

Regulation of Superficial Single Nephron Glomerular Filtration Rates in Infant Rats¹ (36136)

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The development of renal function is a problem which has been receiving increased attention during the past several years. In experimental studies, primary attention has been paid to qualitative aspects of developmental problems and to the sequence of developmental changes [see (2-5) for examples]. Little attempt is being made, however, to differentiate what factors control development of renal function. As an end in itself, and in addition to obtaining base line data for future work, we report on the role of food availability in the regulation of single nephron glomerular filtration rate (SNGFR).

Materials and Methods. Untreated pregnant female rats were obtained either from commercial sources, or from the breeding colony at this institution (UNM). The specific question to be asked was whether animal age, animal size, or kidney weight was related to the control of SNGFR. To provide variation, therefore, in size and weight, litters were either left intact (8 to 16) or reduced to 4 or 6 animals after a suckling period of 5 days. In this way, increased food availability was presented which allowed for a more rapid growth of the animals in litters which were reduced in number.

Micropuncture experiments were done when the animals were between 15 and 33 days old. It has been our experience that the experimental kidney would show sluggish function unless the stomach and gut were empty. Fifteen- to 23-day-old rats were there-

fore removed from the mothers about 3 hr before starting the experiment and were placed in a warm room held at 34°. Thirty- to 33-day-old rats were removed 6 to 7 hr before experimentation. At the time of removal from the mothers, the animals were weighed. If, at the time of anesthetization, the animals had lost more than 1 g of body weight, an equivalent amount of water was administered by stomach tube.

The rats were anesthetized with Inactin (14 mg/100 g of body wt). A catheter was inserted into a jugular vein and an infusion of Ringers solution containing 100 or 200 μ Ci of ³H-inulin/ml was administered at a rate of 0.5 ml/hr. Approximately 90 min after the start of the infusion, the left kidney was prepared for micropuncture, using methods already described for this laboratory (6). No sooner than 2 hr after the start of equilibration, collection of samples was started and continued for approximately 90 min. In no case was an animal used 4 hr after the start of anesthesia. It was, in fact, difficult to use such animals since it has been observed that kidney function became labile at this time. The kidney would blanch sporadically, and tubules would close and open in an unpredictable manner.

Tail blood samples, collected in hematocrit tubes, were obtained just before the start of micropuncture collection and approximately every 30 min thereafter.

It was found that, very often, some negative pressure was required to maintain a steady collection as contrasted to how one makes a collection in adult rats (7). It is suspected that the extra pressure is required to overcome the resistance of the smaller orifice of pipettes used in these studies (7.5-9 μ vs 9-12 μ used in adult rats). In all experiments, technical adequacy of the collection

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procedure was established by meeting criteria previously established in this laboratory. These are as follows: (a) The blocking oil drop was at least five tubular diameters in length. (b) Tubular fluid could be collected into the pipette within a maximum of 15 sec. (c) The collecting pipette filled spontaneously, after the first or second aspiration of fluid to get the collection started (7). (d) Small changes in collection pressure produced corresponding small changes in oil droplet position. (e) Diameter of the tubule did not appear to change in going from prepuncture to collecting conditions (8). This latter criterion was met subjectively by comparing luminal to pipette diameters.

Results. The relationship between age alone and SNGFR was first examined independent of feeding conditions. The results of all micropuncture studies are shown in Fig. 1, wherein SNGFR is plotted as a function of age. In one animal which was 33 days old, it was found at autopsy that the animal had very heavily consolidated lungs. SNGFR was low in this animal. These data are excluded from consideration. The remaining points show 51 data from 9 rats from intact litters, and 101 data from 19 rats from reduced

litters. Although a trend between age and SNGFR can be seen, the relationship is not as well defined as one might expect even for data obtained by micropuncture.

In Fig. 2a and b, SNGFR has been re-plotted as a function of kidney weight and body weights. To allow for identification of the age of each animal in Figs. 1 and 2, Table I shows the age, body weight, and kidney weight of each animal used. The fact that reduction of litter size did result in increased growth is readily seen. Some 20-day-old animals from reduced litters are even larger than 30-day-old animals from the intact litters. The relationship between SNGFR and both kidney weight and body weight is readily apparent. Table II shows the least squares analysis of the regression between SNGFR and kidney weight as well as body weight. This analysis emphasizes several points. The slope of the relationship between SNGFR and kidney weight is less in animals from intact litters than from reduced litters. In fact, the low r value indicates a probability greater than .05 that the slope is no different than zero for this set of data. Although a similar trend is seen for the relationship between SNGFR and body weights, the larger

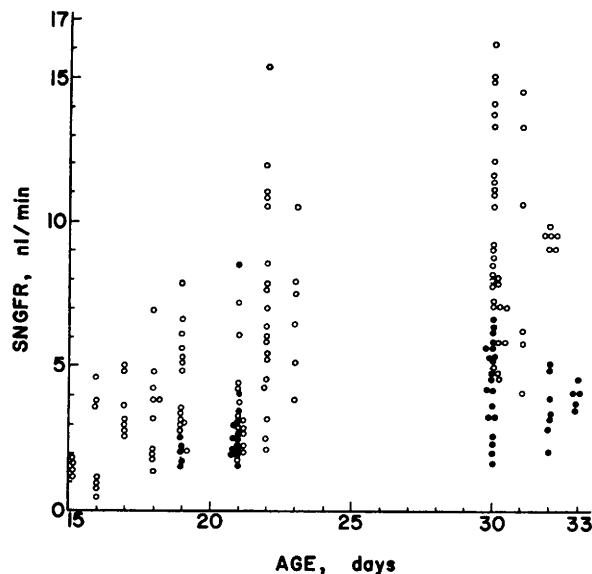


FIG. 1. Relationship between SNGFR and animal age: Each point represents a single determination; (●) data obtained using animals from reduced litters; (○) data obtained using animals from intact litters.

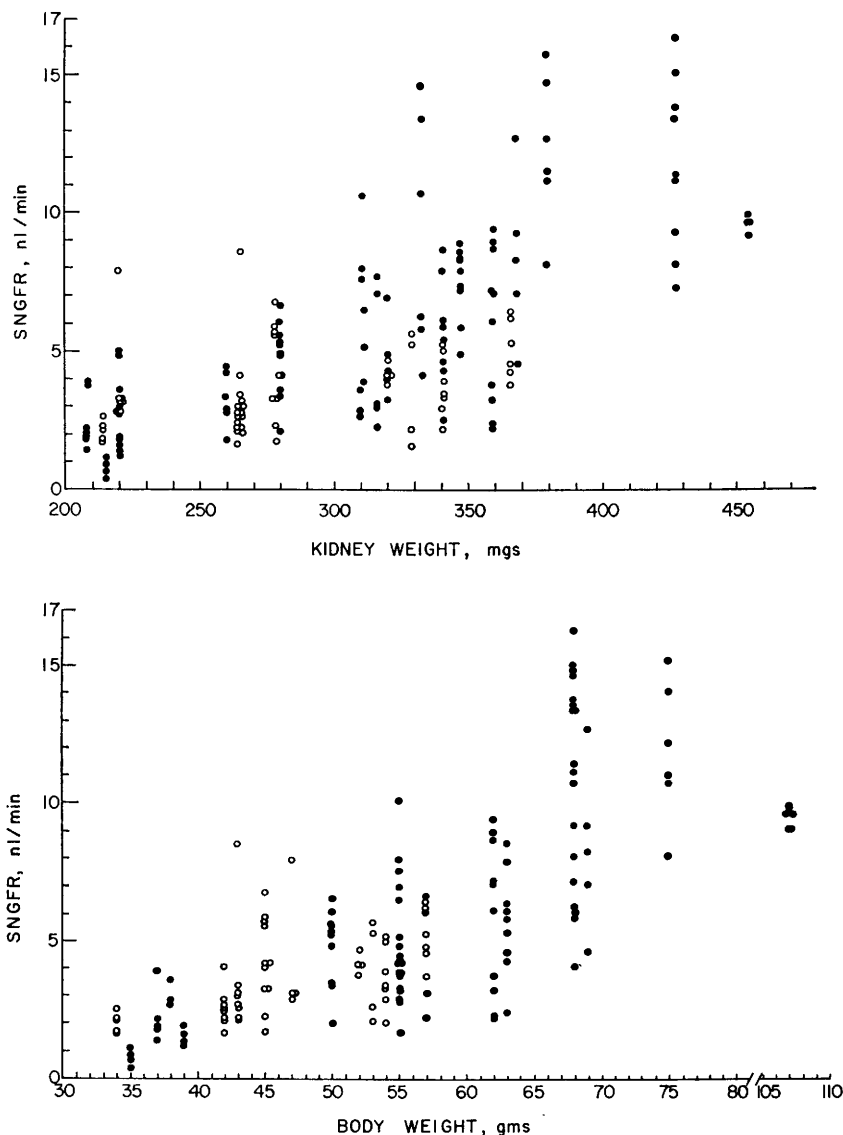


FIG. 2a (top). Relationship between SNGFR and kidney weight: Symbolism is the same as in Fig. 1. (b) (bottom). Relationship between SNGFR and body weight.

slope from reduced litters is not statistically different from that of the intact litters.

Discussion. These studies indicate that age is not the sole determinant of the rate of development of at least one renal function, SNGFR. Increased food availability (which results in increased food intake and growth) is shown to be a determining factor on the rate of development of SNGFR.

The data obtained in these young animals are consistent with the view that young rats

have a relatively high SNGFR. The least squares solution of the relation between SNGFR and body weight shows a slope of 8.71×10^{-2} for intact litters and 14.7×10^{-2} for reduced litters. In studies in this laboratory of mature animals, *i.e.*, larger than 175 g, the corresponding slope was found to be 1.05×10^{-2} (Solomon, unpublished). These data also suggest that over a wider range of animal weights, the use of a linear function between SNGFR and body weight would not

TABLE I. Relationship Between Age, Body Weight, and Kidney Weight of Experimental Animals from Intact and Reduced Litters.

Age (days)	Body wt (g)	Kidney wt (mg)
a. Intact litters		
19	34	213
19	47	220
21	42	264
21	43	265
30	45	278
30	53	329
30	57	366
32	54	340
33	53	320
b. Reduced litters		
15	39	220
16	35	216
16	38	310
17	39	220
18	37	208
18	55	320
19	50	280
21	55	276
21	62	358
22	57	316
22	63	341
23	55	312
30	60	347
30	68	428
30	69	368
30	75	380
31	68	333
32	107	460
32	107	460

have found that SNGFR is related to the length of the proximal tubules in a variety of rodents. It is unlikely that this relationship holds for the two conditions used in this study. SNGFR per milligram of kidney weight is higher in animals from reduced litters compared to those from intact litters. The difference is reduced when SNGFR is related to body weight. If growth, then, of the kidney still primarily reflects an increase in proximal tubular length, one would conclude from these studies that the relationship of SNGFR to proximal tubular length is higher in animals from intact litters. It would, therefore, seem that increased food availability leads to increased animal growth, which in turn may trigger increased kidney growth. Although the kidney shares in the growth response, when food availability is increased it seems to lag when compared to animals on limited food availability.

Summary. The rate of growth of infant rats has been varied by increasing food availability to selected litters. Within the two different populations of infant rats, slow growing versus fast growing, superficial single nephron GFR has little relationship to animal age. Rather, SNGFR is related both to body size and kidney weight. A somewhat better relationship between SNGFR and kidney weight has been found. Fast growing rats show a greater ratio of SNGFR to kidney

TABLE II. Analysis of Relation of SNGFR to Kidney Weight and Body Weight.

	Intact litters		Reduced litters	
	Kidney wt	Body wt	Kidney wt	Body wt
Intercept ^a	1.189	-0.434	-6.819	-2.124
Slope \pm SE ($\times 10^{-2}$) ^a	0.840 \pm 0.547	8.71 \pm 3.58	4.10 \pm 0.421	14.7 \pm 1.99
r	.215	.329	.723	.621

^a Dimensions of kidney wt and body wt are mg and g, respectively; slopes are given in nl/min/unit wt.

be a good approximation. At present, adequate studies allowing for a comparison based on kidney weight do not exist. The growth of the kidney, however, is probably, at least in part, a reflection of increased length of proximal tubule (9).

Recently, Baines and DeRouffignac (10)

weight than do slow growing rats.

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