Renal function in the chinchilla

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Renal function in the chinchilla. Am. J. Physiol. 219(6): 1706-1713. 1970. — Micropuncture and other techniques were used to study renal function in the Chinchilla laniger, a species of rodent able to produce a highly concentrated urine. Urine osmolality ranged from 2,350 to 7,599 mOsm after water deprivation and decreased to a mean of 130 mOsm after water loading. Mean GFR was 3.38 ± 1.02 ml/min or 0.70 ml/min per 100 g body weight. Free water clearance averaged 6.9% of the GFR and did not decline appreciably during saline diuresis. Micropuncture was performed in 22 animals infused at 0.2 ml/min. In 41 end accessible proximal tubules mean single nephron glomerular filtration rate (SGFR) was 45.5 ± 3.8 ml/min. Mean tubule fluid-to-plasma ratio (TF/P) of inulin was 2.71 ± 0.165. TF/P Osm was 1.03 ± 0.06. TF/P Na was 1.04 ± 0.02, and TF/P K was 1.18 ± 0.03. In 14 distal tubules mean SGFR was 57.7 ± 8.1 ml/min, mean TF/P inulin was 9.25 ± 1.27, TF/P Osm was 0.72 ± 0.06, TF/P Na was 0.50 ± 0.04, and TF/P K was 1.77 ± 0.162. In a separate study, fluid from the distal tubule was persistently hypotonic throughout its entire length. (Mean TF/P Osm was 0.52 ± 0.03, n = 27.) Glomeruli were labeled in 10 kidneys by the injection of India ink in vivo. Mean glomerular count per kidney was 48,018 ± 5545.

Urinary concentrating mechanism; tubule water reabsorption; tubule Na reabsorption; tubule K reabsorption.

Harvey and co-workers (20, 32) in their studies of the medullary circulation of Chinchilla laniger noted that these animals excrete a remarkably concentrated urine. Chinchillas deprived of water for 2 weeks remained active and voided urine as concentrated as 6,000 mOsm (32), values comparable to the maximum urinary osmolality achieved by desert rodents (35). We were stimulated by these findings to undertake an investigation, using micropuncture and other techniques, of renal function in the chinchilla.

The family Chinchillidae consists of three genera and seven species and is found only in South America. Chinchilla laniger inhabits an arid environment—rocky slopes at elevations of 800-6,100 m in Peru, Bolivia, Chile, and Argentina to about latitude 52 deg S (10). Adults weigh 0.4-0.7 kg, are slender, have relatively broad heads, large black eyes, round ears, and fine, dense pelage. Chinchillidae are herbivorous and are active throughout the year.

In this study we examine those features of chinchilla renal function related primarily to water conservation.

Methods

Adult male and female chinchillas weighing between 400 and 550 g were used for all experiments. Ten chinchillas were placed in separate cages, deprived of water for as long as 8 days, and their urine was collected under mineral oil. Three animals were given water (30 ml/kg body weight containing 1.7% alcohol) by gastric tube to estimate maximal urinary dilution.

Five chinchillas were used to investigate the urinary concentrating capacity in response to the intravenous administration of solutions of sodium chloride in different concentrations. (One animal received 0.9% saline at 0.31 ml/min, two animals received 3% saline at 0.60 ml/min, and two animals received 5% saline at 0.13 and 0.29 ml/min, respectively.) Each animal was anesthetized with intraperitoneal inactin, 120 mg/kg, and given prime and maintenance solutions containing inulin to achieve a plasma inulin concentration of 30 mg/100 ml. After an hour for equilibration of the test solution was begun. Urine collection periods lasted 10-30 min. Plasma was collected at the midpoint of each period. The GFR, osmolar clearance (Counce), and negative free water clearance (T1H2O) were calculated in the usual way (42).

In 22 animals micropuncture was performed. The animals were allowed free access to water, but were deprived of food 24 hr prior to the experiment. After anesthesia with intraperitoneal inactin, 120 mg/kg, both femoral veins were cannulated. In the right femoral artery a cannula was placed for blood sampling and blood pressure monitoring, and in the left femoral artery a catheter was passed until its tip was positioned just above the renal arteries for the injection of lissamine green. In the first series of experiments, 14 animals were given a priming dose of inulin and a maintenance infusion of Tyrode Ringer solution (containing, mm: NaCl 156.9, NaHCO3 11.9, NaH2PO4 0.4, KCl 2.7, CaCl2 1.8, and MgCl2 0.5) with inulin calculated to maintain the plasma inulin concentration at 100 mg/100 ml. The infusion rate was 0.2 ml/min. Smaller infusion rates were found insufficient to keep the animal in good condition throughout the experiment. The chinchilla was placed on a heated animal table; a 2-cm cruciate incision was made in the left abdominal wall. The kidney was freed of surrounding tissue and placed on a kidney cup. The surface of the kidney was illuminated by a quartz rod and bathed with mineral oil warmed to body temperature. The body temperature was maintained at 37-38 C and monitored by a rectal thermometer.

Glass micropuncture pipets with an external diameter of 8-9 μ at the tip were used. The pipets were siliconized inside and out with a 1% aqueous solution of Siliclad (Clay-Adams) on the day of use and filled with castor oil stained with Sudan black. After 60 min for equilibration, timed micropuncture samples were obtained from the terminal
surface (end-accessible) segments of proximal tubules, and segments of distal tubules were identified by the intra-aortic injection of 0.05 ml of 3% lissamine green (SF, Cryst, Chroma-Gessellschaft). The time for passage of the dye (transit time) through the proximal tubule and loop of Henle was measured. The rate of fluid collection from the tubule was adjusted to keep the castor oil column (5 tubule diam long) just distal to the puncture site. The volume of the sample was measured in a quartz capillary of constant bore, previously calibrated with 51Cr. After the volume was measured, the sample was analyzed for osmolality, inulin, sodium, and potassium as previously described (23, 25).

Recovery experiments of simulated tubule fluid samples are presented in Table 1. Single nephron glomerular filtration rate (SGFR) was calculated from the tubule fluid-to-plasma inulin ratio, and the volume of tubule fluid (VTF) was collected per minute, according to the expression (15)

$$\text{SGFR} = \frac{(\text{TF}/\text{P inulin}) \times \text{VTF}}{\text{VTF}}$$

where SGFR and VTF are in units of nanoliters per minute. In the calculations of TF/P ratios, no correction for plasma water was made.

A second series of eight animals was used to study the osmolality of the distal tubule contents. The animals were subjected to the same experimental preparation and given the same infusion (except that it contained no inulin) at the same rate as described before. A distal tubule was identified and injected with an oil column 4–6 tubular diam long. Special care was taken during the collection: the oil column was usually moving in a distal direction, less than 0.5 mm/min, and the flow of the oil column was observed after the pipet was withdrawn to confirm the direction of flow. The site of puncture was determined by latex injection and microdissection (4). Arterial blood was collected at the midpoint, and urine was obtained at the end of the experiment.

Plasma and urine samples were analyzed for osmolality by the Ramsay-Brown microfreezing point technique (33). (If the urinary samples were sufficiently large, the osmolality was determined by an Advanced osmometer (23).) Inulin, sodium, and potassium were analyzed by methods described before (23). Chloride was determined by the Buchler-Cotlove chloridometer (9), bicarbonate content was determined by the Natelson microgammomter (31), urea was determined by the disudomonozine method (29), and glucose was determined by the alkaline potassium ferrocyanide method (21) read in the AutoAnalyzer (38). Arterial blood gases were determined by micro pH and blood gas analyzing system of the IL gas analyzer model 113-5-1.

Since catheterizing the ureters often resulted in hypoten-

### TABLE 1. Microanalytical control recoveries

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No.</th>
<th>Range</th>
<th>True, mean</th>
<th>Observed, mean</th>
<th>SD</th>
<th>SE, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality, mOsm</td>
<td>7</td>
<td>195-474</td>
<td>299</td>
<td>300</td>
<td>4.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Inulin, mg/100ml</td>
<td>16</td>
<td>160–1,500</td>
<td>563.5</td>
<td>559.8</td>
<td>29.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Na, mEq/liter</td>
<td>8</td>
<td>88–180</td>
<td>128</td>
<td>132</td>
<td>4.1</td>
<td>2.1</td>
</tr>
<tr>
<td>K, mEq/liter</td>
<td>8</td>
<td>4.4–9.0</td>
<td>6.4</td>
<td>6.7</td>
<td>0.24</td>
<td>3.2</td>
</tr>
</tbody>
</table>

### RESULTS

**Chinchilla plasma.** The concentrations of the major solutes of chinchilla plasma are presented in Table 2. Also included are a few measurements of arterial blood gases. These were made at the highest concentrations of total solute, sodium, chloride, and urea, and the low potassium and bicarbonate concentrations.

### TABLE 2. Analyses of chinchilla plasma

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na, mEq/liter</td>
<td>161.1</td>
<td>1.04</td>
<td>57</td>
</tr>
<tr>
<td>K, mEq/liter</td>
<td>3.2</td>
<td>0.07</td>
<td>51</td>
</tr>
<tr>
<td>Cl, mEq/liter</td>
<td>119.2</td>
<td>3.93</td>
<td>9</td>
</tr>
<tr>
<td>HCO₃, mEq/liter</td>
<td>20.1</td>
<td>1.35</td>
<td>9</td>
</tr>
<tr>
<td>Urea nitrogen, mg/100 ml</td>
<td>30.0</td>
<td>1.67</td>
<td>6</td>
</tr>
</tbody>
</table>

**Mean GFR of eight animals was 3.38 ± 1.02 ml/min, or 0.70 ml/min per 100 g body weight (Table 3).** Excluding animal 4, the values were 2.43 ± 0.54 ml/min and 0.52 ml/min per 100 g body weight, respectively.

**Microdissection experiments.** In the first series of 14 animals, mean blood pressure was 90 ± 1.82 mm Hg at the beginning and 90 ± 2.13 mm Hg at the end of the experiment.

**TABLE 2. Analyses of chinchilla arterial blood**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.44</td>
<td>0.03</td>
<td>5</td>
</tr>
<tr>
<td>PO₂</td>
<td>95.0</td>
<td>3.2</td>
<td>5</td>
</tr>
<tr>
<td>PO₂</td>
<td>29.6</td>
<td>1.23</td>
<td>5</td>
</tr>
<tr>
<td>PO₂</td>
<td>39.6</td>
<td>1.23</td>
<td>5</td>
</tr>
</tbody>
</table>

**Anesthetized animal**

- 82.3
- 117.3
- 95.0
- 97.6

**Unanesthetized animal**

- 82.3
- 117.3
- 95.0
- 97.6
Plasma osmolality was unchanged (329 ± 5 71 Osm before, 323 ± 4 3 Osm after), but the hematocrit decreased from 39.4% ± 0.51 before to 35.4% ± 0.81 at the end of the experiments. The transit time for the passage of lisamine green from the glomerulus to the end-accessible proximal tubule convolution averaged 10.9 ± 0.34 sec at the beginning and 15.1 ± 0.53 sec at the end of the experiments. The time for the dye to reach the first surface segment of the distal tubule was 40.4 ± 1.88 sec at the beginning and 42.6 ± 2.19 sec at the end of the experiment.

Tables 4 and 5 and Figs. 2-5 summarize 55 micropuncture collections in 14 animals. The mean single nephron glomerular filtration rate for 41 proximal tubules was 45.5 ± 3.8 nl/min or 17.4 nl/min per g kidney weight; for 14 distal tubules, the values were 57.7 ± 8.1 nl/min or 22.9 nl/min per g kidney weight. The mean SGFRs from the proximal and distal tubules do not differ significantly (P > .1). The combined mean was 48.6 nl/min or 18.6

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**TABLE 4. Micropuncture of superficial nephrons in chinchilla**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Proximal Tubule</th>
<th>Distal Tubule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SE</td>
<td>No.</td>
</tr>
<tr>
<td>Single nephron glomerular filtration rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>nl/min</td>
<td>45.5</td>
<td>3.8</td>
</tr>
<tr>
<td>nl/min per g kidney wt</td>
<td>17.4</td>
<td>1.23</td>
</tr>
<tr>
<td>Osmolality, mOsSO</td>
<td>435</td>
<td>2.4</td>
</tr>
<tr>
<td>TF/P Osm</td>
<td>1.03</td>
<td>0.006</td>
</tr>
<tr>
<td>TF/P Inulin</td>
<td>2.11</td>
<td>0.16</td>
</tr>
<tr>
<td>P/TF Inulin × 100</td>
<td>42.7</td>
<td>2.49</td>
</tr>
<tr>
<td>TF/P Na</td>
<td>1.04</td>
<td>0.02</td>
</tr>
<tr>
<td>TF/P K</td>
<td>1.18</td>
<td>0.038</td>
</tr>
<tr>
<td>TF/P Osm/inulin</td>
<td>0.44</td>
<td>0.028</td>
</tr>
<tr>
<td>TF/P Na/inulin</td>
<td>0.44</td>
<td>0.028</td>
</tr>
<tr>
<td>TF/P K/inulin</td>
<td>0.50</td>
<td>0.033</td>
</tr>
</tbody>
</table>

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**TABLE 5. Reabsorption in loop of Henle of chinchilla**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Proximal Tubule</th>
<th>Distal Tubule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SE</td>
<td>No.</td>
</tr>
<tr>
<td>Mean</td>
<td>31.29</td>
<td>0.364</td>
</tr>
<tr>
<td>se</td>
<td>4.54</td>
<td>0.050</td>
</tr>
<tr>
<td>No. of animals</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>P less than 0.05</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Differences between proximal tubule fluid and distal tubule fluid, i.e., proximal minus distal.

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**FIG. 2. TF/P inulin as a function of intratubular flow rate. Proportional equals single nephron glomerular filtration rate. Flow is expressed in nl/min per g kidney weight. Hyperbolic lines represent, respectively, equations TF/P inulin × V = 17.4 nl/min per g kidney weight (mean SGFR determined from puncture of proximal tubule) and TF/P inulin × V = 22.9 nl/min per g kidney weight. (Mean SGFR determined from puncture of distal tubules).**
FIG. 3. A: TF/P Osm. B: fraction of filtered solute unreabsorbed (TF/P Osm/inulin). Both plotted as a function of filtered water unreabsorbed (P/TF inulin X 100).

FIG. 4. A: TF/P sodium and B: fraction of filtered sodium unreabsorbed (TF/P Na/inulin). Both plotted as a function of fraction of filtered water unreabsorbed (P/TF inulin X 100).
In the proximal tubule, a mean of 57% of the glomerular filtrate was reabsorbed containing isotonic quantities of total solute, sodium, and potassium. In the loop of Henle (distal tubule reabsorption minus proximal tubule reabsorption in the eight animals in which both segments of tubule were punctured, Table 5), 39% of the filtered water, 36% of the filtered solute, 38% of the filtered sodium, and 30% of the filtered potassium were reabsorbed. In the distal tubule, a total of 87% of the filtered water and more sodium than water was reabsorbed, resulting in a significantly hypotonic fluid (TF/P Osm 0.72). Less overall reabsorption of potassium than sodium occurred.

A second series of micropuncture experiments was undertaken in eight animals specifically to ascertain the pattern of fluid osmolality as a function of distal tubule location. As is illustrated by Fig. 6, the fluid was consistently hypotonic throughout the distal tubule (mean TF/P Osm 0.52 ± 0.031, n = 27) and only slightly more concentrated in the distal half (TF/P Osm 0.529 ± 0.031, n = 21) than in the proximal half (TF/P Osm 0.460 ± 0.077, n = 6). In seven of the eight animals, urine was obtained at the end of the experiment and was, in each case, hypertonic (mean U/P Osm 3.275 ± 0.567, n = 7).

Glomerular counts. The mean number of glomeruli in 10 kidneys was 48,018 ± 554 ± SE (Table 6).

**DISCUSSION**

The chinchilla manifests several features which, analogous to other species (26, 35), probably represent adaptations to a limited water supply. One of these is the high serum
The figure of 42.77% however, is the more meaningful value insofar as a mathematical consequence of the variation in the TF/P inulin.

Microinfusion experiments. The chinchilla resembled those in the dog (6) and the monkey (2). Subjects to laparotomy while the other group was not, hypertonic (Fig. 6). These findings in the hydropenic time, and since the animals studied by micropuncture were subjected to lower osmolality, this suggests a third adaptation. Finally, as Buckalew et al. (5) demonstrated in the rat, there is no plateau in the T,H,O response of the chinchilla to a saline infusion.

Proximal tubule. At the end-accessible portion of the proximal tubule of the surface nephron, approximately 57% of the glomerular filtrate is reabsorbed, and the reabsorbat contains isotonic quantities of solute, sodium, and probably potassium. Although the mean TF/P K ratio is significantly higher than the mean TF/P Na ratio, P < .001, the difference (0.16) is small and within the error of the microanalytic method. Fractional reabsorption in the accessible proximal tubule of the chinchilla nephron is thus similar to that in the rat (39), but greater than that in the dog (7). The rate of infusion employed in the present study, however, is sufficient to produce some suppression of proximal tubule reabsorption in the rat (6) and in the dog (14).

Distal tubule. An exact assessment of the contribution of the distal tubule and the loop segments to overall reabsorption cannot be made, because the distal tubule was punctured at various sites along its length, but a reasonably good approximation can be obtained by averaging the distal tubule data. When the glomerular filtrate reaches the distal convoluted segment, 87% of the filtered water and 93% of the filtered sodium have been reabsorbed, resulting in a significantly hypotonic fluid (TF/P Osm 0.72).

To determine the luminal fluid osmolality as a function of distal tubule length, a second series of experiments was undertaken. Each of 27 samples collected in eight animals was distinctly hypotonic to the plasma, and the osmolality of the most distal samples was only slightly greater than it was of those obtained near the beginning of the distal tubule, despite the fact that the final urine was always hypotonic (Fig. 6). These findings in the hydroperic chinchilla resemble those in the dog (6) and the monkey (2).

Recently Lechène et al. (28) reported hypotonicity throughout the distal tubule in rats, in contrast to the earlier findings of Gotschalk and Mylle (19) and Wirz (41). De Rouffignac et al. (11–13) found the fluid to remain hypotonic throughout the distal tubule in Meriones (12) and Psammomys (13) (except for isotonicity at the extreme end of the distal tubule in the nondiuretic Psammomys (30)).

Loop of Henle. In the segment of tubule intervening between the end-accessible portion of the proximal tubule and the distal tubule—roughly equivalent to the loop of Henle (Table 4)—more solute (36%) than water (31%) was reabsorbed, indicating that the reabsorbate in the loop of Henle of the chinchilla is hypertonic, as it is in the rat and the dog.

Single nephron glomerular filtration rate. The mean single nephron glomerular filtration rate in the proximal tubule (45.5 ± 3.8 ml/min) was not significantly different from that in the distal tubule (57.7 ± 0.1) (Fig. 2), suggesting that the technique of collecting fluid in either segment corresponded reasonably well to the tubule fluid flow rate. Overall mean GFR was 40.6 ml/min (or 10.8 ml/min per g kidney weight).

As a rough estimate of the SGFR of nephrons beneath the surface of the kidney, the total GFR per kidney was divided by the number of nephrons per kidney. In eight chinchillas, total GFR per kidney was 1.69 ml/min (or 1.22 ml/min if animal 4 is excluded). The method of Damadian et al. (10) was employed to determine the number of glomeruli per kidney and gave surprisingly reproducible glomerular counts, 48,018 ± 354 se (Table 6); 1.69 × 10^4 ml/min ÷ 48,018 = 35.2 ml/min as the average SGFR per nephron throughout the kidney. This result has at least three possible explanations.

1) The SGFR of deeper nephrons is less than that of superficial nephrons. If this is correct, the intrarenal distribution of nephron filtration rates in the chinchilla is the reverse of that in Psammomys in a saline diuresis (1, 13) and rats fed a low (22) or normal (1, 24) salt diet, in which the SGFR of the juxtamedullary nephron is significantly greater than that of the superficial nephron, but is similar to that in rats fed a high salt diet (22).

2) The SGFR of the superficial nephrons was artifically elevated by micropuncture, a factor stressed recently by Gertz et al. (16) and Schnermann et al. (37). The agreement between distal and proximal tubule SGFR argues against an artifically elevated SGFR but does not exclude the possibility.

3) The animals in which the clearance studies were done were less well hydrated than the animals studied by the micropuncture technique. Since the animals were given the same infusion at the same rate for comparable lengths of time, and since the animals studied by micropuncture were subjected to laparotomy while the other group was not, this possible explanation seems unlikely but cannot be excluded. Clearly, whether the SGFR of deeper nephrons is less than that of superficial nephrons must await determination by direct measurement.

Knowledge of the function of the thin loops of Henle and the juxtamedullary nephrons, the collecting ducts, and the medullary circulation has been limited by the inaccessibility of the medulla to direct investigation. The hamster...
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