Blood Glucose Kinetics in Whole Body and Mammary Gland of Lactating Goats Exposed to Heat

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ABSTRACT
Whole-body and mammary kinetics of blood glucose were measured in lactating goats exposed to thermoneutral, moderate hot, and severe hot environments for 4 d. Milk yields were reduced by 3 and 13% during moderate and severe heat exposure, but heat production was unchanged during the experiment. Concentrations of plasma glucose and free fatty acids did not change during heat exposure. Concentration of thyroxine tended to decrease and concentration of prolactin increased with increasing temperature. Whole-body turnover of blood glucose decreased significantly during both moderate and severe heat exposure. Blood glucose oxidation rate and contribution of blood glucose to total carbon dioxide production were not influenced by heat exposure. Mammary glucose uptake tended to decrease during heat exposure, and this reduction may account for the decreased whole-body turnover of blood glucose. The lactose concentration in milk was decreased on the 4th d of severe heat exposure. A relatively low production of milk lactose was apparently derived from blood glucose. These results suggest that the whole-body turnover of blood glucose decreases in step with a decrease in mammary glucose uptake during heat exposure in lactating goats.

INTRODUCTION
Ruminant animals can reduce heat production and increase heat loss in a hot environment, but they cannot maintain high productivity at high ambient temperatures (19, 23). Blood glucose is an important precursor of milk constituents and energy source for the lactating mammary gland. In particular, milk lactose, the major osmolite in milk, is almost totally synthesized from blood glucose. Therefore, blood glucose metabolism is important in maintenance and productivity of lactating animals. Annison and Linzell (2) first quantitatively measured whole-body and mammary kinetics of blood glucose simultaneously, demonstrating that 60 to 85% of whole-body turnover of blood glucose was taken up by the udder. Blood glucose metabolism of nonlactating sheep was reported to decrease during heat exposure even though feed intake was maintained (27).

The objective of this experiment is to quantify whole-body and mammary blood glucose kinetics in lactating goats exposed to moderately and severely hot environments.

MATERIALS AND METHODS
Animals
Five female Japanese Saanen goats aged 2 to 6 yr, in their first to fifth lactations, 5 to 10 wk postpartum, and weighing 29 to 47 kg were used. They were surgically prepared with skin loops enclosing a carotid artery and the left subcutaneous abdominal vein. Animals were kept in metabolic cages in a controlled environment chamber at 20 ± 1°C for more than a week to become accustomed to experimental procedures and surroundings. They were fed 1000 g lucerne hay cubes and 500 g concentrates daily at 1800 h. The ration contained 11.3 MJ digestible energy per kilogram, 13% crude protein, and 17% crude fiber. Water was given ad libitum. Animals were milked twice daily (0900 and 1800 h). A polyethylene cathe-
ter was inserted into a jugular vein a day before blood sampling commenced.

Experimental Procedure

The experiment consisted of three periods: thermoneutral (20 ± 1°C), moderate heat exposure (30 ± 2°C), and severe heat exposure (35 ± 2°C). Relative humidity was maintained at 70 ± 5% for all temperatures. As milk yield was expected to change as lactation advanced, each experimental period was restricted to 4 d. Animals were exposed to a thermoneutral environment, moderate heat, and severe heat for 4 d, in that order, with a recovery period of 2 d in the thermoneutral environment. One goat died accidentally after moderate heat exposure.

Physiological responses (respiration rate, heart rate, and rectal temperature) were observed and blood samples (10 ml) from the jugular vein collected at 1200 h. Heat production was measured by collecting exhaled gas through a face mask into a Douglas bag. All collections were twice daily on each of the 4 d for 6 min at approximately 1500 h.

Whole-body and mammary kinetics of blood glucose were measured simultaneously on the 4th d of exposure to each environment. A catheter was placed in the carotid artery and two catheters were inserted in the left subcutaneous abdominal vein at least 2 h before the experiment started.

At approximately 1200 h, [U-14C]glucose (New England Nuclear, MA) was infused into jugular vein as a primed continuous infusion (priming dose, 3.0 μCi; infusion rate, .3 μCi/min in .6 mCi/L Krebs-Ringer solution) and p-aminohippuric acid (Sigma Chemical Co., St. Louis, MO) was infused upstream into the subcutaneous abdominal vein (priming dose, 20 mg; infusion rate, 1 mg/min in 2 g/L Krebs-Ringer solution). Each infusion was continued for 6 h, and blood samples were obtained simultaneously from the carotid artery and downstream subcutaneous abdominal vein at 30-min intervals during the latter half of the infusion period. At the thermoneutral environment and moderate heat exposure, four arterial blood samples were collected at 20-min intervals after infusions stopped. Exhaled gas for determination of the specific activity of exhaled carbon dioxide (CO2) was collected by a previously described procedure (27).

Methods of Analyses

Blood. Concentration of plasma glucose was determined enzymically (15). Concentration of plasma free fatty acids (FFA) and thyroxine (T4) were determined by nonesterified fatty acids (NEFA) and T4 test kits (Wako, Osaka, Japan). Isolation of glucose was described previously (28). Concentration of p-aminohippuric acid was determined by the method of Smith et al. (30). A double antibody radioimmunoassay was used for assay of plasma prolactin, as described by Johke (17).

Exhaled Gas. Specific activity of CO2 in exhaled gas was determined by the method described previously (27). Oxygen consumption and CO2 production were determined by automatic gas analyzers (O2, Beckman, Oxygen analyzer, Model 755; CO2, Shimazu, Gas analyzer, Model URA-5).

Milk. Lactose was determined enzymically (15) as glucose after acid hydrolysis as described by Cowie et al. (12). Glucose in milk was disregarded. Lactose was isolated using ion exchange resins (Amberlite IR4B and Dowex 50W) and dissolved in 10 ml of ACSII (Amer- sham International) as described previously (26). Total radioactivity of milk lactose was measured by liquid scintillation counting (Model 3385, Packard).

Calculations

Heat production was calculated from oxygen consumption and CO2 production as described by Young et al. (35). Therefore, estimates slightly overestimate true heat production. Parameters of whole-body metabolism of blood glucose were calculated by the methods of Bergman (6) and Sabine and Johnson (25). Mammary glucose metabolism was calculated by the method of Faulkner et al. (13).

Statistics

Results are expressed as means ± SE. The significance of differences were evaluated by Student's t test comparing thermoneutral means with values obtained under moderate or severe heat exposure.

RESULTS

Physiological Responses

Respiration rate increased markedly (P<.01) while heart rate was not influenced by heat
exposure (Table 1). Rectal temperature was significantly elevated by .8 and 1.0°C during moderate and severe heat exposure.

Feed intake was 1462 and 1398 g/d during the thermoneutral period and moderate heat exposure, but intake tended to reduce gradually to 1200 g/d during severe heat exposure (Figure 1). Water intake was 6.3 ± .7 L/d during the thermoneutral period and increased (P<.05) to 9.7 ± 1.1 and 13.7 ± 2.3 L/d during moderate and severe heat exposure. Milk yield remained stable in the thermoneutral environment, and decreased by 3 and 13% during moderate and severe heat exposure. Heat production was 22.3 kJ/h per kg body weight at thermoneutral environment and was not influenced by heat exposure.

**Blood Constituents**

Concentration of glucose in plasma did not change during heat exposure, but, on day 4 of all environments, tended to be higher than those on the other three days (Figure 2). Concentration of FFA was not influenced by heat exposure, means during moderate and severe heat exposure were 10 and 9% lower than the thermoneutral mean. Concentration of T4 decreased (P<.05) by 18% during moderate heat exposure and by 28% during severe heat exposure. Mean concentration of prolactin was 72 ng/ml in the thermoneutral environment. Plasma prolactin concentration was increased (P<.05) by 48 and 55% during moderate and severe heat exposure.

**Blood Glucose Metabolism and Heat Production**

Whole-body turnover of blood glucose was decreased (P<.05) by moderate and severe heat exposure (Table 2). The proportion of blood glucose oxidized and the proportion of exhaled CO₂ derived from blood glucose did not change during heat exposure.

**Mammary Glucose Metabolism and Milk Production**

In one of the goats, concentrations of p-aminohippuric acid in the subcutaneous abdominal vein did not achieve a plateau. Therefore, data on mammary kinetics of the animal were removed.

Mammary plasma flow tended to reduce on the 4th d of moderate and severe heat exposure (Table 3). The arteriovenous difference of plasma glucose also tended to decrease at higher environmental temperatures. Therefore, net mammary glucose uptake tended to be reduced by approximately 15 and 50%. The contribution of mammary glucose uptake to whole-body glucose utilization decreased during heat exposure, although these changes were not statistically significant (P>.05).

Milk lactose concentration decreased (P<.05) on the 4th d of severe heat exposure. Milk lactose output and the contribution of blood glucose to milk lactose synthesis tended to decrease during severe heat exposure (Table 4).

<table>
<thead>
<tr>
<th>TABLE 1. Effects of moderate (30°C) and severe (35°C) heat exposure for 4 d on physiological responses in lactating goats.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiration rate</strong></td>
</tr>
<tr>
<td>(min⁻¹)</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Thermoneutral (5)¹</td>
</tr>
<tr>
<td>Moderate heat (5)</td>
</tr>
<tr>
<td>Severe heat (4)</td>
</tr>
</tbody>
</table>

¹ In parentheses are numbers of goats.

*Significant at P<.05 compared with the thermoneutral mean.

**Significant at P<.01 compared with the thermoneutral mean.
DISCUSSION

Physiological Responses

A marked increase in respiration rate and hyperthermia were developed by heat exposure in lactating goats. Water intake was clearly increased by heat exposure. The increased water intake may be utilized mainly for heat loss as evaporation from the respiratory tract and excreted as urine, but milk yield tended to reduce during heat exposure. Heat production was not influenced during the heat exposure in the present experiment, although it decreased in nonlactating shorn sheep (27). Johnson et al. (18) reported that in lactating dairy cattle, metabolic rate did not change in hot environments when feed intake was maintained by administering the refused feed directly to the rumen.

Blood Constituents

In ruminants, almost all blood glucose is supplied by gluconeogenesis in the liver and kidney. The plasma glucose concentration of ruminants is lower, and the effect of starvation stress is less than in nonruminant animals. Concentration of plasma glucose in nonlactating shorn sheep did not change during heat exposure (27). Weekes et al. (34) reported that plasma glucose concentration in nonlactating shorn sheep was significantly higher during cold exposure than in a warm environment. Faulkner et al. (13) also observed plasma glucose concentration in lactating goats was higher by approximately 15% during cold exposure than that in a thermoneutral environment. The response of plasma glucose concentration to environmental temperature may be similar for both lactating and nonlactating ruminants.

Plasma FFA concentration was not influenced by heat exposure. Bergman and Hogue (8) reported that FFA concentration in lactating sheep at peak lactation was about 1.8 times higher than that of nonlactating ewes. The average fat content of goat milk is 4.5% (16). The long-chain fatty acids of milk with...
TABLE 2. Effects of moderate (30°C) and severe (35°C) heat exposure for 4 d on whole-body kinetics of blood glucose in lactating goats.

<table>
<thead>
<tr>
<th></th>
<th>Arterial concentration (mmol/L)</th>
<th>Turnover rate (μmol/min)</th>
<th>Pool size (mmol)</th>
<th>Oxidation rate (μmol/min)</th>
<th>Exhaled carbon dioxide derived from blood glucose (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X SE</td>
<td>X SE</td>
<td>X SE</td>
<td>X SE</td>
<td>X SE</td>
</tr>
<tr>
<td>Thermoneutral (5)</td>
<td>3.2 .1</td>
<td>620 .42</td>
<td>37.4 2.8</td>
<td>18 1</td>
<td>7 .5</td>
</tr>
<tr>
<td>Moderate heat (5)</td>
<td>3.3 .2</td>
<td>569* 37</td>
<td>42.3 3.9</td>
<td>18 1</td>
<td>6 .4</td>
</tr>
<tr>
<td>Severe heat (4)</td>
<td>3.6 .5</td>
<td>418* 45</td>
<td>ND</td>
<td>19 1</td>
<td>6 .3</td>
</tr>
</tbody>
</table>

1 In parentheses are numbers of goats.
2 ND = Not determined.
*Significant at P<.05 compared with the thermoneutral mean.

TABLE 3. Effects of moderate (30°C) and severe (35°C) heat exposure for 4 d on mammary plasma flow, arteriovenous difference of plasma glucose, and mammary glucose uptake in lactating goats.

<table>
<thead>
<tr>
<th></th>
<th>Mammary plasma flow (ml/min)</th>
<th>Arteriovenous difference of plasma glucose (mmol/L)</th>
<th>Mammary glucose uptake (μmol/min)</th>
<th>Mammary glucose uptake to whole-body turnover of blood glucose (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X SE</td>
<td>X SE</td>
<td>X SE</td>
<td>X SE</td>
</tr>
<tr>
<td>Thermoneutral (3)</td>
<td>518 176</td>
<td>.70 .10</td>
<td>328 59</td>
<td>60 13</td>
</tr>
<tr>
<td>Moderate heat (3)</td>
<td>418 100</td>
<td>.67 .03</td>
<td>281 66</td>
<td>54 12</td>
</tr>
<tr>
<td>Severe heat (3)</td>
<td>360 106</td>
<td>.56 .17</td>
<td>169 25</td>
<td>37 2</td>
</tr>
</tbody>
</table>

1 In parentheses are numbers of goats.
TABLE 4. Effects of moderate (30°C) and severe (35°C) heat exposure for 4 d on milk lactose concentration, lactose output, and percentage of lactose derived from blood glucose in lactating goats.

<table>
<thead>
<tr>
<th></th>
<th>Lactose concentration</th>
<th>Lactose output</th>
<th>Percentage of lactose derived from blood glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mmol/L)</td>
<td>(μmol/min)</td>
<td>(%)</td>
</tr>
<tr>
<td>Thermoneutral (3)</td>
<td>136</td>
<td>159</td>
<td>61</td>
</tr>
<tr>
<td>Moderate heat (3)</td>
<td>136</td>
<td>154</td>
<td>59</td>
</tr>
<tr>
<td>Severe heat (3)</td>
<td>128*</td>
<td>143</td>
<td>50</td>
</tr>
</tbody>
</table>

1 In parentheses are numbers of goats.

*Significant at P<.05 compared with the thermoneutral mean.

16 and more carbon atoms are derived from plasma lipid (3). Lack of marked changes in plasma FFA suggests that mobilization of fatty acids from adipose tissue occurred in the present experiment in which milk yield was maintained above 1.5 L/d during heat exposure. Cowan et al. (11) measured body fat content in lactating sheep of 65.6 kg body weight and found that the weight of adipose tissue decreased from 9.19 kg at 12 d to 2.28 kg at 41 d and 1.19 kg at 111 d of lactation. Thompson et al. (32) calculated that the output of C18 fatty acids into milk in lactating sheep exposed to 40°C for 2 d was greater than in a thermoneutral environment.

The negative relationship between plasma T4 concentration and environmental temperature is well-known (36). Thyroid hormone enhances lactational intensity (31), but negative correlations between milk yield and plasma T4 concentration have been observed (33). The plasma T4 concentration (67 ng/ml) obtained in the thermoneutral environment was comparable to concentrations (60 ng/ml) obtained in nonlactating sheep (27). The extent of the decrease in plasma T4 concentration during heat exposure was less in the present experiment (18 to 28%) than that in nonlactating sheep (about 50%) (27). Thus, plasma T4 concentration is related negatively to environmental temperature but is not decreased further due to the combined effects of environmental temperature and milk yield.

Prolactin has a significant physiological action for mammary growth and maintenance of milk secretion, but plasma prolactin concentration is not generally correlated highly with milk yield. However, Akers et al. (1) found a strong positive relationship between prolactin secretion rate and milk yield in dairy cattle. Prolactin concentration is also positively related to environmental temperature. In the present experiment plasma prolactin concentration increased with increasing temperature. This result may appear to be inconsistent with the concurrent data on milk yield; however, Koprowski and Tucker (20) found that the prolactin release response to the milking stimulus was lower in summer than in winter.

**Milk Constituents**

Thompson et al. (32) reported that milk lactose concentration did not change in lactating sheep exposed to 40°C for 2 d. Bandaranayaka and Holmes (4) also reported that milk lactose did not change in lactating cows during prolonged heat exposure. However, Findlay (14) described milk lactose decreases in European cattle subjected to temperature in excess of 27°C. Although lactose concentration decreased significantly on the 4th d of severe heat exposure, the concentrations in all environments were within the limits of those for normal lactating goats (16).

**Whole-Body and Mammary Kinetics**

In the present experiment, blood glucose metabolism revealed changes during heat exposure similar to those previously obtained in...
nonlactating sheep (27), although heat production was not influenced. Oxidation rate of blood glucose in the lactating goat was smaller than that in nonlactating sheep, which was consistent with a large amount of blood glucose being used for synthesis of milk constituents.

It has been suggested that the high rate of glucose metabolism during lactation is due to the increased energy intake (21). On the contrary, Bennink et al. (5) demonstrated that blood glucose turnover increased after parturition even when energy intake was maintained constant. Paterson and Linzell (24) demonstrated that the turnover rate of blood glucose correlated positively with milk yield in dairy cows. In the present experiment correlation was positive under both thermoneutral \( r=0.55 \) and heat exposure \( r=0.65, P<.05 \) conditions. This implies that the turnover rate of blood glucose is an important factor that influences milk yield during heat exposure as well as in a thermoneutral environment.

The glucose uptake by the udder was measured simultaneously during determinations of whole-body blood glucose metabolism. The proportion of mammary uptake to whole-body turnover of blood glucose (60 ± 13%) in the present experiment is within the normal range. The proportion was influenced little by moderate heat exposure but decreased to 37 ± 2% by severe heat exposure. Whole-body and mammary kinetics of blood glucose have been neglected in relation to effects of environmental temperature, especially with high environmental temperatures. Faulkner et al. (13) found that in lactating goats exposed to cold mammary glucose uptake decreased to 30% of control, although the glucose turnover rate of nonmammary tissue increased. They concluded that the reduction of glucose uptake and lactose synthesis by the udder are important factors that reduce milk secretion during cold exposure.

It is well-known that glucose is the major precursor of lactose. Bickerstaffe et al. (9) showed in lactating cows that at least 85% of lactose was derived from plasma glucose. Buckley et al. (10) also showed 73 and 67% of lactose carbon were derived from glucose carbon in ad libitum-fed and feed-restricted lactating goats. We obtained a similar result (81 ± 7%) in lactating goats in a previous experiment (26) with the same analytical technique as the present experiment, but the values obtained in the present experiment were consistently lower (50 to 61%) in all environments. The possible reason for this may relate to the sampling time. Blood glucose kinetics was measured 21 to 24 h after feeding, but lactose output into milk was the mean for the whole day. Concerning precursors of milk lactose other than blood glucose, Mepham and Linzell (22) observed gluconeogenesis from glutamate to occur in the mammary gland of lactating goats. However, Scott et al. (29), who used mammary slices from lactating cows, observed that glucose was the major source of lactose carbon, although glycerol was also incorporated into lactose, but alanine, glutamate, lactate, and pyruvate were not incorporated. In the present experiment the decrease in whole-body turnover of blood glucose was of similar magnitude to the reduced glucose uptake by the udder. Consequently, the glucose turnover rate of nonmammary tissue was influenced little by heat exposure. It seems that mammary glucose utilization decreases preferentially during heat stress as well as during cold stress (13). In this regard, Bergman (7), in reviewing bovine ketosis, concluded that lactating animals can prevent the development of severe hypoglycemia by reducing milk production.

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REFERENCES


