

Strain and Sex Differences in Renin Content of Rat Kidneys (34350)

K. CONRADI, J. JELINEK, AND F. GROSS*
(Introduced by H. Bloch)

Department of Pharmacology, University of Heidelberg, Heidelberg Germany

The renin content of kidneys has been studied in the rat under various experimental conditions [for literature see (1)]. Little, however, is known about the significance that sex, age, and strain may have on the amount of renin extractable from the kidney. In adult female Wistar rats, Fisher *et al.* (2) have observed a lower reactivity of the renin-angiotensin-aldosterone system to variations in sodium balance than have other investigators; variations in age and strain of rats were considered to explain this discrepancy (3). To obtain more precise information on the effect of these parameters, juvenile and adult male and female animals of two of the most widely used rat strains, Wistar and Sprague-Dawley, were studied for their renin content.

Material and Methods. Male and female rats of the Wistar (W) and Sprague-Dawley (SD) strains, which had been kept under identical conditions since day 23 of life, were studied in groups of 20 at the ages of 26 days and 130 days. Body weights, kidney weights, and the renin content of the kidneys were measured.

Renin content of the kidneys was determined according to the method described previously (1), but which was slightly modified. The total kidney was homogenized in isotonic saline (6.7 ml/g of kidney) with a Teflon homogenizer cooled in ice water. The process lasted 1 min. Two ml of the homogenate were acidified to pH 2.5 with 0.05 ml of 2 N H_2SO_4 and neutralized 30 min later by 0.05 N KOH. After centrifugation at 3000 rpm for 10 min the supernatant was removed, and 0.06 ml of it was added to 1.5 ml of plasma from rats nephrectomized 16–20 hr previously. The mixture was incubated for

10 min at pH 5.5 and 37°. Angiotensinases were inhibited by the addition of 0.5 ml of 3.8% EDTA. The enzymatic reaction was interrupted by acidification with 0.05 ml of 1 N HCl and by boiling for 5 min. After centrifugation (15 min at 3500 rpm) the concentration of angiotensin in the supernatant was determined by rat bioassay. For the bioassay we used male rats (weighing 180–200 g), which had been nephrectomized 16–20 hr previously, anesthetized with urethan (1.4 g/kg sc) and pretreated with pentolinium (0.3 ml of a 0.5% solution ip).

Blood pressure was measured by a mercury manometer inserted into the left carotid artery. Pressor response to the intravenous injection of 0.1 ml of the supernatant (diluted 1:2 with isotonic saline) was compared with that elicited by standard doses of angiotensin II-amide (5, 10, 20 m μ g) in a three-point bioassay. All intravenous injections were given into the left jugular vein; the volume injected was kept constant at 0.1 ml. From the angiotensin activity found in 0.1 ml of supernatant the total amount per kidney (renin content) and the amount per gram of renal tissue (renin concentration) were calculated.

Results. The data are summarized in Table I. The body weight, kidney weight, renin concentration, and renin content were similar for the sexes of the same strain of juvenile animals, but differed significantly between the strains. Whereas body and kidney weights were smaller in Wistar rats ($p < 0.01$), the renin concentration was higher ($p < 0.01$) than in Sprague-Dawley rats. Consequently, total renin content of the kidneys was the same for the two strains.

In adult rats a marked sex difference was evident; male rats had a significantly higher body and kidney weight ($p < 0.01$) than fe-

* Requests for reprints to be addressed to Prof. F. Gross.

TABLE I. Body Weight, Kidney Weight, Relative and Absolute Content of Renin in the Kidney (expressed as angiotensin II) in Female (F) and Male (M) Wistar and Sprague-Dawley Rats 26 and 130 Days Old (mean \pm SEM).

Group	Wistar				Sprague-Dawley			
	(days):		26		130		26	
	F	M	F	M	F	M	F	M
Body wt (g)	42.8 ± 0.55	44.4 ± 0.7	192 ± 3.7	297 ± 5.0	55.3 ± 1.3	52.7 ± 1.0	260 ± 4.5	394 ± 12.2
Kidney wt (mg)	221 ± 4.3	220 ± 3.5	569 ± 8.0	911 ± 11.0	315 ± 4.3	293 ± 5.2	851 ± 20.4	1302 ± 36.1
Renin (expressed as angiotensin II)								
(μ g/g of kidney)	73.7 ± 2.3	72.2 ± 1.7	71.2 ± 2.0	50.3 ± 2.0	54.4 ± 1.7	56.8 ± 3.5	58.7 ± 3.4	32.1 ± 1.6
(μ g/kidney)	16.2 ± 0.5	15.9 ± 0.4	40.5 ± 1.3	45.7 ± 1.7	17.1 ± 0.7	16.5 ± 0.9	49.8 ± 2.9	41.2 ± 1.8
No. of kidneys	18	20	20	20	20	18	18	20

males. Whereas concentration of renin in the females was the same as in juvenile animals, it was lower in the males of the two strains ($p < 0.01$). Sprague-Dawley rats had a higher body and kidney weight but a lower renin concentration than Wistar rats. Total renin content in the large kidneys of male Sprague-Dawley rats was the same as in the small kidneys of female Wistar rats, owing to the low concentration of the former and the high concentration of the latter. There was a sex difference within the two strains, as male Wistar rats had a significantly higher renin content than did corresponding female rats, whereas in the Sprague-Dawley strain the ratio was reversed; the females had significantly higher values (Fig. 1). In adult animals the negative correlation between kidney weight and renin concentration was independent of the strain and sex differences observed (Fig. 2).

Discussion. Although the kidneys of both sexes of juvenile rats had the same weight, in adults of both strains the kidneys of males were larger than those of females. As the number of glomeruli is independent of kidney growth, it may be assumed that kidneys of female rats contain more glomeruli per mm^3 of renal tissue than do kidneys of male animals. This assumption agrees with an observation published by Arataki in 1926

(4). That the renin concentration in adult male rats is lower than that in females indicates the amount of renin in the individual

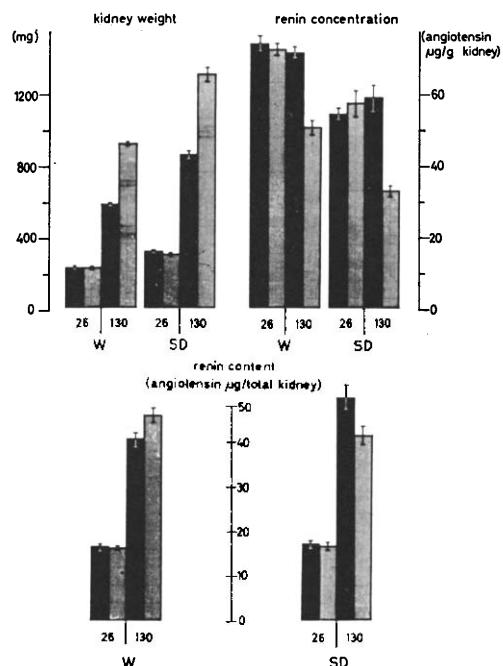


FIG. 1. Kidney weight (mg), renin concentration, and total renin content per kidney (μ g of angiotensin II) in female (black columns), and male (grey columns) rats of 26 and 130 days of age; W = Wistar strain, SD = Sprague-Dawley strain; vertical bars indicate SEM.

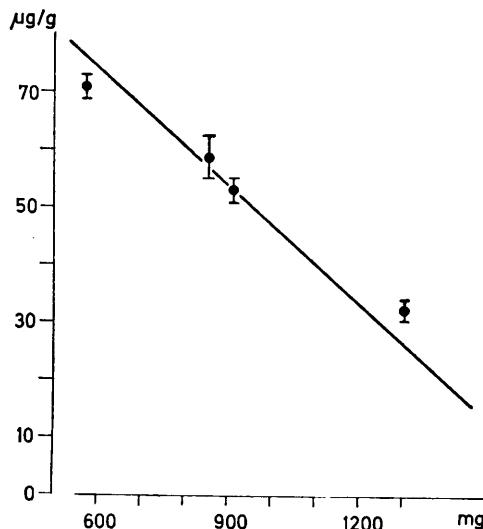


FIG. 2. Correlation between kidney weight (mg) (abscissa) and renin concentration (μg of angiotensin/g of kidney) (ordinate) for kidneys of adult male and female Wistar and Sprague-Dawley rats.

glomerulus is similar in both sexes to that in young animals. The larger kidney of male rats may depend on the "renotrophic" effect of the male hormone, which obviously does not affect the glomerular system and the production of renin in the juxtaglomerular cells.

The observed strain differences in renin concentration indicate that the larger kidneys of Sprague-Dawley rats do not contain more glomeruli than the kidneys of Wistar rats, and that the renin content of the glomeruli is of a similar order in the animals of both strains. The total renin content might differ slightly, however, since kidneys of adult female Sprague-Dawley rats contain little more

renin than those of female Wistar rats.

The results obtained show that to determine the renin content of kidneys one should take into account age, sex, and strain of the rat. Whether the differences observed in renal renin concentration affect the responses to various procedures that influence release, production, or storage of renin within the kidney remains to be investigated.

Summary. The body weight, kidney weight, renin content, and renin concentration of kidneys were determined in juvenile and adult male and female rats of the Wistar and the Sprague-Dawley strains. In juvenile rats, there was no sex difference in the various parameters; a strain difference was noted, however, as body and kidney weights were smaller and renin concentration higher in Wistar than in Sprague-Dawley rats. In adult animals a sex difference was observed, male rats of both strains having a higher body and kidney weight than females. Renin concentration in males was generally lower than in females. A negative correlation between kidney weight and renin concentration was found in adult rats, independent of sex and strain. It is concluded that renin stores in the glomeruli of males and females are similar in both sexes and strains.

1. Gross, F., Brunner, H., and Ziegler, M., *Recent Progr. Hormone Res.* **21**, 119 (1965).
2. Fisher, E. R., Tamura, M., and Masson, G. M. C., *Proc. Soc. Exptl. Biol. Med.* **118**, 1191 (1965).
3. Fisher, E. R. and Klein, H. Z., *Proc. Soc. Exptl. Biol. Med.* **121**, 142 (1966).
4. Arataki, M., *Am. J. Anat.* **36**, 399 (1962).

Received July 10, 1969. P.S.E.B.M., 1969, Vol. 132.