Time in Minutes	Blood Glucose Concentration (mg.%)	
	Anesthetized	Unanesthetized
-20	68 ± 3	69 ± 4
-10	68 ± 2	68 ± 4
0	69 ± 3	70 ± 4
10	*95 ± 5[2]	**121 ± 6[3]
20	**126 ± 6	**148 ± 6
30	**116 ± 6	**153 ± 6
40	**120 ± 5	**143 ± 5
50	**109 ± 5	**133 ± 6
60	**104 ± 6	**127 ± 7
70	*94 ± 6	**119 ± 6
80	90 ± 7	**113 ± 6
90	86 ± 8	**108 ± 6
100	81 ± 8	**107 ± 7
110	75 ± 8	**108 ± 6
120	78 ± 8	**103 ± 6
130	75 ± 9	**99 ± 7
140	76 ± 9	**98 ± 6
150	73 ± 9	**96 ± 6
160	74 ± 9	**94 ± 6
170	75 ±10	*91 ± 6
180	74 ± 9	*91 ± 6

[1]Each value represents the mean of 10 sheep ± standard error

[2]* ($p < 0.05$)

[3]** ($p < 0.01$)

TABLE II

THE AVERAGE BLOOD ACETATE, PROPIONATE, AND BUTYRATE CONCENTRATIONS IN ANESTHETIZED AND UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INJECTION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME[1]

Time	Concentration of Volatile Fatty Acids in (mg.%)					
	Anesthetized			Unanesthetized		
	Acetate	Propionate	Butyrate	Acetate	Propionate	Butyrate
-20	9.2 ± 1	0.3 ± 0.1	0.4 ± 0.1	7.3 ± 1	0.2 ± 0.1	0.2 ± 0.1
-10	8.7 ± 1	0.3 ± 0.1	0.3 ± 0.1	8.2 ± 1	0.2 ± 0.1	0.2 ± 0.1
0	9.2 ± 1	0.2 ± 0.1	0.2 ± 0.1	7.8 ± 1	0.3 ± 0.1	0.2 ± 0.1
10	13.9 ± 1	0.5 ± 0.1	**51.9 ± 7 [3]	*13.5 ± 1[2]	0.5 ± 0.1	**33.5 ± 2
20	**18.7 ± 2	0.5 ± 0.1	**29.4 ± 4	**15.8 ± 2	0.5 ± 0.1	**18.7 ± 1
30	**18.3 ± 2	0.5 ± 0.1	**15.5 ± 3	**15.5 ± 2	0.5 ± 0.1	**8.8 ± 1
40	**18.1 ± 2	0.5 ± 0.1	**8.6 ± 3	**16.8 ± 1	0.5 ± 0.1	**3.4 ± 0
50	*16.9 ± 2	0.4 ± 0.1	3.0 ± 3	**15.5 ± 2	0.4 ± 0.1	1.2 ± 0.2
60	*14.4 ± 2	0.3 ± 0.1	1.2 ± 0.1	*13.6 ± 2	0.3 ± 0.1	0.5 ± 0.1
70	12.8 ± 2	0.3 ± 0.1	0.5 ± 0.1	12.3 ± 1	0.3 ± 0.1	0.3 ± 0.1
80	10.4 ± 1	0.3 ± 0.1	0.4 ± 0.1	11.4 ± 2	0.3 ± 0.1	0.3 ± 0.1
90	9.7 ± 1	0.3 ± 0.1	0.2 ± 0.1	10.9 ± 1	0.3 ± 0.1	0.2 ± 0.1
100	9.0 ± 1	0.3 ± 0.1	0.3 ± 0.1	10.4 ± 1	0.3 ± 0.1	0.2 ± 0.1
110	9.6 ± 1	0.3 ± 0.1	0.2 ± 0.1	10.7 ± 1	0.3 ± 0.1	0.2 ± 0.1
120	9.3 ± 1	0.3 ± 0.1	0.2 ± 0.1	10.4 ± 1	0.3 ± 0.1	0.2 ± 0.1
130	8.5 ± 1	0.3 ± 0.1	0.2 ± 0.1	9.8 ± 1	0.3 ± 0.1	0.2 ± 0.1
140	7.1 ± 1	0.3 ± 0.1	0.2 ± 0.1	9.6 ± 1	0.3 ± 0.1	0.2 ± 0.1
150	8.2 ± 1	0.3 ± 0.1	0.2 ± 0.1	9.3 ± 1	0.3 ± 0.1	0.2 ± 0.1
160	7.4 ± 1	0.3 ± 0.1	0.2 ± 0.1	9.1 ± 1	0.3 ± 0.1	0.2 ± 0.1
170	6.6 ± 1	0.2 ± 0.1	0.2 ± 0.1	9.4 ± 1	0.3 ± 0.1	0.2 ± 0.1
180	6.8 ± 2	0.2 ± 0.1	0.2 ± 0.1	9.4 ± 1	0.3 ± 0.1	0.2 ± 0.1

[1]Each value represents the mean of 10 sheep ± standard error

[2]* ($p < 0.05$)

[3]** ($p < 0.01$)

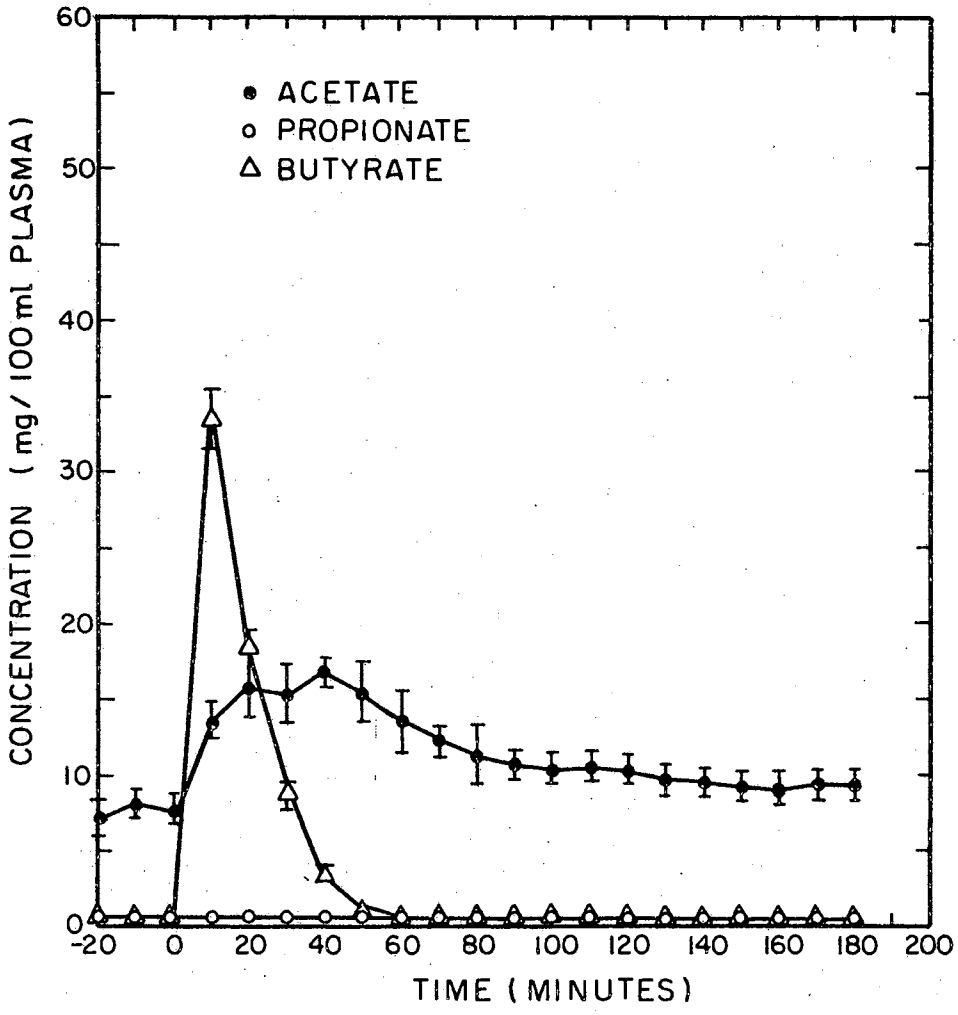

Figure 2. The Average Blood Acetate, Propionate, and Butyrate Concentrations in Unanesthetized Sheep Before and Following the Intravenous Injection of Sodium Butyrate (2.5 mMoles/ Kg.) at Zero Time

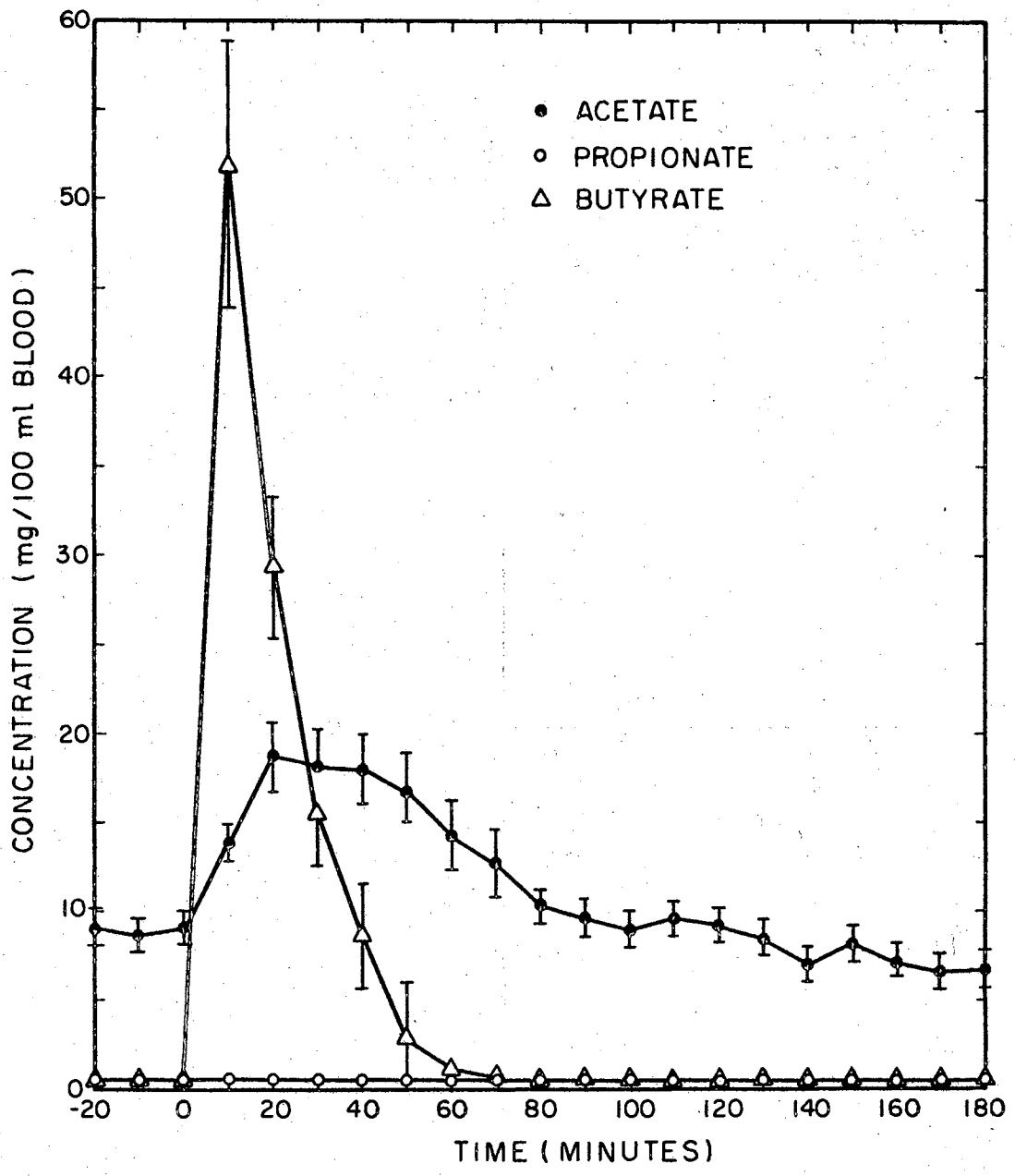

Figure 3. The Average Blood Acetate, Propionate, and Butyrate Concentrations in Anesthetized Sheep Before and Following the Intravenous Injection of Sodium Butyrate (2.5 mMoles/Kg.) at Zero Time

sheep. Following the butyrate injection, there was a highly significant increase ($p < 0.01$) in the blood acetate concentrations at 20, 30, and 40 minutes in the anesthetized sheep, and at 20, 30, 40, and 50 minutes in the unanesthetized sheep. Also, there was a significant increase in blood acetate levels ($p < 0.05$) at 60 minutes following butyrate administration in the anesthetized sheep, and at 10 and 60 minutes in the unanesthetized sheep. There were no significant changes in the blood propionate concentrations in either the anesthetized or unanesthetized sheep following the butyrate injection. The intravenous infusion of sodium butyrate in both the anesthetized and unanesthetized sheep resulted in a highly significant increase ($p < 0.01$) in blood levels of butyrate at 10, 20, 30, and 40 minutes following the butyrate injection. Comparison of the butyrate levels between the anesthetized and unanesthetized sheep showed that there was a highly significant difference ($p < 0.01$) at 20 minutes and a significant difference ($p < 0.05$) at 10, 30, 50, and 60 minutes following the butyrate injection. There was not a significant difference in the blood acetate levels between the anesthetized and unanesthetized sheep following the butyrate injection. Figure 4 illustrates the changes in blood acetate concentrations in both the anesthetized and unanesthetized sheep.

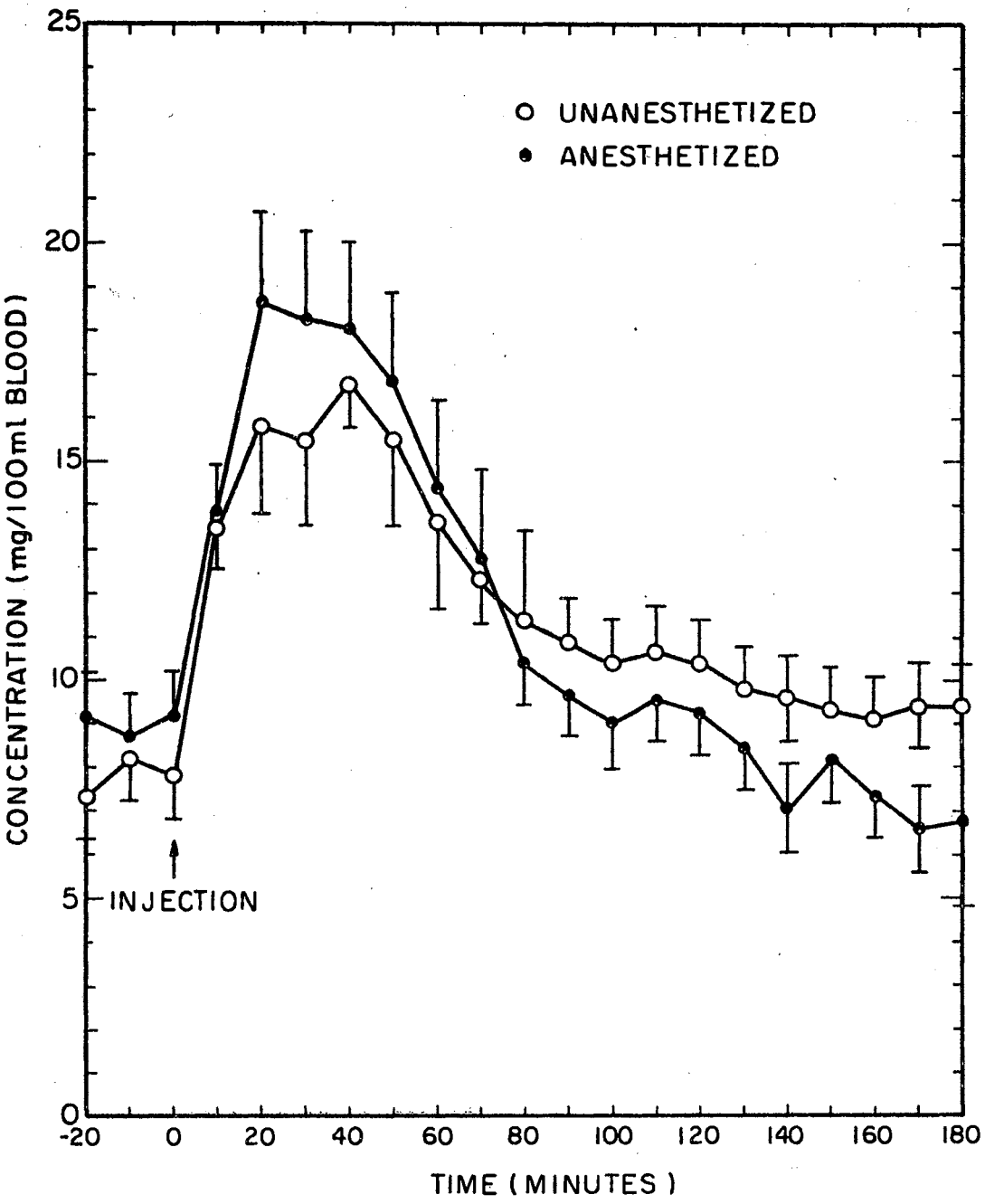

Figure 4. The Average Blood Acetate Concentrations in the Anesthetized and the Unanesthetized Sheep Before and Following the Injection of Sodium Butyrate (2.5 mMoles/Kg.) at Zero Time.

CHAPTER V

DISCUSSION

It has been well established that the liver is the primary organ for butyrate metabolism in the ruminant animal. However, there has been much controversy among investigators in regard to butyrate metabolism by the liver. The main controversy is concerned with the possible glycogenic or ketogenic function of butyrate as discussed earlier. In regard to the glycogenic role of butyric acid, there have been several investigations dealing with the effect of sodium butyrate on blood glucose. In this respect, the results of this experiment have demonstrated that the intravenous infusion of sodium butyrate into both the anesthetized and unanesthetized sheep resulted in an increase in blood glucose within ten minutes following the butyrate injection. In 1952, Potter (34) reported that the administration of butyric acid into insulin-treated, hypoglycemic lambs relieved the insulin induced hypoglycemic convulsions and produced an increase in blood glucose. Jarrett, Potter, and Tilsell (17) in 1952 reported that the administration of butyric acid into sheep resulted in a rapid increase in blood glucose as well as a gradual increase in pyruvic acid. It was then postulated that the butyrate induced hyperglycemic response was possibly due to glycogenolysis mediated through the release of epinephrine from the adrenal medulla.

Other researchers have observed an increase in blood glucose following the administration of butyrate. Ash, et al. (5) observed a similar

hyperglycemic response to butyrate administration in insulin treated sheep. Working on the hypothesis that the increase in blood sugar was due to butyrate causing the release of epinephrine from the adrenal medulla, they then injected the same sheep with epinephrine. It was found that epinephrine injected into sheep resulted in an increase in blood lactate along with the expected increase in blood glucose. Since previous injections of butyric acid did not produce an increase in blood lactate along with the elevation in blood sugar, they then postulated that the hyperglycemic response was not due to butyrate induced epinephrine release from the adrenal medulla.

In 1965, Phillips et al. (32) clearly demonstrated that butyrate administration into adrenalectomized insulin treated sheep resulted in an increase in blood glucose within fifteen minutes following the injection. Further experiments by Phillips et al. (32), using adrenalectomized lambs, demonstrated that butyrate administration resulted in an increase in liver phosphorylase activity which occurred immediately after the injection but prior to the hyperglycemic response. Also, corresponding to the increase in phosphorylase activity, a decrease in liver glycogen was observed. Phillips et al. (32) further noted a five-fold increase in plasma ketone bodies following butyrate injection. However, the studies of Ash, et al. (5) clearly demonstrated that the injection of β-hydroxybutyrate into lambs did not produce a hyperglycemic response. The results from the experiments of Phillips and Black (31) and Phillips et al. (32) have indicated the possibility of butyrate acting directly upon the liver to increase phosphorylase activity or, as postulated in Phillips et al. (32), butyrate may induce the release of glucagon from the pancreas which would in turn produce an increase in liver phosphorylase activity.

In 1966, Trenkle and Kuhlemeier (42) failed to demonstrate the hyperglycemic response following butyrate injection. Instead, they reported that the concentration of blood glucose decreased following the butyrate injection. The differences between the results obtained in the investigation reported herein to those obtained by Trenkle and Kuhlemeier (42) could possibly be due to the experimental procedure. Trenkle and Kuhlemeier measured blood glucose concentrations at one and two hour intervals following the butyrate injection. The results of the current experiment support those of Jarrett et al. (17) and Phillips et al. (32) in that the hyperglycemic response occurs within minutes following the butyrate injection and then it gradually decreases toward that of normal preinjection glucose levels. It therefore seems probable that the failure of Trenkle and Kuhlemeier (42) to demonstrate butyrate induced hyperglycemia was due to the fact that they failed to take blood samples early after injection.

Studies on the effect of the blood glucose concentration upon the butyrate induced hyperglycemic response in sheep has been studied by Kronfeld (19) and Phillips and Black (31). Kronfeld (19) reported that when blood glucose levels were near normal (40 mg.%), butyrate administration increased the blood glucose levels 5 to 50 mg.%. When blood glucose levels were low (20-25 mg.%), the effects were even more profound in that blood glucose levels were increased 50 to 80 mg.%. On the other hand, Kronfeld (19) reported that when blood glucose levels were high (60-80 mg.%) prior to the injection, butyrate administration decreased the blood glucose levels.

The current investigation does not agree with the latter findings of Kronfeld (19) since the blood glucose levels prior to butyrate

administration reported herein are within Kronfeld's "high" range but these sheep still exhibited a marked hyperglycemic response to butyrate. The fact that the butyrate induced hyperglycemic response is not dependent upon the blood glucose level at the time of administration has been shown by other investigators. For example, Phillips and Black (31) demonstrated that when butyrate was injected into nursing 2-week old lambs whose blood glucose levels were over 100 mg.%, a hyperglycemic response resulted which was much the same as in the fasted, insulin hyperglycemic lambs. In the investigation reported herein, the average blood glucose levels prior to the injection of butyrate were 68.6 mg.% in the anesthetized sheep and 68.9 mg.% in the unanesthetized sheep. The administration of sodium butyrate resulted in an elevation in blood glucose in both the anesthetized and unanesthetized sheep (Figure 1). Hungate (16) reported that a decrease in liver glycogen was not found in excised livers perfused with butyrate, indicating that butyrate does not produce liver glycogenolysis directly. Further investigation is needed to elucidate the butyrate induced glucostatic mechanism in the ruminant animal.

In regard to the role of the pancreas in this hyperglycemic response, Manns and Boda (22) have demonstrated that the administration of butyrate acts directly upon the pancreas to stimulate the release of insulin. The possibility of a butyrate induced release of glucagon by the pancreas was not investigated by these workers. Additional experiments may ascertain the role of the pancreas with respect to the butyrate induced hyperglycemic response.

The possibility of butyrate being directly converted into glucose has been studied by several investigators. The studies of Leng and Annison (20) and Ash, et al. (5) have demonstrated that the incorporation

of radioactive labelled butyrate into glucose involves no net synthesis of glucose. Weinmen (43) has shown that the incorporation of radioactive labelled volatile fatty acids into glucose does not necessarily mean a net synthesis of glucose.

In this investigation, the intravenous injection of sodium butyrate into anesthetized and unanesthetized sheep resulted in an increase in blood acetate levels following the butyrate injection as illustrated in Figures 2, 3, and 4. Spahr, et al. (39) have demonstrated that perfusing the goat rumen with butyrate resulted in the conversion of butyrate to β-hydroxybutyric acid. Pennington (27) demonstrated that butyrate was readily converted into acetoacetate in vitro. Pennington (27) was measuring the ability of the rumen epithelial tissue of the sheep to metabolize the volatile fatty acids. It was found that butyric acid was metabolized by rumen epithelial tissue to a greater extent than either acetic or propionic acids, and that a large part of the butyric acid was converted to ketone bodies. Acetic acid was shown to be converted to ketone bodies, but no ketone bodies were derived from propionate. Leng and Annison (20) postulated that the incorporation of ^{14}C-1-butyrate into β-hydroxybutyrate indicated a continual breakdown and resynthesis of acetoacetyl-CoA through acetyl-CoA. These studies support the ketogenic role of butyrate metabolism in the ruminant animal. The basis for the ketogenic role is the metabolism of butyrate via the TCA cycle through acetyl-CoA as an intermediate. Thus, for every two carbons contributed to the TCA cycle by butyrate, two carbons are lost in the form of carbon dioxide.

Since nonradioactive labelled butyrate was used throughout this investigation, it is difficult to ascertain the exact metabolic pathways

involved in the elevation of blood acetate levels following the butyrate administration. It is known that acetyl-CoA may be synthetized from acetate in the presence of ATP and CoA. Also, it is known that butyrate is oxidized via the TCA cycle through acetyl-CoA. Thus, the infusion of large amounts of butyrate may serve as a supply for acetyl-CoA producing an equilibrium change in acetyl-CoA synthesis and a possible increase in acetate levels which normally would be readily oxidized via the TCA cycle. Little is known about the exact pathways involved in butyrate metabolism.

In conclusion, it was observed that the administration of sodium butyrate into anesthetized and unanesthetized sheep resulted in an increase in blood glucose within a few minutes following injection, and an increase in blood acetate levels as well as the expected increase in blood butyrate levels. Additional experiments need to be designed in order to study the exact mechanism of this butyrate induced hyperglycemic response. It has been postulated by Phillips, et al. (32) that butyrate induces the release of glucagon from the pancreas which in turn produces the increase in liver phosphorylase activity. The results reported herein do not eliminate this possibility and, in fact, make this suggestion even more attractive.

CHAPTER VI

SUMMARY AND CONCLUSIONS

The effects of intravenous sodium butyrate on blood glucose in sheep have been reported by several investigators. Since the results of these studies failed to agree, an experiment was designed to study further the effects of the intravenous injection of sodium butyrate on blood glucose levels in anesthetized and unanesthetized sheep. Another objective was to measure the blood levels of acetate, propionate, and butyrate following butyrate administration.

The following results were observed:

1. The intravenous injection of sodium butyrate into anesthetized sheep resulted in a highly significant increase in blood glucose concentration ($p < 0.01$) at 20, 30, 40, 50, and 60 minutes following the butyrate injection, and a significant increase in blood glucose concentration ($p < 0.05$) at 10 and 70 minutes following the injection of butyrate.
2. The intravenous injection of sodium butyrate into unanesthetized sheep resulted in a highly significant increase in blood glucose concentration ($p < 0.01$) at all time intervals between 10 and 150 minutes following the butyrate injection; and a significant increase in blood glucose concentration ($p < 0.05$) at 160, 170, and 180 minutes following the injection of butyrate.
3. There was a highly significant increase in blood acetate

concentration ($p < 0.01$) at 20, 30, and 40 minutes in the anesthetized sheep and at 20, 30, 40, and 50 minutes in the unanesthetized sheep following the butyrate injection. Also, following the butyrate injection, there was a significant increase in blood acetate levels ($p < 0.05$) at 60 minutes in the anesthetized sheep, and at 10 and 60 minutes in the unanesthetized sheep.

4. There was no change in blood propionate concentration in either the anesthetized or unanesthetized sheep following the injection of butyrate.
5. There was a highly significant increase in blood butyrate concentration ($p < 0.01$) at 10, 20, 30, and 40 minutes following the butyrate injection in both the anesthetized and unanesthetized sheep.

Rumen and hepatic tissues are the primary organs for butyrate metabolism in the ruminant animal. There has been much controversy among researchers regarding the possible glycogenic or ketogenic role of butyrate in hepatic tissue. Several investigators have observed a hyperglycemic response following the injection of butyrate (5,17,19,32,34), whereas other researchers have failed to demonstrate this butyrate induced hyperglycemic response (42). The results of this study have clearly demonstrated that the intravenous infusion of sodium butyrate resulted in an increase in blood glucose concentrations in both the anesthetized and unanesthetized sheep. Also, the intravenous infusion of sodium butyrate resulted in an increase in blood concentrations of acetate which has been demonstrated by other researchers (2). The exact mechanism by which butyrate induces the increase in blood glucose has not yet been fully

explained. Further investigations into the role of the pancreas and liver in this butyrate induced hyperglycemic response are needed.

A SELECTED BIBLIOGRAPHY

1. Annison, E. F., K. J. Hill, and D. Lewis. "Studies on the Portal Blood of Sheep. 2. Absorption of Volatile Fatty Acids From the Rumen of the Sheep." Biochemical Journal, Vol. 66 (1957), 592-599.

2. Annison, E. F., R. A. Leng, D. B. Lindsay, and R. R. White. "The Metabolism of Acetic Acid, Propionic Acid and Butyric Acid in Sheep." Biochemical Journal, Vol. 88 (1963), 248-252.

3. Annison, E. F., and D. Lewis. Metabolism in the Rumen. London: Metheun and Co., Ltd.; New York: John Wiley and Sons, Inc., 1959.

4. Annison, E. F., and R. R. White. "Further Studies on the Entry Rates of Acetate and Glucose in Sheep." Biochemical Journal, Vol. 84 (1962), 526-552.

5. Ash, R. W., R. J. Pennington, and R. S. Reid. "The Effect of Short-Chain Fatty Acids on Blood Glucose Concentration in Sheep." Biochemical Journal, Vol. 90 (1964), 353-360.

6. Barcroft, J., R. A. McAnally, and A. T. Phillipson. "Absorption of Volatile Acids From the Alimentary Tract of the Sheep and Other Animals." Journal of Experimental Biology, Vol. 20 (1944), 120-129.

7. Black, A. L., M. Kleiber, and A. M. Brown. "Butyrate Metabolism in the Lactating Cow." Journal of Biological Chemistry, Vol. 236 (1961), 2399-2403.

8. Bost, J., E. Dorleac, and A. Guehenneux. "Variations du Taux Plasmatique Des Acides Gras Non Esterifies Au Cours De L'Anesthesie General Chez le Mouton." Comptes Rendus Des Seances De la Societe De Biologie et De Ses Filiales, Vol. 160 (1966), 2113-2117.

9. Carroll, E. J., and R. E. Hungate. "The Magnitude of the Microlual Fermentation in the Bovine Rumen." Applied Microbiology, Vol. 2 (1954), 205-214.

10. Davis, C. L., R. E. Brown, J. R. Staubus, and W. O. Nelson. "Availability and Metabolism of Various Substrates in Ruminants. I. Absorption and Metabolism of Acetate." Journal of Dairy Science, Vol. 43 (1960), 231-249.

11. Doughtery, R. W., Ed. Physiology of Digestion in the Ruminant. Washington: Butterworths, 1965.

12. Elsden, S. R. "The Fermentation of Carbohydrates in the Rumen of the Sheep." Journal of Experimental Biology, Vol. 22 (1947), 51-62.

13. Goetsch, D. D. "Liver Enzyme Changes During Rumen Development in Calves." American Journal of Veterinary Research, Vol. 27 (1966), 1187-1192.

14. Gray, F. V. "The Absorption of Volatile Fatty Acids From the Rumen." Journal of Experimental Biology, Vol. 24 (1947), 1-10.

15. Holter, J. B., S. Lakshmanan, and J. C. Shaw. "Determination of Volatile Fatty Acids in Bovine Blood by Isotope Dilution." Journal of Dairy Science, Vol. 42 (1959), 358-362.

16. Hungate, Robert E. The Rumen and Its Microbes. New York and London: Academic Press, 1966.

17. Jarrett, I. G., B. J. Potter, and O. H. Filsell. "Lower Fatty Acids in the Intermediary Metabolism of Sheep." Australian Journal of Experimental Biology and Medical Science, Vol. 30 (1952), 197-205.

18. Kleiber, M., A. L. Black, M. A. Brown, J. Luick, C. F. Baxter, and B. M. Tolbert. "Butyrate as a Precursor of Milk Constituents in the Intact Dairy Cow." Journal of Biological Chemistry, Vol. 210 (1954), 239-247.

19. Kronfeld, D. S. "The Effects of Blood Sugar and Ketone Bodies of Butyrate Acetate, and β-hydroxybutyrate Infused Into Sheep." Australian Journal of Experimental Biology and Medical Science, Vol. 35 (1957), 257-266.

20. Leng, R. A., and E. F. Annison. "Metabolism of Acetate, Propionate and Butyrate by Sheep-Liver Slices." Biochemical Journal, Vol. 86 (1963), 319-327.

21. Leng, R. A., J. W. Steel, and J. R. Luick. "Contribution of Propionate to Glucose Synthesis in Sheep." Biochemical Journal, Vol. 103 (1967), 785-790.

22. Mann, J. G., and J. M. Boda. "Insulin Release by Acetate, Propionate, Butyrate, and Glucose in Lambs and Adult Sheep." American Journal of Physiology, Vol. 212 (1967), 747-755.

23. Masson, M. J., and A. T. Phillipson. "The Absorption of Acetate, Propionate, and Butyrate From the Rumen of Sheep." Journal of Physiology, Vol. 113 (1951), 189-206.

24. McCandless, F. L., and J. A. Dye. "Physiological Changes in Intermediary Metabolism of Various Species of Ruminants Incident to Functional Development of Rumen." American Journal of Physiology, Vol. 162 (1950), 434-446.

25. Nelson, N. "A Photometric Adaption of the Somogyi Method for the Determination of Glucose." Journal of Biological Chemistry, Vol. 153 (1944), 375-380.

26. Phillipson, A. T., and R. A. McAnally. "Studies on the Fate of Carbohydrates in the Rumen of the Sheep." Journal of Experimental Biology, Vol. 19 (1942), 199-214.

27. Pennington, R. J. "The Metabolism of Short-Chain Fatty Acids in Sheep. 1. Fatty Acid Utilization and Ketone Body Production by Rumen Epithelium and Other Tissues." Biochemical Journal, Vol. 51 (1952), 251-258.

28. Pennington, R. J. "The Metabolism of Short-Chain Fatty Acids in the Sheep. 2. Further Studies With Rumen Epithelium." Biochemical Journal, Vol. 56 (1954), 410-416.

29. Pennington, R. J., and W. H. Pfander. "The Metabolism of Short-Chain Fatty Acids in the Sheep. 5. Some Interrelationships in the Metabolism of Fatty Acids and Glucose by Sheep-Rumen Epithelial Tissue." Biochemical Journal, Vol. 65 (1957), 109-111.

30. Pennington, R. J., and T. M. Sutherland. "The Metabolism of Short-Chain Fatty Acids in the Sheep. 4. The Pathway of Propionate Metabolism in Rumen Epithelial Tissue." Biochemical Journal, Vol. 63 (1956), 618-628.

31. Phillips, R. W., and A. L. Black. "The Effect of Volatile Fatty Acids on Plasma Glucose Concentration." Comparative Biochemistry and Physiology, Vol. 18 (1966), 527-536.

32. Phillips, R. W., A. L. Black, and R. Moller. "Butyrate Induced Glycogenolysis in Hypoglycemic Lambs." Life Sciences, Vol. 4 (1965), 521-525.

33. Phillipson, A. T. "Fermentation in the Alimentary Tract and the Metabolism of the Derived Fatty Acids." Nutritional Abstracts and Reviews, Vol. 17 (1947), 12-18.

34. Potter, B. J. "Relief of Hypoglycemic Convulsion With Butyric Acid." Nature (London), Vol. 170 (1952), 541.

35. Ramsey, H. A., and C. L. Davis. "Metabolism of N-Butyrate by the Adult Goat." Journal of Dairy Science, Vol. 48 (1965), 381-390.

36. Reid, R. L. "Studies on the Carbohydrate Metabolism of Sheep. VI. Interrelationships Between Changes in the Distribution and Levels of Glucose and in the Levels of Volatile Fatty Acid in the Blood of Lambs." Australian Journal of Agricultural Research, Vol. 4 (1953), 213-223.

37. Schambye, P. and A. T. Phillipson. "Volatile Fatty Acids in Portal Blood of Sheep." Nature (London), Vol. 164 (1949), 1094-1095.

38. Somogyi, M. "Notes on Sugar Determination." Journal of Biological Chemistry, Vol. 195 (1952), 19-23.

39. Spahr, S. L., E. M. Kesler, and R. J. Flipse. "Utilization of Blood Acetate and Butyrate by the Isolated, Perfused Goat Rumen." Journal of Dairy Science, Vol. 48 (1965), 228-233.

40. Steel, R. G., and J. H. Torrie. Principles and Procedures of Statistics. New York, Toronto, London: McGraw-Hill Book Company, Inc., 1960.

41. Taylor, T. A., and H. A. Ramsey. "Metabolism of N-Butyrate and Propionate by Rumen Epithelium." Journal of Dairy Science, Vol. 48 (1965), 505-509.

42. Trenkle, A., and K. V. Kuhlemeier. "Relationship of Rumen Volatile Acids, Blood Glucose and Plasma Nonesterified Fatty Acids in Sheep." Journal of Animal Science, Vol. 25 (1966), 1111-1115.

43. Weinman, E. O., E. H. Strisower, and I. L. Chaikoff. "Conversion of Fatty Acids to Carbohydrates: Application of Isotopes to This Problem and Role of the Krebs Cycles as a Synthetic Pathway." Physiology Reviews, Vol. 37 (1957), 252-272.

APPENDIX A

TABLE III

BLOOD GLUCOSE CONCENTRATIONS IN ANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INJECTION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Glucose Mg.%										Mean ± $S_{\bar{x}}$
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	
-20	76	60	79	68	55	77	53	77	65	68	68 ± 3
-10	64	72	76	70	53	73	58	78	70	73	69 ± 2
0	79	71	74	68	52	75	54	75	69	76	69 ± 3
10	76	108	99	111	91	95	77	110	74	106	95 ± 5
20	148	141	129	144	114	129	104	141	90	124	126 ± 3
30	76	106	127	119	116	142	123	131	100	121	116 ± 3
40	118	138	129	95	116	140	119	132	93	120	120 ± 5
50	106	141	117	86	97	123	101	118	87	117	109 ± 5
60	114	136	124	80	79	112	88	106	90	114	104 ± 6
70	97	107	110	68	73	106	86	106	70	113	94 ± 6
80	98	116	67	59	110	78	97	72	115	---	90 ± 7
90	93	119	55	55	114	67	93	68	100	---	86 ± 8
100	88	90	50	48	110	67	93	66	103	---	81 ± 8
110	94	46	49	100	64	83	68	99	---	---	75 ± 8
120	103	106	40	47	94	70	85	59	101	---	78 ± 8
130	97	106	40	46	65	77	66	106	---	---	75 ± 9
140	108	99	41	43	54	76	66	101	---	---	74 ± 9
150	86	104	42	48	55	75	66	107	---	---	73 ± 9
160	96	107	39	50	56	78	64	104	---	---	74 ± 9
170	109	111	41	44	55	79	65	99	---	---	75 ±10
180	91	113	48	44	55	73	64	101	---	---	74 ± 9

TABLE IV

BLOOD GLUCOSE CONCENTRATIONS IN UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Glucose Mg.%										Mean ± $S_{\bar{x}}$
	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	
-20	88	62	74	59	68	81	50	74	64	65	69 ± 4
-10	93	60	64	53	70	85	61	71	65	61	68 ± 4
0	93	61	66	55	75	88	63	72	65	62	70 ± 4
10	150	132	113	114	114	148	102	134	111	95	121 ± 6
20	159	138	160	145	158	174	124	160	147	119	148 ± 6
30	179	142	140	160	157	172	146	165	149	116	153 ± 6
40	166	120	129	155	144	156	146	148	152	116	143 ± 5
50	168	103	114	132	138	160	124	142	132	115	133 ± 6
60	164	88	108	118	136	153	122	145	125	110	127 ± 7
70	137	89	102	124	136	145	109	126	119	106	119 ± 6
80	132	81	105	103	130	142	107	115	111	105	113 ± 6
90	134	75	105	95	125	132	110	112	90	103	108 ± 6
100	146	69	100	96	120	132	104	115	87	101	107 ± 7
110	139	72	108	94	118	129	107	116	93	100	108 ± 6
120	120	65	102	99	113	128	100	119	88	97	103 ± 6
130	127	66	99	77	113	125	104	84	92	---	99 ± 7
140	122	66	104	74	112	119	99	106	91	89	92 ± 6
150	124	65	94	73	107	116	101	105	87	90	96 ± 6
160	126	60	89	68	103	107	98	112	90	88	94 ± 6
170	109	60	92	65	98	108	97	115	83	84	91 ± 6
180	110	54	90	62	97	106	97	115	91	87	91 ± 6

TABLE V

BLOOD ACETATE CONCENTRATIONS IN ANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Acetate Mg.%										Mean ± $S_{\bar{x}}$
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	
-20	9.5	13.6	13.6	8.1	6.2	10.2	----	8.7	7.8	5.6	9.2 ± 1
-10	10.1	14.6	13.6	5.0	6.2	11.2	5.7	7.6	6.8	5.8	8.7 ± 1
0	7.3	14.2	16.8	6.7	7.8	10.2	9.6	7.2	6.4	6.0	9.2 ± 1
10	11.3	19.6	14.6	13.9	12.2	12.8	12.7	21.3	9.3	11.2	13.9 ± 1
20	18.3	34.0	24.6	15.3	15.0	20.4	16.0	21.3	10.0	12.2	18.7 ± 2
30	22.7	25.2	21.0	15.3	15.0	24.8	22.9	16.0	11.3	9.2	18.3 ± 2
40	21.7	30.8	----	13.9	15.2	22.2	----	17.1	13.3	11.0	18.1 ± 2
50	19.3	30.2	26.0	10.5	14.4	21.6	13.4	10.5	9.3	14.2	16.9 ± 2
60	15.0	22.8	22.2	12.4	11.4	19.4	10.4	10.7	7.5	12.0	14.4 ± 2
70	12.7	22.2	20.6	8.6	10.4	16.8	9.5	10.2	7.7	9.0	12.8 ± 2
80	11.2	----	18.4	6.6	6.6	15.2	8.9	9.8	7.2	9.2	10.4 ± 1
90	8.0	----	20.6	6.3	7.4	13.8	6.9	10.2	6.0	8.2	9.7 ± 1
100	11.2	----	15.6	4.7	6.4	13.8	5.4	10.2	6.1	7.8	9.0 ± 1
110	7.9	----	20.0	6.4	6.8	11.6	6.5	10.0	6.9	10.6	9.6 ± 1
120	11.8	----	16.2	5.4	6.6	11.0	7.4	----	5.8	10.4	9.3 ± 1
130	7.2	----	19.6	5.1	6.4	----	7.8	6.4	5.7	10.0	8.5 ± 1
140	9.8	----	14.6	4.8	5.4	----	5.6	6.1	4.0	----	7.1 ± 1
150	8.4	----	14.6	5.7	5.6	----	6.2	7.6	7.7	9.8	8.2 ± 1
160	8.9	----	15.0	4.6	4.4	----	6.6	7.2	5.4	----	7.4 ± 1
170	9.0	----	11.6	4.5	4.4	----	5.2	6.1	5.5	----	6.6 ± 1
180	8.7	----	16.0	5.3	4.0	----	4.9	4.2	5.1	----	6.8 ± 2

TABLE VI

BLOOD ACETATE CONCENTRATIONS IN UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Acetate Mg.%										Mean ± $S_{\bar{x}}$
	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	
-20	9.6	6.0	6.1	5.0	9.4	9.4	8.8	4.4	7.4	----	7.3 ± 1
-10	10.4	6.9	5.7	3.8	11.2	12.9	7.1	5.9	7.6	10.8	8.2 ± 1
0	10.4	4.7	5.4	4.5	9.9	12.6	7.1	6.5	10.0	6.8	7.8 ± 1
10	15.1	11.7	9.2	9.1	20.7	19.3	10.8	11.5	11.4	16.4	13.5 ± 1
20	16.6	13.2	14.4	8.6	25.7	21.1	16.1	12.5	13.0	16.7	15.8 ± 2
30	12.4	9.5	14.7	14.2	25.2	18.9	----	10.2	16.1	18.8	15.5 ± 2
40	21.7	15.8	11.6	19.5	20.7	20.9	15.9	12.0	17.4	14.3	16.8 ± 1
50	19.7	8.5	8.9	8.6	26.7	20.0	14.0	10.1	11.8	26.6	15.5 ± 2
60	20.4	6.5	9.8	11.8	18.3	14.4	11.9	9.3	10.1	23.3	13.6 ± 2
70	13.8	7.8	9.9	10.4	22.1	17.0	11.0	9.4	9.4	12.3	12.3 ± 1
80	14.7	7.7	7.7	8.1	16.1	16.5	14.0	7.6	10.2	11.6	11.4 ± 2
90	14.4	5.8	9.3	6.3	19.2	16.1	10.3	8.4	----	8.9	10.9 ± 1
100	10.4	4.5	----	5.5	18.8	15.0	8.2	9.7	11.0	10.8	10.4 ± 1
110	13.9	5.3	9.1	4.2	18.3	14.3	12.0	9.5	9.3	11.3	10.7 ± 1
120	13.5	5.4	6.6	5.6	18.0	15.2	11.2	7.6	9.3	11.9	10.4 ± 1
130	12.1	3.5	5.5	6.8	18.2	11.7	11.1	6.3	9.8	13.3	9.8 ± 1
140	11.0	5.0	6.1	4.7	18.0	9.7	11.8	9.0	9.4	10.8	9.6 ± 1
150	7.2	3.9	10.0	5.4	17.0	11.2	9.7	7.8	8.0	12.5	9.3 ± 1
160	9.1	3.3	7.5	6.1	15.0	8.7	14.3	8.1	8.4	10.3	9.1 ± 1
170	9.0	3.5	7.2	6.8	15.8	12.7	8.8	7.4	10.5	12.1	9.4 ± 1
180	7.1	3.7	7.4	5.1	15.3	14.4	10.5	7.4	10.4	13.0	9.4 ± 1

TABLE VII

BLOOD PROOIONATE CONCENTRATIONS IN ANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time	Blood Propionate Mg.%										Mean ± $S_{\bar{x}}$
Minutes	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	
-20	0.2	0.5	0.8	0.3	0.3	0.3	---	0.2	0.2	0.2	0.3 ± 0.1
-10	0.2	0.4	0.5	0.2	0.3	0.2	0.1	0.2	0.2	0.2	0.3 ± 0.1
0	0.2	0.4	0.5	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.2 ± 0.1
10	0.2	0.7	0.5	0.7	0.3	0.5	0.4	0.4	0.4	0.4	0.5 ± 0.1
20	0.2	0.9	0.7	0.7	0.5	0.5	0.4	0.4	0.4	0.4	0.5 ± 0.1
30	0.2	0.9	0.5	0.4	0.5	0.5	0.3	0.4	0.4	0.4	0.5 ± 0.1
40	0.2	0.9	---	0.3	0.5	0.5	---	0.5	0.4	0.4	0.5 ± 0.1
50	0.3	0.9	0.5	0.3	0.4	0.3	0.3	0.2	0.4	0.4	0.4 ± 0.1
60	0.3	0.5	0.7	0.3	0.3	0.3	0.2	0.2	0.2	0.4	0.3 ± 0.1
70	0.2	0.5	0.7	0.3	0.3	0.2	0.2	0.2	0.2	0.4	0.3 ± 0.1
80	0.2	---	0.7	0.2	0.3	0.2	0.2	0.2	0.2	0.4	0.3 ± 0.1
90	0.2	---	0.7	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.3 ± 0.1
100	0.2	---	0.7	0.4	0.2	0.2	0.2	0.3	0.2	0.2	0.3 ± 0.1
110	0.2	---	0.7	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.3 ± 0.1
120	0.2	---	0.7	0.2	0.2	0.2	0.2	---	0.2	0.3	0.3 ± 0.1
130	0.2	---	0.7	0.2	0.2	---	0.2	0.3	0.2	0.2	0.3 ± 0.1
140	---	---	0.7	0.2	0.2	---	0.2	0.3	0.1	0.2	0.3 ± 0.1
150	0.2	---	0.7	0.2	0.2	---	0.2	0.3	0.2	0.2	0.3 ± 0.1
160	---	---	0.7	0.2	0.2	---	0.2	0.3	0.1	0.2	0.3 ± 0.1
170	---	---	0.3	0.2	0.2	---	0.2	0.3	0.1	0.2	0.2 ± 0.1
180	---	---	0.2	0.2	0.2	---	0.2	0.3	0.1	0.2	0.2 ± 0.1

TABLE VIII

BLOOD PROPIONATE CONCENTRATIONS IN UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time	Blood Propionate Mg.%										Mean ± $S_{\bar{x}}$
Minutes	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	
-20	0.1	0.2	0.3	0.2	0.4	0.2	0.3	0.2	0.2	---	0.2 ± 0.1
-10	0.2	0.2	0.2	0.2	0.3	0.3	0.4	0.2	0.2	0.2	0.2 ± 0.1
0	0.3	0.1	0.2	0.2	0.3	0.3	0.4	0.2	0.2	0.3	0.3 ± 0.1
10	0.4	0.4	0.5	0.3	0.9	0.5	0.5	0.5	0.5	0.6	0.5 ± 0.1
20	0.4	0.4	0.5	0.3	0.9	0.5	0.5	0.5	0.5	0.8	0.5 ± 0.1
30	0.4	0.4	0.5	0.3	0.9	0.5	---	0.5	0.5	0.8	0.5 ± 0.1
40	0.4	0.4	0.5	0.3	0.9	0.4	0.4	0.4	0.5	0.6	0.5 ± 0.1
50	0.4	0.2	0.5	0.3	0.9	0.4	0.4	0.2	0.4	0.6	0.4 ± 0.1
60	0.4	0.3	0.2	0.2	0.5	0.4	0.3	0.3	0.4	0.4	0.3 ± 0.1
70	0.3	0.1	0.2	0.2	0.5	0.4	0.3	0.2	0.3	0.4	0.3 ± 0.1
80	0.2	0.1	0.2	0.2	0.5	0.4	0.3	0.2	0.3	0.3	0.3 ± 0.1
90	0.3	0.2	0.2	0.2	0.4	0.4	0.3	0.2	---	0.2	0.3 ± 0.1
100	0.3	0.2	---	0.2	0.4	0.4	0.3	0.4	0.3	0.2	0.3 ± 0.1
110	0.3	0.2	0.2	0.2	0.5	0.4	0.3	0.3	0.3	0.3	0.3 ± 0.1
120	0.3	0.2	0.2	0.2	0.4	0.4	0.3	0.2	0.2	0.3	0.3 ± 0.1
130	0.3	0.1	0.2	0.2	0.4	0.3	0.3	0.4	0.2	0.4	0.3 ± 0.1
140	0.3	0.1	0.2	0.2	0.4	0.2	0.3	0.2	0.2	0.3	0.2 ± 0.1
150	0.2	0.1	0.3	0.2	0.5	0.3	0.3	0.2	0.2	0.3	0.3 ± 0.1
160	0.2	0.1	0.2	0.2	0.5	0.3	0.4	0.2	0.2	0.3	0.3 ± 0.1
170	0.2	0.1	0.2	0.2	0.5	0.4	0.3	0.2	0.2	0.3	0.3 ± 0.1
180	0.2	0.1	0.2	0.2	0.5	0.4	0.3	0.2	0.2	0.4	0.3 ± 0.1

TABLE IX

BLOOD BUTYRATE CONCENTRATIONS IN ANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Butyrate Mg.%										Mean ± $S_{\bar{x}}$
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	
-20	0.2	0.4	0.6	0.3	0.3	0.3	----	----	----	----	0.4 ± 0.1
-10	0.2	0.4	0.5	0.2	0.3	0.1	0.1	----	----	----	0.3 ± 0.1
0	0.2	0.4	0.5	0.2	0.2	0.1	0.1	----	----	----	0.2 ± 0.1
10	36.6	50.6	36.0	42.0	76.0	46.2	75.9	----	----	----	51.9 ± 7.0
20	14.4	36.4	30.2	18.8	37.0	29.8	39.4	----	----	----	29.4 ± 4.0
30	4.4	20.0	13.8	8.9	22.2	17.6	21.9	----	----	----	15.5 ± 3.0
40	0.4	13.0	----	3.1	17.4	9.2	----	----	----	----	8.6 ± 3.0
50	0.4	3.6	2.6	0.9	7.0	4.3	2.3	----	----	----	3.0 ± 3.0
60	0.2	1.8	1.3	0.5	2.6	2.0	0.6	----	----	----	1.2 ± 0.1
70	0.2	1.0	0.6	0.3	0.9	0.4	0.5	----	----	----	0.5 ± 0.1
80	0.2	----	0.5	0.2	0.8	0.7	0.3	----	----	----	0.4 ± 0.1
90	0.2	----	0.5	0.2	0.3	0.2	0.2	----	----	----	0.2 ± 0.1
100	0.2	----	0.4	0.4	0.3	0.2	0.2	----	----	----	0.3 ± 0.1
110	0.2	----	0.4	0.2	0.2	0.2	0.1	----	----	----	0.2 ± 0.1
120	0.2	----	0.4	0.2	0.2	0.2	0.2	----	----	----	0.2 ± 0.1
130	0.2	----	0.4	0.2	0.2	----	0.2	----	----	----	0.2 ± 0.1
140	----	----	0.3	0.2	0.2	----	0.1	----	----	----	0.2 ± 0.1
150	0.2	----	0.3	0.2	0.1	----	0.1	----	----	----	0.2 ± 0.1
160	----	----	0.3	0.2	0.1	----	0.2	----	----	----	0.2 ± 0.1
170	----	----	0.4	0.2	0.1	----	0.1	----	----	----	0.2 ± 0.1
180	----	----	0.4	0.2	0.1	----	0.1	----	----	----	0.2 ± 0.1

TABLE X

BLOOD BUTYRATE CONCENTRATIONS IN UNANESTHETIZED SHEEP BEFORE AND FOLLOWING THE INTRAVENOUS INFUSION OF SODIUM BUTYRATE (2.5 mMOLES/KG.) AT ZERO TIME

Time Minutes	Blood Butyrate Mg.%										Mean ± $S_{\bar{x}}$
	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	
-20	0.1	0.2	0.3	0.2	0.3	0.2	0.2	0.1	0.2	----	0.2 ± 0.1
-10	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.2 ± 0.1
0	0.4	0.1	0.2	0.2	0.2	0.3	0.2	0.1	0.2	0.2	0.2 ± 0.1
10	30.8	21.2	30.6	27.9	47.5	34.8	32.8	34.4	38.1	36.7	33.5 ± 2.0
20	19.9	13.9	15.1	11.1	23.8	21.0	22.9	19.2	19.3	20.5	18.7 ± 1.0
30	6.1	5.3	9.1	5.4	10.7	7.0	----	7.2	14.0	14.5	8.8 ± 1.0
40	2.4	2.5	3.6	2.1	3.3	2.3	3.4	2.3	6.3	5.5	3.4 ± 0.3
50	1.2	0.7	1.0	0.4	1.6	0.8	0.9	0.6	1.6	2.9	1.2 ± 0.2
60	0.6	0.3	0.6	0.3	0.7	0.4	0.2	0.3	0.6	1.1	0.5 ± 0.1
70	0.4	0.2	0.4	0.2	0.4	0.3	0.4	0.3	0.3	0.4	0.3 ± 0.1
80	0.3	0.2	0.3	0.2	0.3	0.3	0.4	0.3	0.3	0.2	0.3 ± 0.1
90	0.2	0.2	0.3	0.2	0.4	0.2	0.3	0.2	----	0.2	0.2 ± 0.1
100	0.2	0.1	----	0.2	0.3	0.2	0.3	0.3	0.3	0.2	0.2 ± 0.1
110	0.2	0.1	0.2	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.2 ± 0.1
120	0.2	0.1	0.2	0.2	0.2	0.3	0.2	0.3	0.3	0.2	0.2 ± 0.1
130	0.2	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.2 ± 0.1
140	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.3	0.3	0.3	0.2 ± 0.1
150	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.2	0.2	0.1	0.2 ± 0.1
160	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.3	0.3	0.1	0.2 ± 0.1
170	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.3	0.3	0.2	0.2 ± 0.1
180	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.3	0.3	0.2	0.2 ± 0.1

VITA

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