Importance of Blood Glucose and Ketones in the Evaluation of Nutritional State of the Ruminant

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The concentrations of glucose and ketones (acetoacetate and 3-hydroxybutyrate) in the blood should be useful clinicoc hemical signs of the nutritional condition of the ruminant. The concentration of glucose or ketones in the blood at any instant represents an equilibrium between the rate of entering of these substances into the blood stream and the rate of removal of them from it. Homeostasis of blood glucose level can be maintained by interactions between the forces to raise blood glucose and the forces to lower blood glucose. Glucagon, epinephrine, glucocorticoid, and growth hormone act for the former forces, while only insulin for the latter.

The ruminant metabolism is greatly influenced by the extensive microbial fermentation of ingested foodstuffs which occurs in the rumen. Dietary carbohydrates are largely converted into volatile fatty acids (VFA) such as acetate, propionate and butyrate, so that little glucose is absorbed from the alimentary tract. The important point to emphasize is that an input of glucose is essential to meet certain obligatory outputs such as lactose synthesis in milk production, supply of energy to the fetus, synthesis of triglycerides in adipose tissue and respiration of brain cells and working muscles. 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.

Most tissues can utilize ketones. However, there are only two major sites of ketogenesis, namely the liver and the wall of the rumen-reticulum. The principal precursors of ketones are free fatty acids (FFA) derived from mobilized body fat and butyrate absorbed from the rumen content. As glucose becomes less available in the body, FFA and ketones become more important energy-supplying blood components.

The objects of this paper are to show several features of changes in the concentrations of blood glucose and ketones and to consider the significance of these changes for the evaluation of nutritional conditions of the ruminant.

Developmental changes of blood glucose concentration in the ruminant

In Table 1 changes of blood glucose concentr-
trations in whole blood, plasma and red cells are shown from our experiments. The fall in blood glucose concentration involves two components, the loss of glucose from the red cells, and a slower decline in plasma glucose concentration. The decline in blood glucose is closely paralleled by a fall in blood potassium, most of which is due to a loss of potassium from the red cells. For example, the potassium concentrations of the red cells of 1-week-old calves, those of 11-week-old calves and those of adult cows were 95±2 (SD), 21±3 and 25±3 mEq/l, respectively. The changes in glucose and potassium contents of the red cells are associated with the replacement of fetal cells by an adult type cells.

In Table 2 plasma glucose concentrations of fed ruminants are summarized from our various experiments. Plasma glucose concentration of goat fetuses in the late pregnancy is exceedingly low, but plasma fructose concentration of these fetuses is 74±25 (SD) mg/dl. After the birth fructose in the fetal plasma is rapidly replaced by glucose.

During the postnatal period in which only milk or liquid milk replacer is fed, the carbohydrate metabolism of the ruminant resembles that of the non-ruminant, since the forestomach (rumen, reticulum and omasum) remains to be immature. As milk enters directly into the abomasum via closure of the esophageal groove, the suckling ruminant exhibits alimentary hyperglycemia after milk consumption. In the experiments using the kid and calf, the suckling ruminant shows the ability to synthesize glucose from propionate or amino acids as well as the weaned ruminant. In our experiment in which the ruminoreticular compartment of the kid has been surgically removed, the ruminant can survive more than a year as a single-stomached animal by eating palatable solid food.

If the amount of milk is restricted and solid foods are given, solid consumption increases at 3 to 6 weeks of age. The increase in solid consumption induces rapid forestomach development. A high positive correlation of 0.82 is obtained between the cumulative solid intake and the ruminoreticular development in the young goat. Early weaning of dairy calves from 3 to 6 weeks of age has been reported. After weaning major source of energy of the ruminant changes from milk to VFA.

Feeding programs have an influence upon the decreasing patterns of blood or plasma glucose in young calves. At the age of weaning the calves seem to suffer most severely from the shortage of gluconeogenic substances, and the hypoglycemic conditions may become a stimulus for an increased solid intake by the mechanism based on chemostatic regulation. In this case glucose concentration in plasma may be more susceptible to nutritional balance of glucose pool in the body than that in whole blood or red cells.

In contrast to young calves, mature cows do not show the postprandial hyperglycemia even after ingestion of milk. In our experiment using a rumen-bypassed lactating cow, plasma glucose concentration does not rise in the post-feeding period. We suspect an alteration of carbohydrate metabolism in the mature cow, in which much of alimentary source of glucose might be

| Table 2. Jugular plasma glucose concentrations of fed ruminants |
|---------------------------|---------------------|
| Japanese meat-type goats  | Plasma glucose concentration (mg/dl) |
| Fetuses                   | 14±6*(3)**          |
| Suckling animals of 1-3 days of age | 104±19(6)         |
| Milk-fed animals of 5 wk of age | 84±21(6)          |
| Weaned animals of 12 wk of age | 60±1(3)           |
| Japanese beef cattle (Wagyu) | 133±22(8)         |
| Suckling animals of 1-2 wk of age | 107±12(4)         |
| Early-weaned animals of 11 weeks of age | 70±10(8)      |
| Mature nursing cows       | 68±2(4)            |
| Holstein cows             | 82±4(4)            |
| Rumen-bypassed heifers    | 68±2(4)            |
| Rumen-bypassed lactating cows | 111±8(6)        |
| Dexamethasone-injected cows | (24 hr post-injection of 10 mg Dex.) |

* SD
** Figure in parenthesis is number of animals used.
metabolized to lactate or other metabolites in the brush border of small intestine cells. Intraruminal administration of 500 g of 1,2-propanediol to lactating cows shows the tendency to increase the plasma glucose concentration by 7 mg/dl in 4 hr post-feeding. Intramuscular injection of 10 mg dexamethasone induces the hyperglycemia (Table 2) in 24 hr post-injection. In this case diminished glucose utilization may occur rather than increased gluconeogenesis. Except the pharmacological treatments it is difficult for the lactating cow to raise blood glucose concentration by any feeding treatment.

Significance of jugular plasma glucose and ketone concentrations in the ruminant

In the lactating cow the plasma glucose concentration is very sensitive to the uptake of VFA from the rumen and to their subsequent metabolism. The glucose requirement is continuously high in relation to the dietary supply of glucogenic substances. As a consequence the balance in carbohydrate metabolism may be precarious.

In Table 3 plasma glucose, ketone and FFA concentrations of normal lactating cows, spontaneously ketotic cows and diabetic goats are shown from our original data. The values of normal lactating cows serve as controls. Intraruminal administration of 500 ml tributyrin (glyceryl tributyrate) to normal lactating cows before morning feeding causes temporary decrease in plasma glucose concentration and temporary increase in plasma ketone concentration. Maximum changes of these values are at 3 hr post-administration, and these changes disappear at 24 hr post-administration. Plasma insulin concentrations increase from 13±5 (SD) µU/ml (pre-administration) to 85±59 at 3 hr post-administration. The appetite of the cows is not depressed by this treatment. Storry and Rook note the considerable decrease and increase in plasma glucose concentration of lactating cows associated with the butyric and propionic acid infusions respectively.

The changes of plasma glucose and ketone concentrations of spontaneously ketotic cows appear to be similar to those of tributyrin-treated cows. However, in the ketotic cows, the appetite is depressed; insulin secretion can be depressed; and plasma FFA concentration is elevated. In the ketotic cows, overproduction of ketones may be caused primarily by greater oxidation of FFA in the liver, because ketone production from the alimentary source of butyrate at the ruminal wall may be depressed by loss of appetite. Alloxan-diabetic goats differ from ketotic cows in the plasma glucose concentration. Diabetic goats exhibit much higher glucose concentration than normal or ketotic cows due to the lack of insulin-mediated glucose utilization processes.

In cows fed high-concentrate diets there is a changed pattern of rumen fermentation resulting in higher rates of propionate production and a lower ratio of acetate/propionate. This gives rise to higher levels of blood glucose and higher glucose entry rates than when a normal high roughage diet is fed. In Table 4 postprandial changes of plasma glucose and ketone concentrations of high-producing cows fed high-
concentrate diets are shown from our unpublished data. Plasma glucose level decreases in several hours after intake of high-concentrate diets. The same trend has been shown in the literature.\textsuperscript{13,14}\n
In Table 4 plasma ketone level increases gradually in the post-feeding period. There are negative correlations of $-0.68$ and $-0.62$ between plasma glucose and plasma acetoacetate and between plasma glucose and plasma 3-hydroxybutyrate concentration, respectively. According to Radloff et al.\textsuperscript{10}, in the lactating cow, blood glucose level is a controlling factor in ketogenesis. At low glucose levels ketogenesis increases, whether it be from rumen acids in the fed animal or FFA in the fasted animal.

Although plasma glucose concentration decreases to some extent postprandially as shown in Table 4, it must return to the pre-feeding level after about 5 or 7 hr post-feeding. Supply of gluconeogenic materials such as propionate and amino acids must be prerequisite for this. As shown in Table 3, the extent of change in plasma ketone concentration is much larger than that in plasma glucose concentration. So plasma ketone level may become a useful index for the sufficiency in meeting glucose requirement of the ruminant. During 24-hr period the homeostatic control of blood glucose and ketone concentrations must be maintained in the ruminant. Nutritional and management cares are important for this.

**References**


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