The spiny mouse (Acomys cahirinus) completes nephrogenesis before birth

Hayley Dickinson,1,2 David W. Walker,1 Luise Cullen-McEwen,2 E. Marelyn Wintour,1 and Karen Moritz2

1Department of Physiology and 2Department of Anatomy and Cell Biology, Monash University, Clayton, Victoria, Australia

Submitted 4 November 2004; accepted in final form 25 February 2005

Dickinson, Hayley, David W. Walker, Luise Cullen-McEwen, E. Marelyn Wintour, and Karen Moritz. The spiny mouse (Acomys cahirinus) completes nephrogenesis before birth. Am J Physiol Renal Physiol 289: F273–F279, 2005. First published March 1, 2005; doi:10.1152/ajprenal.00400.2004.—The spiny mouse is relatively mature at birth. We hypothesized that like other organs, the kidney may be more developed in the spiny mouse at birth, than in other rodents. If nephrogenesis is complete before birth, the spiny mouse may provide an excellent model with which to study the effects of an altered intrauterine environment on renal development. Due to its desert adaptation, the spiny mouse may have a reduced cortex-to-medulla ratio compared with C57/BL mice, although the total glomerular volume is similar. The cortex-to-medulla ratio of the spiny mouse is significantly smaller. The spiny mouse is the first rodent species shown to complete nephrogenesis before birth. This makes it an attractive candidate for the study of fetal and neonatal kidney development and function. The reduced total nephron number and cortex-to-medulla ratio in the spiny mouse may contribute to its ability to highly concentrate its urine under stressful conditions (dehydration).

glomerular number; urine osmolality; unbiased stereology

THE SPINY MOUSE (Acomys cahirinus) is a nocturnal rodent species native to regions of Africa and Europe, where it inhabits sandy deserts and rocky terrains (41). Spiny mice are an ideal rodent model for perinatal research as they have a relatively long gestation period (39–40 days); small litter size (1–4, usually 1–3); and precocial (covered with fur and capable of moving around and self-feeding soon after birth) pups, which show an advanced stage of development. At birth they have a fur coat, open eyes and ears, and are capable of locomotion and thermoregulation due to their sophisticated sensory and motor capabilities (15). Self-feeding begins within a few days of birth (14), weaning occurs at 2–3 wk, and sexual maturity is reached at ~2 mo (31). Spiny mice have been studied extensively as a possible model for mature-onset or chemical diabetes and obesity in humans (11, 16, 19, 20, 22, 36, 40). Spiny mice are used as a precocial rodent model in comparative developmental studies with altricial (naked, blind, and incapable of moving around soon after birth) rodents, such as rats (4, 6, 7, 13, 23, 25, 29), and have been used to examine the role of odor and pheromones in maternal, paternal, and neonatal behaviors (32, 33). Organogenesis of the liver (24), lung (29), and some brain regions (6–8) is shown to be complete during the fetal period in the spiny mouse, unlike other rodents such as the house mouse and rat, where these processes continue into the neonatal period. Very little is known about the kidney and its functionality in the spiny mouse.

Orci et al. (30) examined changes in the basement membrane thickness of glomeruli in aged and diabetic spiny mouse kidneys using electron microscopy. They showed an age-dependent increase in basement membrane width, which appeared to be accelerated in diabetic animals (30). The spiny mouse is known to concentrate the urea in its urine to 4.8 M (38) and conserve its blood volume during dehydration as effectively as the Saharan camel (21). Development of the kidney has not previously been examined in the spiny mouse. We therefore chose to investigate the development of the kidney throughout gestation in the spiny mouse from the initial invasion of the Wolffian duct through to complete nephron endowment. We hypothesized that like other organs the kidney may be more developed in the spiny mouse at birth than other rodents. Furthermore, we hypothesized that, like the camel (1), due to its desert adaptation, the spiny mouse will have a reduced cortex-to-medulla ratio, however an equivalent total nephron number to the laboratory (C57/BL) mouse.

The process of nephron formation is complex and depends on a series of reciprocal inductive interactions between the epithelial ureteric bud, a caudal branch of the Wolffian (mesonephric) duct, and the mesenchymal cells of the metanephric mesenchyme (blastaema). The environment and time taken for nephrogenesis completion vary significantly among different mammalian species. In some species, such as humans (18) and sheep (28), nephrogenesis is completed within an intrauterine environment. The rat, with a gestational length of 21 days, undergoes nephrogenesis from embryonic day 12.5 (E12.5) to postnatal days 7–10 (PN7–10), with only 20% of its nephrons present at birth (26). This is similar to the house mouse, which has a gestational length of 20 days and undergoes nephrogenesis from E11 to PN5–7, and the pig, which has a gestational length of 16 wk and undergoes nephrogenesis from E20 to PN21–28. These are all examples of species whereby nephrogenesis continues after birth (18). While the issue of induction vs. completion of nephron endowment and branching morphogenesis after birth has not been specifically described, the fact that the rat has only 20% of its full endowment of nephrons at 21 days of gestation (of a 21- to 22-day gestation) strongly suggests that new nephrons are being induced (26). Similarly, a newborn mouse kidney, as shown by Cebrian et al. (9), has only ~8,000 glomeruli, of which the authors included glomer-
ulii ranging from the S-shaped body stage to morphological maturity. Again, this strongly suggests that nephrons are still to be induced to reach the full endowment of ~11,000 nephrons in the mouse kidney (9). The spiny mouse may prove to be advantageous to current rodent models in studying and understanding the development of organs throughout human gestation as development of many organs is completed within a similar environment, making comparisons and discoveries more applicable.

Many factors have been shown to influence renal development, and it has been suggested by numerous animal models that compromised renal development may underlie an increased susceptibility to the development of adult diseases such as hypertension (27). If nephrogenesis is completed before birth, the spiny mouse may provide an excellent model with which to study the effect of maternal factors, such as diabetes or an altered intrauterine environment on renal development in a rodent.

MATERIALS AND METHODS

Animals. All experiments were approved in advance by Monash University Department of Physiology and Anatomy and Cell Biology Animal Ethics Committees and conducted in accordance with the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes.

The spiny mice used in this study were obtained from our own laboratory colony, started in 2002 from five breeding pairs imported by Dr. David W. Walker from the University of Amsterdam. The animals were fed standard rat and mouse cubes (Specialty Feeds, Melbourne, Australia) with water available ad libitum. Spiny mice were housed in standard rat cages (40 × 26 × 15 cm) with a wire lid, and ambient room temperature was set at 25 ± 1°C with 30–50% humidity. Precise-time matings are not possible in this species due to the lack of visible vaginal plugs; therefore, a postpartum estrus exhibited by the spiny mouse within 24 h of giving birth was used to determine gestational ages. Experimental females were paired with a male at ~150 days of age and allowed to naturally conceive and deliver their first litter with no human intervention. The first 24-h period after birth of the first litter is deemed to be the day of conception of litter 2 and the next day as day 1 of gestation. Kidneys were collected from both fetal (gestational age 18, 21, 24, 28, 32, 35, 38) and neonatal ages (postnatal age 1, 4, 8, 15, 30) to study the timing of kidney development in the spiny mouse and from eight adult male spiny mice (at 10 wk of age) for the determination of glomerular number (Table 1). In addition, kidneys from four adult male mice of a C57/BL genetic background (12) (at 30 days of age) were also collected for comparative reasons. All animals were killed by an overdose of anesthetic (Nembutal) administered intraperitoneally (120 mg/kg).

Tissue preparation. All kidneys were removed, weighed, and immersion fixed in 10% buffered formalin for 48 h. Kidneys to be examined for development of the spiny mouse kidney were dehydrated in serial alcohols, embedded in paraffin wax, and sectioned at 10 μm. Sections were then stained with hematoxylin and eosin and coverslipped.

Following fixation, kidneys used to determine glomerular number were dehydrated overnight in 70% ethanol, decapsulated, reweighed, cut into three pieces, and further dehydrated in graded alcohols. Kidneys were then processed into glycolmethacrylate blocks (Technovit 7100, Kulzer, Wehrheim, Germany) and exhaustively sectioned at a nominal thickness of 15 (spiny mice) or 20 μm (C57/BL mice). During serial sectioning, every tenth and eleventh section were sampled, with the first section chosen at random. The sections were stained with a periodic acid-Schiff reaction and coverslipped.

Table 1. Body weights, kidney weights, and kidney weight-to-body weight ratios of spiny mice throughout gestation and into early adult life

<table>
<thead>
<tr>
<th>Age, day(s)</th>
<th>Body Wt, g</th>
<th>Total Kidney Wt, mg</th>
<th>Total Kidney Wt-To-Body Wt Ratio, mg/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>0.08, 0.07</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>0.27±0.01</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>0.84±0.02</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>1.43±0.04</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>2.70±0.07</td>
<td>7</td>
<td>48.00±0.20</td>
</tr>
<tr>
<td>35</td>
<td>4.19±0.04</td>
<td>4</td>
<td>80.00±0.03</td>
</tr>
<tr>
<td>38</td>
<td>5.23±0.09</td>
<td>8</td>
<td>120.00±0.86</td>
</tr>
<tr>
<td>Neonatal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5.65±0.16</td>
<td>4</td>
<td>120.00±0.20</td>
</tr>
<tr>
<td>4</td>
<td>7.37</td>
<td>1</td>
<td>140.00</td>
</tr>
<tr>
<td>8</td>
<td>10.20</td>
<td>1</td>
<td>180.00</td>
</tr>
<tr>
<td>13</td>
<td>12.04</td>
<td>1</td>
<td>190.00</td>
</tr>
<tr>
<td>30</td>
<td>30.25</td>
<td>1</td>
<td>203.00</td>
</tr>
<tr>
<td>Young adult</td>
<td>33.68±0.81</td>
<td>8</td>
<td>207.00±0.80</td>
</tr>
</tbody>
</table>

Values are means ± SE. n, No. of mice.

Tissue analysis. Kidney development sections were examined and photographed using light microscopy. The beginning of metamorphic development was described by the invasion of the ureter and the subsequent condensation of mesenchyme around it. The beginning of glomerular formation was described by the presence of comma- and S-shaped bodies (nephrogenic zone), and the absence of the nephrogenic zone was deemed to be the completion of nephrogenesis.

Kidney volume and cortex-to-medulla ratio. Kidney volume was estimated by means of the Cavalieri principle (17). The tenth section of each pair was placed onto a light microscope (Olympus BH2) adapted for projection such that the field of vision was projected onto a table in a semidarkened room at a final magnification of ×28.25, and a stereological test grid (2 × 2 cm) was placed on the bench. Points on the grid overlying the kidney were counted as cortex (PC), medulla (PM), or renal pelvis (Pp). The cortex was defined as the area superficial to the arcuate arteries (10). Kidney volume (VKid) was estimated using the following formula

\[ V_{\text{Kid}} = 10 \times P_c \times a(p) \times T \]  

(1)

where 10 is the reciprocal of the sampling fraction, Pc is the total number of points counted (sum of Pc, PM, Pp), a(p) is the area associated with each grid point, and T is the section thickness.

Glomerular number and volume. Glomerular number and volume were determined using unbiased stereological methods as previously described by Bertram (2). The total number of glomeruli in a kidney was estimated using a physical dissector/fractionator combination (39). A 2 × 2-cm grid was placed over each field of view, and points falling on kidney tissue (PKid), glomeruli (PGlom), and renal corpuscles (PCorp; the filtration unit of the kidney made up of Bowman’s capsule and the glomerulus) were counted. Glomeruli sampled by an unbiased counting frame on the field of view on the tenth section that were not present in the eleventh section were counted. Glomeruli sampled in the eleventh section that were not present in the tenth section were counted to double the efficiency of the technique. This process was repeated for each complete pair of sections. The number of section pairs used for counting glomeruli in each kidney was ~25 (spiny mice) and 15 (C57/BL mice). Total nephron number \( N_{\text{glomeruli, Kid}} \) was then estimated using the following formula

\[ N_{\text{glomeruli, Kid}} = \frac{V_{\text{Kid}}}{V_{\text{glomeruli}} \times \lambda} \]  

(2)
where 10 is the reciprocal of the sampling fraction, \( P_S \) is the number of points overlying all kidney sections, \( P_F \) is the number of points overlying complete kidney sections, \( \frac{1}{2} f_a \) is the fraction of the total section area used to count glomeruli, and \( Q \) is the actual number of glomeruli counted. The glomerulus was defined as the glomerular tuft. Mean glomerular tuft volume (\( V_{\text{Glom}} \)) was estimated using the following formula

\[
N_{\text{Glom, Kid}} = 10 \times P_S \times P_F \times \frac{1}{2} f_a \times Q 
\]

where \( V_{V(\text{Glom, Kid})} \) is the volume density of glomeruli in the kidney and was estimated by dividing \( P_{\text{Corp}} \) by \( P_{\text{Kid}} \). \( N_{V(\text{Glom, Kid})} \) was calculated by dividing \( N_{\text{Glom, Kid}} \) by \( V_{\text{Kid}} \). The coefficient of variation was found to be 2.3%, when one kidney was counted three times.

**Urine osmolality.** Approximately 20 \( \mu l \) of urine were collected from eight male spiny mice and eight C57/BL mice at 0800. Droplets of urine were collected in a sterile pasteur pipette when mice were picked up. Due to the very small volumes of urine produced by the spiny mice, samples were collected over 4 days and pooled before analysis. C57/BL mice gave sufficient urine in 1 day. Urine was stored at \(-20^\circ C\) until analysis. Osmolality was measured by freezing-point depression using an Advanced Osmometer 2020 (Advanced Instruments, Needham Heights, MA).

![Fig. 1. Metanephric development in the spiny mouse. A: embryonic day 18 (E18) fetus showing ureteric bud (UB) surrounded by condensing mesenchyme (CM) and Wolffian duct (WD). B: E21 fetus showing UB with multiple branches, S-shaped bodies (SSB), and comma-shaped bodies (CSB). C: E28 fetus showing clear nephrogenic zone (NZ) with SSB and CSB, immature glomeruli (IMG), and the developing collecting duct system (CD). D: E35 fetus showing mature glomeruli (G) and medullary rays (MR). There still appears to be an active NZ along the very edge of the kidney. E: E38 fetus showing glomeruli (G) throughout the cortex and note the absence of CSB, SSB, and NZ. F: postnatal day 1 (PN1) neonate showing many glomeruli (G) at the periphery of the kidney.](image-url)

**Table 2. Body weights, kidney weights, and kidney volumes for male spiny mice at postnatal age 10 wk and male C57/BL mice at postnatal age 30 days**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Spiny Mice ((n = 8))</th>
<th>C57/BL Mice ((n = 4))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body, g</td>
<td>33.68±0.81*</td>
<td>22.49±0.77</td>
</tr>
<tr>
<td>Left kidney, g</td>
<td>0.102±0.006*</td>
<td>0.157±0.009</td>
</tr>
<tr>
<td>Right kidney, g</td>
<td>0.104±0.004*</td>
<td>0.164±0.009</td>
</tr>
<tr>
<td>Total kidney, g</td>
<td>0.207±0.008*</td>
<td>0.321±0.016</td>
</tr>
<tr>
<td>Total kidney wt-to-body wt ratio</td>
<td>0.0061±0.0002*</td>
<td>0.0143±0.0003</td>
</tr>
</tbody>
</table>

Values are means ± SE. \( n \), No. of mice. *\( P < 0.001 \) between groups.
Table 3. Glomerular number and volume estimates in the left kidney for male spiny mice at postnatal age 10 wk and male C57/BL mice at postnatal age 30 days

<table>
<thead>
<tr>
<th>Stereological Analysis</th>
<th>Spiny Mice (n = 8)</th>
<th>C57/BL Mice (n = 4)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume, mm³</td>
<td>0.106±0.007†</td>
<td>0.160±0.011</td>
</tr>
<tr>
<td>Cortex-to-medulla ratio</td>
<td>1.276±0.065;‡</td>
<td>1.671±0.063‡</td>
</tr>
<tr>
<td>Glomerular number</td>
<td>7.245±2.80‡</td>
<td>11.421±5.36</td>
</tr>
<tr>
<td>Glomerular volume, mm³</td>
<td>$3.634±0.184‡$</td>
<td>$2.298±0.168$</td>
</tr>
<tr>
<td>Total glomerular volume, mm³</td>
<td>$2.620±0.147$</td>
<td>$2.619±0.194$</td>
</tr>
<tr>
<td>Corpuscle volume, mm³</td>
<td>$3.755±0.216‡$</td>
<td>$2.512±0.147$</td>
</tr>
<tr>
<td>Total corpuscle volume, mm³</td>
<td>$2.708±0.174$</td>
<td>$2.859±0.162$</td>
</tr>
</tbody>
</table>

Values are means ± SE. *No. of mice. †Results comparable to previously published data (Ref. 12).‡P < 0.01, ‡P < 0.001 between groups.

Statistics. All results are given as means ± SE. P values were determined by means of an independent sample t-test using the computer-based statistics program SPSS.

RESULTS

Metanephric development. At E18, kidney development had begun in the spiny mouse, with the invasion of the ureteric bud into the metanephric mesenchyme, which subsequently condenses around the ureteric bud (Fig. 1A). The developing Wolffian duct and ureteric bud are visible, suggesting that the kidney has started development although the first glomerulus is not yet present. At E21 (Fig. 1B), the kidney has taken on a more definitive shape, while the first branch of the ureteric bud is still clearly visible, multiple branching events have taken place, and distinct comma- and S-shaped bodies have developed. At E24 (not shown), the kidney is undergoing many branching events with comma- and S-shaped bodies forming the periphery of the kidney. Very few immature glomeruli are present. By E28 (Fig. 1C), the nephrogenic zone can be clearly seen along the periphery of the kidney with multiple comma- and S-shaped bodies. Immature glomeruli are also identifiable toward the developing medulla of the kidney. The collecting duct system is visible within the developing medulla. At E32 (not shown), the nephrogenic zone is still very clear along the periphery of the kidney with many comma- and S-shaped bodies present. Few mature glomeruli can be seen toward the medulla of the kidney. At E35 (Fig. 1D), few comma- and S-shaped bodies are still evident and definitive glomeruli are present in increased numbers. Glomeruli appear more mature at this age with the presence of Bowman’s capsule. Medullary rays are clearly visible, stretching from the medulla toward the cortex. Nephrogenesis is close to completion at this time point, with the presence of mature glomeruli in the outer cortex. However, there still appears to be an active nephrogenic zone close to the edge of the kidney. By E38 (Fig. 1E), comma- and S-shaped bodies are completely absent and glomeruli are present throughout the outer cortex to the edge of the kidney. It is by this time point that nephrogenesis is completed in the spiny mouse, 2 days before birth. By PN1 (Fig. 1F), although the kidney has its full endowment of nephrons, tubular development and nephron migration toward the medulla continue through early neonatal life.

Glomerular number. As shown in Table 2, the spiny mouse is considerably larger ($P < 0.001$), although kidney weights are significantly less ($P < 0.001$) and thus kidney volumes were less ($P < 0.01$; Table 3), than the C57/BL mouse. Thus the kidney weight-to-body weight ratios were significantly smaller in the spiny mouse compared with the C57/BL mouse ($P < 0.001$; Table 2). Glomerular number was $\sim$36% less ($P < 0.001$) in spiny mice than in C57/BL mice (Table 3). Mean glomerular and corpuscle volumes were significantly greater in spiny mice than C57/BL mice ($P < 0.001$, $P < 0.01$; Table 3). Total glomerular and corpuscle volumes were very similar in both species of mouse (Table 3). Cortex-to-medulla ratios between the two species were significantly different, with spiny mice having a significantly smaller ratio than C57/BL mice ($P < 0.01$; Table 3). Figure 2 shows that these smaller ratios appear to be due to the increased size of the medulla, particularly the increased thickness and length of the renal papillae in the spiny mouse kidney.

Urine osmolality. Mean urine osmolality was very similar between spiny mice (2,104 ± 376 mosmol/kgH₂O) and C57/BL mice (2,365 ± 264 mosmol/kgH₂O) measured under standard laboratory conditions.

DISCUSSION

The spiny mouse is the first rodent species shown to complete nephrogenesis before birth. It is fair to say that growth and segmentation of nephrons are likely to occur after birth in many species; however, the spiny mouse, like humans and sheep, has its full endowment of nephrons before birth,
whereas the mouse and rat do not. The spiny mouse like the laboratory (C57/BL) mouse and rat belong to the rodent species; however, the spiny mouse is precocial and the laboratory mouse and rat are altricial. These developmental differences are the likely explanation for the different completion times of nephrogenesis in these species. Spiny mice have a longer gestational period, small litter size, precocial young, and organogenesis of major organs, including the kidney as shown here, is complete before birth. Mice and rats continue nephrogenesis in these species. Spiny mice have a longer, thicker, and more densely packed with tubules than in the renal papillae in the spiny mouse kidney appear to be hypertrophied (3). Osmolality was not different between spiny mice and C57/BL mice when measured under normal laboratory conditions (i.e., food and water ad libitum).

Another interesting comparison between species is total glomerular number and individual glomerular size. The sheep and rat are two species that have been examined using similar unbiased stereological techniques to those used here. As would be expected with increasing animal size and thus kidney size, total glomerular number and also individual glomerular size increase (see Table 5). The spiny mouse is therefore very interesting as it shows a significantly reduced total nephron number, an increased individual glomerular volume, and a similar total glomerular volume to the similarly sized C57/BL mouse. This therefore shows that whereas the spiny mouse has fewer nephrons, each individual glomerulus is bigger and hence total glomerular volume is similar. The significance of these differences is not completely understood. The increased individual glomerular volume is not thought to be due to hypertrophy in the spiny mouse kidney. The animals used in this study were young, having just reached sexually maturity, and as such we believe this to be an environmental or genetic adaptation in the spiny mouse, not an age- or disease-related change. We speculate that the spiny mouse, by having a smaller number of large glomeruli, requires each nephron to have larger tubules to match filtration with reabsorption. This would permit greater reabsorption and more concentrated urine. The spiny mouse is known to highly concentrate its urine, as is common in desert species (21). As shown in Fig. 2, the renal papillae in the spiny mouse kidney appear to be longer, thicker, and more densely packed with tubules than in the C57/BL mouse. This suggests an increased capacity for water and solute reabsorption in the spiny mouse kidney. It has been reported that the relative medullary thickness of the spiny mouse is 9.4, whereas that of the house mouse is only 8 (3). This is consistent with the decreased cortex-to-medulla ratio seen here in the spiny mouse kidney compared with the C57/BL mouse. The camel is another animal that has a low cortex-to-medulla ratio (1) and is well known for its ability to withstand extended periods without water and produce highly concentrated urine (35). It is known that the ability to concentrate urine depends on the length of the loops of Henle and collecting ducts that traverse the renal medulla (34) and the maximum length of the loop of Henle is directly proportional to medullary thickness (3). Osmolality was not different between spiny mice and C57/BL mice when measured under normal laboratory conditions (i.e., food and water ad libitum). This is not particularly surprising as neither species of mouse was under any stress. In an early study by Horowitz and Borut (21) in 1970, it was shown that the spiny mouse is able to withstand extended periods without water and produce highly concentrated urine (35). It is known that the ability to concentrate urine depends on the length of the loops of Henle and collecting ducts that traverse the renal medulla (34) and the maximum length of the loop of Henle is directly proportional to medullary thickness (3). Osmolality was not different between spiny mice and C57/BL mice when measured under normal laboratory conditions (i.e., food and water ad libitum). This is not particularly surprising as neither species of mouse was under any stress. In an early study by Horowitz and Borut (21) in 1970, it was shown that the spiny mouse is able to

### Table 5. Stereological estimates from recent literature of kidney volume, nephron number, and mean and total glomerular volumes in adult sheep and rats compared with spiny mice and C57/BL mice

<table>
<thead>
<tr>
<th>Stereological Estimate</th>
<th>Sheep</th>
<th>Rats</th>
<th>C57/BL Mice</th>
<th>Spiny Mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney weight/volume</td>
<td>67.8 g</td>
<td>1,025 mm³</td>
<td>0.157 g/0.160 mm³</td>
<td>0.102 g/0.106 mm³</td>
</tr>
<tr>
<td>Glomerular number</td>
<td>402,787</td>
<td>26,996</td>
<td>11,421</td>
<td>7,245</td>
</tr>
<tr>
<td>Mean glomerular volume, mm³ × 10⁻³</td>
<td>4.3</td>
<td>1.022</td>
<td>0.229</td>
<td>0.363</td>
</tr>
<tr>
<td>Total glomerular volume, mm³</td>
<td>17</td>
<td>0.027</td>
<td>0.00262</td>
<td>0.00262</td>
</tr>
</tbody>
</table>

Results are from Ref. 42 for sheep and Ref. 5 for rats.
KIDNEY DEVELOPMENT IN THE SPINY MOUSE

withstand longer periods of dehydration than the rat by maintaining an almost constant blood plasma volume. It would be interesting to further investigate the effects of water deprivation on the spiny mouse and compare the ability to concentrate urine to that of the C57/BL mouse. In addition, we would measure the length of the loops of Henle in both species to examine the relationship between kidney structure (renal papilla length and density) and function (urinary concentrating ability).

In recent years, it has become clear that the final number of nephrons in the mammalian kidney can be influenced by many factors (stress hormones, deficiencies of vitamin A, iron, and hyperglycemia) altering the maternal and fetal environment preceding the completion of nephrogenesis (27). In some cases disruption of nephrogenesis has been correlated with the adult onset of cardiovascular and renal disease. Of all the animal models currently available, only the sheep and guinea pig complete nephrogenesis before birth, as do humans (Table 4). It is now possible to add the spiny mouse to this list of potentially useful animals in which to examine the impact of an altered intrauterine environment on kidney development and the programming of adult disease. It should be especially useful to study the effects of maternal diabetes type 2 on the offspring, as spiny mice can be induced to develop insulin resistance by merely altering the normal diet to one of high fat, such as birdseed (36). It is hoped that with the knowledge of the mouse genome, screening studies can be utilized to further understand the “programming” effects of an altered intrauterine environment in a rodent species that completes nephrogenesis before birth.

ACKNOWLEDGMENTS

The authors thank Michelle Kett, Lisa Hutton, and Jake Pomeranz for invaluable guidance, assistance, and support.

GRANTS

This work was supported by grants from the March of Dimes and the National Health and Medical Research Council of Australia. H. Dickinson is funded by a Faculty of Medicine Postgraduate Research Scholarship.

REFERENCES


