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Compensatory adaptation of structure and function following progressive renal ablation

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Compensatory adaptation of structure and function following renal ablation. A systematic evaluation of the structural and functional changes following progressive renal ablation was performed in the rat. During a four-week interval following surgery, renal mass increased 31% in control animals (group A), 81% in uninephrectomized rats (group B) and 168% in animals subjected to approximately 70 to 75% ablation (group C). Mean nephron glomerular filtration rate (MNGFR) was estimated from the clearance of inulin (C_{in}) of the remaining renal tissue and total glomerular counts four weeks after surgery. The MNGFR rose from 47 nl/min in group A, to 76 nl/min in group B and 112 nl/min in group C with surgically induced renal insufficiency. These data indicate that the adaptive changes in structure and function which occur following segmental loss of renal tissue are proportional to the mass of tissue which is removed.

Compensation adaptative de la structure et de la fonction après ablation rénale. Une évaluation systématique des modifications structurales et fonctionnelles survenant après ablation rénale croissante chez le rat a été faite. Dans un délai de quatre semaines après l'intervention la masse rénale augmente de 31% chez les animaux témoins (groupe A), de 81% chez les rats uninéphrectomisés (groupe B) et de 168% chez les animaux soumis à une ablation d'environ 70 à 75% (groupe C). La filtration glomérulaire moyenne par néphron (MNGFR) a été évaluée à partir de la clearance de l'inuline du tissu rénal restant et de la numération des glomérules 4 semaines après l'intervention. Cette filtration glomérulaire passe de 47 nl/min dans le groupe A à 76 nl/min dans le groupe B et à 112 nl/min dans le groupe C atteint d'insuffisance rénale induite chirurgicalement. Ces résultats indiquent que les modifications adaptatives de la structure et de la fonction qui surviennent après la perte d'un fragment de tissu rénal sont proportionnelles à la masse de tissu enlevée.

Following the reduction of renal mass, remarkable adaptive changes result in an increase in size and function of the remaining tissue. Previous studies have shown that after 50% renal ablation by unilateral nephrectomy, the intact kidney rapidly grows and exceeds the weight of a control kidney by approximately 40% within three to four weeks [1], while glomerular filtration rate (GFR) for the whole kidney and superficial nephrons increases by 65 to 75% [1–3].

However, it is not clear whether compensatory changes increase progressively in proportion to the amount of tissue surgically removed or destroyed by disease. This correlation has important implications in understanding the adaptive response which occurs in renal insufficiency. In the present study a systematic evaluation of the structural and functional changes following progressive renal ablation was performed. The data indicate that adaptive changes are closely linked to the amount of tissue removed and demonstrate no limit to the growth or functional response.

Methods

Experiments were performed on male Sprague-Dawley rats (Charles River Breeding Laboratories, Wilmington, MA). Three groups were prepared under ether anesthesia. Group A served as controls and a sham operation was performed on the left kidney. Group B animals underwent left nephrectomy. In group C approximately 70 to 75% of total renal tissue was ablated by excising the upper and lower poles of the left kidney and removing the right kidney 12 to 18 hr later. Special care was taken to prevent damage to the adrenal glands. Partial nephrectomy was performed by tightening a pursestring suture around the poles to control bleeding and excising the tissue beyond the suture. The protocol used in the surgical preparation of these groups is shown in Fig. 1.

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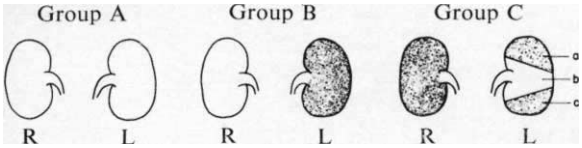

Fig. 1. *Surgical protocol employed in groups A, B and C. Shaded areas* represent tissues ablated at day 1 to 2.

Immediately following operation the excised renal tissue was weighed in tared bottles to determine wet weight.

At the time of surgery, three rats weighing within 5 g of each other were allocated to each of the three groups. The initial body wt was 243 ± 7 g (mean ± SEM), and ranged from 150 to 350 g. Following operation animals in groups A and B were pair-fed against the group C rat of each threesome during the remaining period of study in order to maintain a similar dietary intake. Standard laboratory chow (Purina) pellets were ground to facilitate accurate weighing, and contained 23% protein. Chemical analysis of nitric acid digests of this food showed a sodium concentration of 17.2 mEq/100 g and a potassium concentration of 24.3 mEq/100 g. The adequacy of this method to provide a constant caloric intake was demonstrated by a similar increase in weight gain and final body wt among the animals in each set of three (Table 1). This measure was introduced since preliminary experiments in our laboratory and in others [4] have shown a close correlation between kidney and body wt and between the rate of gain of body wt and caloric intake of the animal.

Four weeks later animals were anesthetized with Inactin (Promonta, Hamburg) (120 to 160 mg kg), tracheostomy was performed and polythylene catheters were secured into the external jugular vein and bladder for the administration of solutions and collection of urine, respectively. Following the administration of isotonic saline equal to 1% of body wt, a priming dose of 10 μCi of inulin-methoxy-^{3}H (New England Nuclear Corp.) was given, followed by a sustaining dose of 10 μCi in a volume of 1.2 ml/hr. Inulin clearance was determined by the average of four ten-minute urine collections and blood samples obtained from the tail at the midpoint of each collection. The concentration of inulin-methoxy-^{3}H was measured in a liquid scintillation counter (Tri-Carb). At the termination of the final urine collection, 2 ml of blood was collected for measurement of blood urea nitrogen (BUN) concentration. In addition, rats were randomly selected from each of the three groups for the determination of total glomerular counting. In these animals, 1 ml of India Ink (Gunther Wagner C11 1432 A) was slowly injected into the left carotid artery as a marker for glomerular counting. Mean whole kidney GFR and GFR/100 g of body wt was not different in animals selected for glomerular counting, compared to their respective groups. Studies performed in six animals during the slow injection of ink showed that mean aortic blood pressure remained stable while kidney tissue became grossly discolored. After the animal was killed, kidneys were decapsulated, extraneous fibrous tissue was excised from the remnant in group C rats, wet kidney wt was determined and kidneys were fixed in 10% formaldehyde solution. Random kidneys were selected from group C for the histological examination of sections cut at four micra and stained with hematoxylin-eosin. There was no evidence of interstitial fibrosis, glomerular obsolescence or tubular atrophy. Minimal amounts of scar tissue were present at the edges of these kidneys trimmed for weighing.

The initial weight of excised kidney tissue was known

Table 1. Summary of changes in renal function and mass[a]

	Group A (N=26)	Group B (N=26)	Group C (N=26)
BUN, *mg/100 ml*	20.8±0.9	26.3±0.9[b]	71.2±7.0[c]
Increase in body wt, *g*	70.4±8.4	79.7±8.0	71.5±8.4
Increase in kidney wt, %	30.5±4.1	80.6±7.1[b]	167.5±11.0[c]
Increase in kidney wt, *g*	0.54±0.06[d]	0.79±0.07[b]	0.94±0.05[b]
C_{in}, *μl/min*	3447±112	2651±132[b]	1105±131[c]
C_{in}, *μl/min/100 g of body wt*	1060±41	801±36[b]	340±36[c]
C_{in}, *μl/min/g of kidney wt*	1290±53	1473±62[e]	734±69[c]

[a] Values are mean ± SEM. BUN, blood urea nitrogen concentration; C_{in}, clearance of inulin.
[b] $P<0.001$ compared to group A.
[c] $P<0.001$ compared to groups A and B.
[d] Total for both kidneys.
[e] $P<0.05$ compared to group A.

for groups B and C rats. To determine the rate of change of wet kidney wt during the four-week interval between surgery and the final clearance studies for group A rats, the weight of tissue in the animal at the initiation of the study had to be estimated. In these calculations it was assumed that the weight of the right and left kidney in the same animal was approximately equal and that kidney wts were approximately equal between different animals of similar body wt. Based on these two assumptions, the initial renal mass estimated to be remaining in the animal following surgery was calculated in the following way:

$$\textit{Group C:}\ \mathrm{CLb} = \mathrm{CR} - (\mathrm{CLa} + \mathrm{CLc}),$$
$$\textit{Group B:}\ \mathrm{BR} = \mathrm{BL},$$
$$\textit{Group A:}\ \mathrm{AR} = \mathrm{AL} = (\mathrm{BL} + \mathrm{CR}) \div 2.$$

The meaning of the symbols used in these formulae is shown in Fig. 1. By these calculations, total ablation averaged $71.9 \pm 1.0\%$ (mean ± SEM) (with a range of 58 to 82%) for group C, so that 28.1% of initial renal mass remained following surgery.

The rate of change in weight (% growth) of AR, AL, BR and CLb was determined from the calculated initial and measured final weights.

In order to measure the total number of glomeruli present in the kidneys or kidney remnant, we used a modification of the method described by Damadian, Shwayri and Bricker [5]. The formaldehyde-fixed specimens were macerated in 25% HCl for 19 hr at 50°C. Preliminary studies had shown that this period of time was necessary for satisfactory maceration of fixed tissue, in contrast to a shorter time interval for fresh specimens. The digest was diluted in distilled water to a final volume of 20 ml and stirred mechanically while ten aliquots were drawn into 50-μl pipettes from different levels of the solution. The total number of glomeruli in each aliquot was counted under a dissecting microscope (magnification, ×40). The sum of all glomeruli counted, multiplied by the appropriate dilution factor, was used to calculate the number of glomeruli in the original specimen. The coefficient of variance (SD/mean × 100) for counting ten aliquots from each specimen averaged 10.8 ± 0.8 in 29 determinations in this study and 10.4 ± 0.5 in 31 determinations in a separate group of kidney samples not included in this report. This small variation indicates adequate precision in counting. Further, statistical analysis of the data showed that mixing was adequate as evidenced by the means and variances of the glomerular counts fitting a Poisson distribution. Mean nephron glomerular filtration rate (MNGFR) was calculated as the quotient of the average inulin clearance (C_{in}) and total glomerular count for individual animals. The concentration of BUN was determined by the Autoanalyzer method [6]. Values expressed represent the mean ± SEM. Student's t test was used for statistical comparison unless otherwise noted.

Results

To determine whether the basic assumptions regarding similarity of kidney wts in the same animal and between different animals of approximately equal body wt were valid, the relationship between kidney wt and body wt was studied in 105 normal rats weighing from 150 to 450 g. The regression line ± SD is shown in Fig. 2 and illustrates a different relationship for animals weighing less than 150 g. Since the initial body wt of all animals used in this study was over 150 g and varied by 5 g or less in any set of three rats, the high coefficient of correlation ($r = 0.82$, $P < 0.001$) suggests that for a given body wt kidney mass can be accurately estimated. Moreover, when the right and left kidneys of the same animals were compared, a difference of only 2.4% was found, the right kidney being heavier. Although this difference was statistically significant by paired analysis ($P < 0.001$), the relative difference for the purpose of estimating initial kidney wt was small. In 60 rats allocated to either group B or group C, wet weights of BL and CR were compared, and a difference of only 3.6% was found, a value not statistically significant ($P > 0.10$). It seems reasonable, therefore, that the calculations described provide an accurate estimate of the weight remaining after initial surgery.

The mean GFR as the absolute value and factored

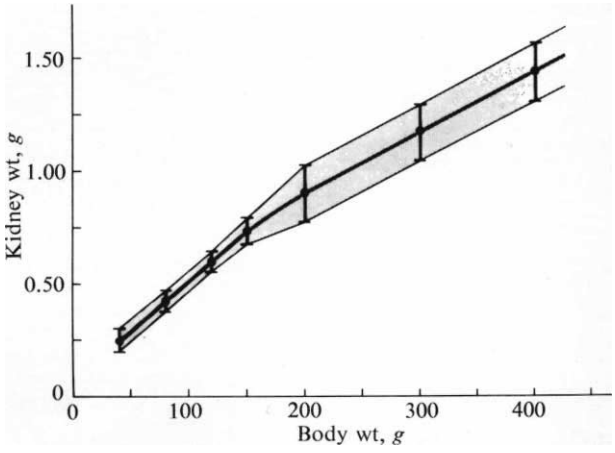

Fig. 2. *Relation of kidney wt and body wt for male Sprague-Dawley rats.* For rats weighing more than 150 g, kidney wt = 0.358 + 0.0027 body wt ($r = 0.82$, $P < 0.001$, $N = 313$). For rats weighing less than 150 g, kidney wt = 0.069 + 0.004 body wt ($r = 0.96$, $P < 0.001$, $N = 83$). These slopes are significantly different ($P < 0.005$). The *shaded area* represents the mean ± 1 SD of kidney wt in relationship to body wt.

by body wt and kidney wt for each group of animals is shown in Table 1. C_{in} was 1060 ± 41 μl min 100 g of body wt in group A and 801 ± 36 in group B. Therefore, as a result of compensatory changes, the whole animal GFR was 76% of control in animals with 50% ablation of renal tissue. A marked reduction in GFR was found in group C animals and averaged 340 ± 36 μl/min/100 g of body wt, 32% of control value. A BUN value at the termination of the study reflected the changes in renal function and averaged, in mg/100 ml, 20.8 ± 0.9, group A; 26.3 ± 0.9, group B; and 71.2 ± 7.0, group C. Renal insufficiency in group C animals was not associated with a metabolic acidosis since, in an additional group of five rats with an average GFR of 382 ± 32 μl/min/100 g of body wt, the arterial blood pH was 7.40 ± 0.02 as compared to 7.43 ± 0.03 in six control (group A) animals. Despite these marked differences in renal function, the rate of gain in body wt in the interval following surgery was not significantly different among the three groups ($P > 0.50$) and averaged 74 g. When C_{in} is expressed per gram of kidney wt, the average value in group B was 1473 ± 62, 14% greater than the control value of 1290 ± 53 ($P < 0.05$), suggesting that compensatory increase in filtration rate was greater than the increase in mass, as previously reported [1]. In contrast, C_{in} was only 734 ± 69 μl/min/g of kidney wt in group C (57% of control, $P < 0.001$). The relatively lower C_{in} per unit of wet weight tissue probably reflects the reduced glomerular density in the remnant kidney, as discussed in the following.

Progressive ablation of renal tissue resulted in a proportional increase in rate of tissue growth, as shown in Table 1 and Figs. 3 and 4. Kidney wt rose 30.5 ± 4.1% in control, sham-operated rats, while an 80.6 ± 7.1% increase occurred in group B animals, following uninephrectomy ($P < 0.001$). Therefore, compensatory changes, due to removal of one-half of renal mass, accounted for approximately 50% greater rate of growth. The hypertrophied right kidney in group B, four weeks after surgery, weighed 37.2 ± 4.9% more than the right kidney of control animals (BR/AR) ($P < 0.001$), a value which corresponds to earlier reported values [1]. In group C, with ablation of an average of 72% of kidney mass, a marked increase in renal mass of 167.5 ± 11.0% occurred ($P < 0.001$ compared to groups A and B), representing nearly 140% increase over control growth. Since each group C animal had varying amounts of tissue removed (range, 58 to 82% ablation of total renal mass), an attempt was made to correlate compensatory response with calculated renal ablation. It can be seen (Fig. 4) that a highly significant correlation exists between percent of ablation and increase in renal mass. In making statistical comparison of the increase in renal mass among the three groups, kidney wt was also computed on the log scale to reflect the relative increase in kidney wt, and, with this computation, $P < 0.001$ for comparisons of groups B and C with group A and for group C with group B was found.

The absolute increase in wet kidney wt among the three groups was also compared. In control rats the

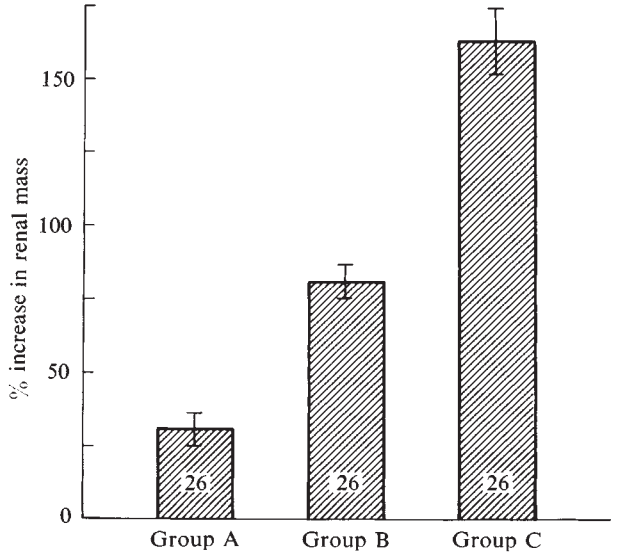

Fig. 3. *Compensatory renal hypertrophy.* Percent increase in kidney mass four weeks following surgery for group A (control), group B (50% nephrectomy) and group C (75% nephrectomy). *Bars* represent mean ± SEM. Number of observations made in each group is shown in *insert on bar.*

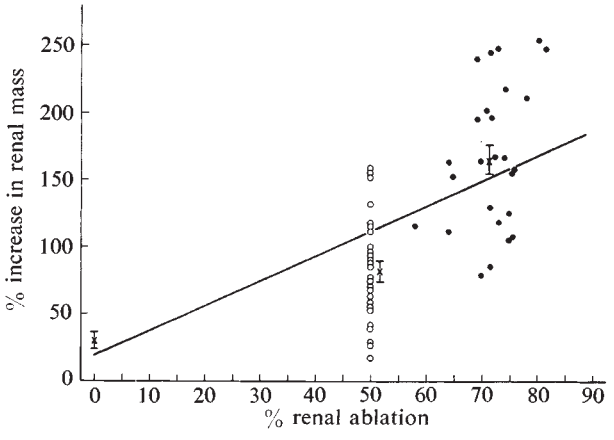

Fig. 4. *Correlation of percent increase in renal mass (I) with percent renal ablation (A) for all group A, B and C rats in this study.* The equation $I = 20.211 + 1.757$ A shows a highly significant correlation ($r = 0.77$, $P < 0.001$). The individual data points for group B animals are represented by *open circles* and those for group C, by *closed circles.* The mean for each group is shown by an X with SEM also shown.

Table 2. Total number of glomeruli and calculated mean nephron glomerular filtration rate (MNGFR)

Group No.	Group A				Group B		Group C	
	Left kidney	Right kidney	Total	MNGFR *nl/min*	Right kidney	MNGFR *nl/min*	Remnant kidney	MNGFR *nl/min*
10	34,040	34,440	68,480	54.0	30,120	114.6	11,040	77.7
11	35,760	39,280	75,040	43.7	39,280	66.7	8,320	139.0
12	33,960	39,960	73,920	56.6	37,600	73.4	8,600	155.0
17	45,480	32,320	77,800	52.2	—	—	5,500	133.8
18	37,320	32,480	69,800	49.9	35,480	55.5	10,720	85.0
19	37,480	39,760	77,240	51.3	35,880	93.9	14,920	116.1
21	41,120	42,400	83,520	37.8	43,960	57.1	25,800	118.7
24	—	—	—	—	43,840	85.0	—	—
25	43,480	44,460	88,120	37.6	—	—	11,880	102.4
29	37,880	33,320	71,200	49.5	35,720	77.7	4,160	99.0
30	32,080	33,560	65,640	40.2	36,360	59.1	5,560	89.5
Mean	37,860	37,216	75,076	47.3	37,582	75.9	10,650	111.6
± SEM	1,368	1,426	2,187	2.2	1,447	6.5	1,982	8.0
P compared to group A						< 0.001		< 0.001
P compared to group B								< 0.005

two kidneys increased by 0.54 ± 0.06 g while the remaining kidney in the uninephrectomized animal rose 0.79 ± 0.07 g ($P < 0.001$). In group C the kidney remnant increased 0.94 ± 0.05 g, an amount greater than the increase in the single kidney in group B, although the difference was not significant ($P > 0.10$). The absolute increase in renal mass was significantly greater in the group C remnant than in both kidneys combined in group A animals ($P < 0.001$).

There were $75{,}076 \pm 2187$ glomeruli in control animals, or approximately 37,500/kidney (Table 2). The number of glomeruli in the remaining kidney following uninephrectomy ($37{,}582 \pm 1447$) was virtually identical. In group C rats, an average of $10{,}650 \pm 1982$ glomeruli was found, less than 30% of control single kidney values. The reduced number of glomeruli relative to the amount of tissue ablated in group C reflects the increased density of glomeruli in the predominantly cortical tissue removed from upper and lower poles and may explain the low C_{in}/g of kidney wt observed in group C. To establish this point, eight animals were injected with India ink and resection comparable to group C was performed, i.e., left upper and lower pole and right nephrectomy. The calculated total ablation averaged 73.2% in these eight rats as compared to 71.9% in group C animals. The glomerular density (glomeruli/g of kidney wt) was nearly twice as great in the combined resected upper and lower poles ($55{,}768 \pm 1511$) as in the remnant ($29{,}799 \pm 1305$) ($P < 0.001$).[1] Furthermore, the number of glomeruli in the remnant portion in these eight animals was not significantly different from the number counted in the group C remnant kidney ($P > 0.10$).

MNGFR increased in a manner that was similar to the change in renal mass (Fig. 5). Nephron filtration rate rose from 47.3 ± 2.2 nl/min in control rats to 75.9 ± 6.5 nl/min in the hypertrophied kidney of group B animals ($P < 0.001$). The changes found in the remnant kidney in group C were striking where MNGFR averaged 111.6 ± 8.0 nl/min ($P < 0.005$ compared to group B). These data indicate a 60% increase in MNGFR in the uninephrectomized rat and 136% increase following approximately 70 to 75% renal ablation compared to control values. The MNGFR in group C rats was 47% more than that in group B.

Discussion

Adaptive renal changes which occur following the partial loss of total nephron mass are well known and include an increase in mass of the remaining tissue and a rise in filtration rate per nephron. Most previous studies of compensatory growth have utilized the model of unilateral nephrectomy, in which the remaining kidney increases in size sufficient to exceed the weight of a control kidney by approximately 40% [1]. In these studies, however, which compared the ratio of the final weight of the experimental to that of the

[1] An average of 0.414 ± 0.014 g was excised from the upper and lower pole of each kidney and contained $22{,}980 \pm 746$ glomeruli. The remnant portion of the same kidneys weighed 0.484 ± 0.031 g and contained $14{,}270 \pm 775$ glomeruli. The total glomerular count, therefore, in the poles plus remnant averaged $37{,}250 \pm 964$, a value not different than in control kidneys from group A animals.

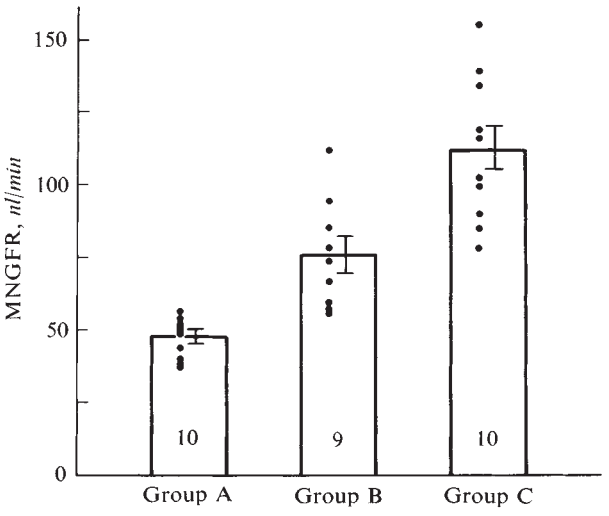

Fig. 5. *Mean nephron glomerular filtration rate (MNGFR) in groups A, B and C. Bars* represent mean ± SEM. Individual observations made in each group are represented by *closed circles.*

control kidney, the rates of growth were not estimated. Whole kidney GFR and superficial nephron GFR have been shown to rise 65 to 75% [1–3], so that the final GFR is approximately 80% of the expected normal value. Moreover, these changes occur rapidly after surgery and apparently reach maximum levels within about four weeks.

The extent to which remaining nephrons can compensate for a reduction in their number after more extensive losses has been less well studied because of the difficulty in quantifying the amount of renal mass removed and in providing appropriate controls. However, in dogs subjected to five-sixths nephrectomy, C_{in} was not reduced in proportion to the amount of tissue removed, suggesting an adaptive increase in function [7]. Platt, Roscoe and Smith demonstrated that after surgical ablation of an estimated 80% of renal tissue in the rat, the weight of the renal remnant approached 50% of the normal weight of the two kidneys and creatinine clearance nearly reached normal levels [8]. Using a similar animal model, Morrison and Howard [9] examined C_{in} before and after removal of approximately 75% of renal mass. In a small number of animals glomerular counts were made, by the method of Kunkel [10], allowing an estimation of MNGFR. Their data showed that MNGFR was more than twice as great in the partially nephrectomized rat as in the control. Although these studies clearly indicate that compensatory changes in mass and function occur after extensive surgical ablation, as in animals subjected to unilateral nephrectomy, it is not possible to correlate either index with the amount of tissue removed. The present experiments were, therefore, designed so that the rate of growth and alterations in nephron function of the normal kidney and remaining tissue following progressive surgical ablation could be compared quantitatively.

Results of the present study demonstrated a striking and progressive increase in renal mass and MNGFR that was directly proportional to the amount of tissue removed. While kidney wt in controls increased 31% in the four-week interval after surgery, renal mass rose 81% and nearly 170% in rats with 50 and 75% surgical ablation, respectively. Subtracting the rate of control growth, increments of 50 and 140% occurred in the two experimental groups, which were due to compensatory changes. When calculated in terms of absolute mass, the increment of 0.94 g found in the remnant kidney was as great as that found in the whole remaining kidney after unilateral nephrectomy, 0.79 g. The change in renal mass observed in these experiments does not necessarily reflect the growth in individual nephron segments. For example, in a previous study in which the volume of the proximal and distal convoluted tubule was measured in normal rats and compared to values in the hypertrophied kidney of uninephrectomized rats, differences were found in the two segments [2]. The greatest increment was found in the proximal tubule which increased in proportion to the change in filtration rate, while volume in the distal tubule increased only one-half as much. A report by Oliver [11] also demonstrated a disproportionate increase in the volume of the proximal tubule, as compared to other segments, in rats with three-quarter nephrectomy.

In these experiments the use of paired-feeding has special significance. Previous reports [4] and other experiments in our laboratory (unpublished) have shown that nitrogen and caloric intake have an important influence on the rate of normal and compensatory growth. Other reports of compensatory growth and function in 70 to 80% ablated animals do not mention this important factor. Since group C animals have reduced food intake for one to two weeks after surgery, the difference in renal growth among the three groups may have been obscured had group A and B animals not been fed according to the consumption of their group C mate.

In association with changes in renal growth, there was striking and progressive increase in MNGFR which occurred in direct proportion to the extent of ablation. The average value of 47.3 nl/min in control animals rose 60% to 75.9 following uninephrectomy and approximately 130% to 112 after ablation of three-fourths of renal mass. It seems very likely that values found in group C animals, with renal insufficiency, reflected the actual rates which occurred due

to compensatory changes since a close correspondence was found between single nephron glomerular filtration rate (SNGFR), measured by micropuncture analysis in superficial nephrons, and MNGFR measured by the quotient of C_{in} and the total glomerular count. In additional experiments designed to study the distribution of nephron filtration rate and the pattern of cortical blood flow in the remnant kidney (unpublished studies), the ratio of SNGFR (average of four measurements) and MNGFR was determined simultaneously in eight animals and averaged 1.00 ± 0.09. It is of interest that in the original description of the method used in these experiments for glomerular counting, Damadian et al [5] found that some glomeruli in regions of scarring were perfused but nonfiltering. Although progressive interstitial fibrosis and glomerular obsolescence has been described in the remnant kidney six to nine months after surgery [9], there was no evidence of a similar process in kidneys from group C animals four weeks after operation. While the possibility cannot be discounted that perperfused but nonfiltering glomeruli were included in our glomerular counts, this condition would have resulted in an underestimation of actual MNGFR. The difference between the high rates of nephron filtration rate found in this study and previously reported micropuncture values of SNGFR in animals with renal insufficiency [3, 12, 13] is unclear.

Previous workers have suggested that compensatory renal growth is due to an increase in renal work in the form of increased tubular reabsorption of sodium [14–17], or due to changes in the concentration of organ-specific humoral substances that control renal mass [18–20]. Recent work from this laboratory has demonstrated that reabsorptive work performed by the kidney is not a sufficient stimulus for compensatory growth. In those experiments a chronic increase in GFR and tubular reabsorption of sodium of approximately 30% was induced both by the administration of methylprednisolone [21] and by diversion of one ureter into the peritoneal cavity [22], without increasing renal mass. Taken together these data which fail to support the work hypertrophy theory and the presently demonstrated closely linked correlation between renal growth and extent of ablation are consistent with the theory that mass may be regulated, at least in part, by an organ-specific humoral substance.

The parallel and progressive adaptive increases in both renal mass and single nephron filtration, demonstrated in this study, have obvious clinical importance in relationship to surgical ablation of renal tissue. While these experiments demonstrate the marked capacity of adaptive nephron response, they do not imply that similar changes occur in all instances of renal insufficiency. For example, in renal insufficiency produced by experimental glomerulonephritis, Rocha, Marcondes and Malnic [23] recently showed that measured single nephron GFR values were reduced below normal and that they varied widely. Therefore, it seems likely that the magnitude of the compensatory renal response is dependent upon the amount of intact cortical tissue spared by the disease process.

Acknowledgments

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