Renal Urea Handling in Goats Fed High and Low Protein Diets

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ABSTRACT
Four female goats first were fed a high protein diet and later a low protein diet. Renal urea handling was studied during feeding of both diets. Glomerular filtration rate was measured with [hydroxymethyl-carbon-14]inulin. Glomerular filtration rate dropped about 60% when nitrogen intake was restricted. Urea concentration of plasma fell from 6 mM on high protein diet to .6mM on low protein diet. On low protein diet the rate of urea filtration at the glomeruli was only 4% of that on high protein diet, 22 versus 519 μmol/min. In addition, tubular urea reabsorption in percentage of filtered urea rose up to 92% on low protein diet. As a result of all these renal changes following dietary nitrogen restriction, urinary urea excretion was only .6% of urinary urea excretion on high protein diet. In goats as in other ruminants, renal mechanisms effectively contribute to urea conservation during protein deprivation.

INTRODUCTION
Effects of altering nitrogen intake on renal function of ruminants has been studied widely. In ruminants, protein deprivation causes effective conservation of urea by the kidneys. This involves a decrease in urea concentration of blood plasma, a corresponding decrease in the amount of urea filtered at the glomeruli, and an enhancing of tubular reabsorption of urea (5).

In addition to these two urea-saving mechanisms during low protein intake, a fall in glomerular filtration rate (GFR) has been reported in sheep (2, 4, 12), cattle (10), reindeer (15), and llama (1). Also, in goats endogenous creatinine clearance during restricted protein intake decreased (6), but its significance to urea conservation was not considered. According to Harmeyer and Martens (5), conclusive evidence from goats that GFR decreases during feeding of low protein diets has yet to be presented. Our paper describes renal responses in goats to reduced intake of nitrogen, with special attention to the quantitative significance to urea conservation referable to decreased GFR and to increased tubular reabsorption.

MATERIAL AND METHODS
Animals and Feeding
Four adult female goats weighing 34 to 45 kg were restrained in individual metabolism cages by collars. Room temperature was 19 to 23°C. Goats were fed twice daily. They were allowed free access to drinking water. The high protein diet (HP) consisted of hay, grain mix, and molasses. Calculated crude protein content of the dry matter was about 14%. On the low protein diet (LP, crude protein <2%) animals were fed straw and a mixture of sugar (49%), starch (43%), and molasses (8%). Rations were equal in energy content (providing the energy requirement for maintenance). Body weight remained unchanged on HP and LP. Goats were given 3 g NaCl in the grain mix daily on both diets. An acclimatization period of 3 wk following change of diet was allowed before clearance procedures.

Sampling Procedures and Measurement of GFR
For calculation of GFR [hydroxymethyl-14C]inulin was chosen because it proved a tracer of native inulin (9). On test day goats were prepared before sampling by fixed permanent cannulae in both jugular veins and by retention catheter in the urinary bladder. Infusion solution contained 80 μCi [hydroxymethyl-14C]inulin and 3 g unlabeled native inulin in 100 ml saline. It was infused constantly into blood at .5 ml/min after a priming dose of 8 ml. Infusion time was 60 min. Urine was collected in 20-min periods. Blood samples

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TABLE 1. Means and their SE of plasma urea concentrations, urea urine to plasma concentration ratios (U/P), and renal measures for three goats on high (HP) and low (LP) protein diet. Number of observations was six.

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<thead>
<tr>
<th></th>
<th>HP</th>
<th>LP</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>SE</td>
</tr>
<tr>
<td>Plasma urea (mM)</td>
<td>5.9</td>
<td>.1</td>
</tr>
<tr>
<td>Urea U/P ratio</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>Urine flow rate (ml/min)</td>
<td>.74</td>
<td>.14</td>
</tr>
<tr>
<td>Urea clearance (ml/min)</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Urea excretion (μmol/min)</td>
<td>232</td>
<td>45</td>
</tr>
<tr>
<td>Potassium excretion (μmol/min)</td>
<td>160</td>
<td>39</td>
</tr>
<tr>
<td>Sodium excretion (μmol/min)</td>
<td>31</td>
<td>13</td>
</tr>
<tr>
<td>Urine osmolality (mosm/kg H₂O)</td>
<td>942</td>
<td>173</td>
</tr>
</tbody>
</table>

*Significance of differences between the two groups: *P<.05; **P<.01; ***P<.001.

were collected from the jugular vein on the side opposite that of infusion, at the midpoint of each urine collection period. Blood was sampled into heparinized centrifuge tubes.

**Chemical Analyses**

Urea concentration of plasma and urine was measured according to Talke and Schubert (14) adapted to the Gilford System 3500 Computer Directed Analyzer (Gilford Instrument Company, OH). [Hydroxymethyl−¹⁴C]inulin (Code CFA.400) was from the Radiochemical Centre (Amersham, England). Radioactivity of samples was measured by liquid scintillation counting. Sodium and potassium concentrations were measured by flame photometry (Coming-EEL, model 430, Halstead Essex, England), and osmolality was measured by the freezing point depression method with a Fiske osmometer (Fiske Associates, Inc., Uxbridge, MA).

**Calculations and Statistics**

Renal clearance of inulin was calculated and used as an estimate for GFR. For each animal the last two periods of infusion time were used as test periods for clearance calculation. The quantity of urea filtered per minute was calculated by multiplying plasma urea concentration by GFR. Reabsorbed urea is the difference between filtered and excreted urea and was percentage of filtered urea. Results are means and SE. Comparisons of renal functions between high and low protein diets were by unpaired t-tests.

**RESULTS**

Urea concentrations of plasma and renal excretory functions are in Table 1. On LP, urea concentration was 10% of that on HP. No difference in urine flow rate between these two diets.
diets was significant. On LP, urine urea concentration was low (about 5 mM), and urea excretion rate was only .6% of that on HP. Reducing dietary nitrogen had no significant effect on urine osmolality or sodium excretion, but urine excretion of potassium was lower on LP, reflecting differences in dietary potassium contents.

During inulin infusion one goat showed a rapidly increasing urine flow rate and decreasing urine osmolality on both diets. With the exception of GFR, data from these experiments had to be excluded because there is an effective washout of medullary urea in the beginning of water diuresis (13). A stable urine flow is, therefore, of critical importance when normal renal urea handling is evaluated.

The GFR dropped almost 60% when nitrogen intake was reduced (Table 2, Figure 1). Thus, the quantity of filtered urea on LP was only 4% of that on HP (Figure 2). As expected, percentage of tubular reabsorption of urea increased on LP, but its actual quantity was smaller than on HP (Table 2).

**DISCUSSION**

The quantity of urea excreted by kidneys is affected by plasma concentration which influences the filtered urea load. The amount of ingested nitrogen determines the urea concentration if other factors are kept constant (11). Reduction of dietary nitrogen may notably decrease urea concentration of plasma. Ide (6) found exceptionally low urea in goats, and so did we. As a consequence of decreasing
plasma urea concentration, the amount of filtered urea falls in the same proportion. It is decreased further by reduction of GFR. In our study GFR fell 58%, resulting in an equivalent decrease of filtered urea.

The fall of GFR as a renal response to restricted nitrogen intake is independent of plasma urea concentration (3, 15). Hence, urea excretion declines even if plasma urea concentration rises. This may happen, for example, when on the low protein diet the energy supply is not sufficient and body proteins are an energy source (7, 8, 15), which leads to an elevation of the plasma urea concentration and corresponding changes in filtered urea loads.

Tubular reabsorption of urea increased in goats on LP up to 92% of filtered urea. However, the actual quantity of urea reabsorbed was less than one-tenth of the quantity reabsorbed on HP. Thus, its contribution to nitrogen economy of goats on reduced nitrogen intake is far less significant than restriction of filtered urea brought about not only by fall in plasma urea concentration but also by decrease in GFR.

Harmeyer and Martens (5) mentioned a lag period of several months associated with renal responses to changes in nitrogen intake. However, no such delay was observed by others (2, 4, 6, 10, 12, 15). Both GFR and tubular reabsorption responded to change of diet as soon as the animal was adapted to it, i.e., in 2 or 3 wk.

The concentrating ability of mammalian kidney decreases when animals are deprived of protein. Reduction in urine osmolality following lowering in dietary protein intake has been described in sheep (2, 12) and reindeer (15). In our study mean urine osmolality was higher on HP diet than on LP diet, but the difference was not statistically significant. Restriction of water intake or a greater number of samplings might have revealed the declined renal concentrating ability on the LP diet even in the goat.

ACKNOWLEDGMENTS

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REFERENCES