Functional and Hemodynamic Adaptation to Progressive Renal Ablation

By Joel M. Kaufman, Norman J. Siegel, and John P. Hayslett

ABSTRACT

Removal of renal tissue stimulates functional and anatomical adaptation in the remaining renal parenchyma. Since recent studies have demonstrated no apparent limitation in compensatory growth following progressive surgical ablation, experiments were performed to determine the changes in glomerular filtration rate and renal blood flow. After removal of 50% of the renal mass mean nephron glomerular filtration rate increased 60%, and after ablation of 75% of the renal tissue it increased 150%. These changes paralleled the increases in renal growth under the same conditions. In comparison, mean glomerular blood flow rose 90% and 240% after 50% and 75% nephrectomy, respectively; these changes in relation to the changes in glomerular filtration rate resulted in a progressive fall in the filtration fraction. Intrarenal blood flow distribution was examined with labeled microspheres. The marked increase in renal blood flow after surgical ablation was characterized by a disproportionate rise in blood flow to the inner cortex. The present investigation, therefore, describes the remarkable functional changes that occur as overall glomerular filtration rate declines and provides further insight into the mechanism responsible for maintaining water and electrolyte homeostasis after loss of functioning renal mass.

KEY WORDS renal blood flow compensatory adaptation rat mean nephron blood flow mean nephron glomerular filtration rate

Remarkable compensatory changes in renal mass and function occur following surgical removal of renal tissue and after damage by some disease processes. Although most studies have examined the contralateral kidney after unilateral nephrectomy, recent experiments have demonstrated that the extent of compensatory renal adaptation correlates directly with the amount of renal tissue removed (1). Although adaptive changes in renal function are responsible for maintaining water and electrolyte homeostasis (2), the factors that control and influence such changes are not well understood. Therefore, the relationship between compensatory increases in glomerular filtration rate and renal hemodynamics following progressive ablation were studied.

Methods

Experiments were performed on male Sprague-Dawley rats (Charles River Breeding Laboratories) weighing 150-200 g at the beginning of the study. Three groups were prepared under ether anesthesia. Group A rats served as controls, and a sham operation was performed on their right kidneys. Group B rats underwent 50% ablation of the total renal mass by right nephrectomy. In group C, approximately 70-75% of the total renal mass was removed by right nephrectomy and upper and lower pole nephrectomy of the left kidney, using a method described previously (1). At the time of surgery, three rats weighing within 10 g of each other were allocated, one to each of the three groups. Following surgery, rats in groups A and B were pair-fed against the group C rat in each threesome during the remaining period of study to maintain a similar caloric intake. The contents of the diet and the importance of paired feeding have been described previously (1). After 3-4 weeks, each threesome was assigned to a specific study protocol.

Changes in glomerular filtration rate and renal blood flow were measured, and an estimate was made of the mean nephron glomerular filtration rate and the mean glomerular blood flow. Rats were anesthetized with Inaktin (Promonta, Hamburg) (80-100 mg/kg, ip). A tracheostomy was performed, and polyethylene catheters (PE50) were secured into the external jugular vein, the left carotid artery, and the bladder for the administration of solutions and the collection of urine. After replacement of surgical losses with isotonic saline (0.15 M NaCl) equal to 1% of the body weight, a priming dose of 10 μc of 3H-methoxy-inulin (New England Nuclear Corporation) was given, followed by a sustaining dose of 10 μc/hour in a volume of 1.2 ml. After a 45-minute equilibration period, inulin clearance was determined by the average of three 10-minute urine collections. Blood samples were obtained from the tail at the midpoint of each urine collection; at the termination of the final
urine collection, a blood sample (0.1 ml) was drawn from the left renal vein. The concentration of $^3$H-methoxy-inulin was determined using a Tri-Carb liquid scintillation counter. After completion of clearance periods, India ink (1 ml) was slowly injected as a marker for glomerular counting. In preliminary studies, blood pressure was shown to remain stable during blood withdrawal and India ink injection. After measuring wet kidney weight, the blackened kidney was fixed in 10% formaldehyde for glomerular counting by a modification of the method of Damadian et al. (3). The formaldehyde-fixed specimens were macerated for 19 hours in 25% HCl at 50°C. The digest was diluted in distilled water to a final volume of 20 ml and stirred mechanically while ten samples were drawn into 50-µliter pipettes from different levels of the solution. The total number of glomeruli in each sample was counted under a dissecting microscope, and the sum of all glomeruli counted multiplied by the appropriate dilution factor gave the number of glomeruli in the original specimen. This method has a coefficient of variation of 5.4%, and the glomerular counts fit a Poisson distribution (1).

The following formulas were used to estimate mean nephron glomerular filtration rate (MNGFR) and mean glomerular blood flow (MGBF).

\[
MNGFR = \frac{C_{in} \text{(µliters/min)}}{\text{total glomerular count}},
\]

\[
MGBF = \frac{\text{RBF (µliters/min)}}{\text{total glomerular count}},
\]

where \(C_{in}\) = inulin clearance and RBF = renal blood flow. The following formulas were used to calculate renal plasma flow and renal blood flow.

\[
E_{in} = \frac{A_{in} - V_{in}}{A_{in}},
\]

where \(E_{in}\) indicates inulin extraction, \(A_{in}\) indicates arterial inulin concentration, and \(V_{in}\) indicates renal vein inulin concentration. Consequently, renal plasma flow (RPF) can be expressed as

\[
RPF = \frac{C_{in}}{E_{in}},
\]

Total renal blood flow (RBF) is given by

\[
RBF = \frac{RPF}{1 - Hct},
\]

where Hct = hematocrit.

The distribution of intrarenal blood flow was evaluated using isotopically labeled microspheres. To compensate for changes in the contour and the volume of the kidney that occur during compensatory adaptation, microspheres with different isotopes were injected before and 4 weeks after surgical ablation. A previous study (4) has demonstrated that this method is reproducible, that the microspheres are removed in a single circulation, and that the initial injection does not alter glomerular filtration rate, renal blood flow, or the distribution of intrarenal blood flow. In all experiments, the microspheres (15 ± 2µ, 3M Corporation) were diluted with normal saline to a final concentration of 60,000/0.1 ml, and one drop of Tween 80 was added. Immediately before injection, each sample was mixed for 1-2 minutes by an ultrasonic dismembranator (Artek Systems GRP).

Rats were anesthetized with sodium pentobarbital (30 mg/kg, ip), the left carotid artery was catheterized, and 0.1 ml of microspheres labeled with $^{85}$Sr was injected. The appropriate surgery for group A, B, or C was performed, and the rats were pair-fed for 4 weeks. After 4 weeks, the right carotid artery was catheterized during sodium pentobarbital anesthesia, and 0.1 ml of microspheres similarly prepared but labeled with $^{14}$Ce was injected. The rats were then killed, renal mass was removed and weighed, and each kidney or remnant was sectioned sagittally. Each sagittal section was placed on a Stadie-Riggs microtome; the outer 0.5 mm of cortex was removed and labeled zone A, the second 0.5-mm slice was marked zone B, and the remainder of the section was marked zone C. Since microspheres 15 ± 2µ in diameter lodge only in afferent arterioles or glomeruli (5), zone C was interpreted as reflecting flow to deep cortical and juxtamedullary glomeruli. The activity (counts/min) of each isotope in each zone was determined in a gamma counter (Packard), and correction of the Ce count for Sr overlap was made. The proportion of flow to each zone was calculated as A/A + B + C, B/A + B + C, or C/A + B + C for each isotope. Since the $^{85}$Sr-labeled microspheres were injected prior to surgery and $^{14}$Ce-labeled spheres were injected 4 weeks after surgical ablation, relative changes in proportional flow to any zone could be expressed by dividing the proportional flow measured with $^{14}$Ce-labeled microspheres by that measured with $^{85}$Sr-labeled microspheres. A ratio of 1.00 would indicate that no change in the proportional flow from control conditions had occurred.

Renal blood flow in each zone was calculated as follows: renal blood flow per zone = total renal blood flow × proportional flow per zone.

The number of glomeruli in each cortical zone was counted in six rats from each of the three groups following injection of India ink 4 weeks after surgery. The kidneys were then sectioned as they were in the microsphere experiments; the pieces were weighed and fixed in 10% formaldehyde, and glomerular counts were determined. Since new nephrons are not formed in the compensatory response to renal ablation, the glomerular density (total number of glomeruli/kidney weight) in different renal zones of the surgically ablated rats compared with that in the same zones of control rats provided a relative index of compensatory growth. Changes in glomerular density in zone C reflected the increase in tubular mass in the medullary as well as the deep cortical areas of the kidney. The glomerular density in each zone in group B and C rats was divided by the mean number of glomeruli in the corresponding zone of group A rats. This value was termed the zonal hypertrophy index.

Superficial nephron glomerular filtration rate and mean nephron glomerular filtration rate were compared in a separate series of experiments in which both measurements were performed simultaneously in groups A, B, and C. The experimental protocol was the same as that used in the clearance and blood flow studies, except that exposure and fixation of the left kidney for micropuncture was performed by previously...
described methods (6). Urine formed by the left experimental kidney was collected through a bladder catheter after the right ureter was ligated close to the bladder and then severed proximal to the tie. In these experiments a priming dose of 50 μc of 3H-methoxy-inulin was injected in a volume of 0.5 ml, and a sustaining infusion of 75 μc/hour in a volume of 1.2 ml was established. After a 45-minute equilibration period, three 30-minute urine collections were obtained to determine the inulin clearance of the left kidney or kidney remnant. Plasma inulin was determined from a blood sample obtained from the tail at the midpoint of each collection period. Concomitantly the superficial nephron glomerular filtration rate was measured in four to five proximal surface tubules during a 4-minute collection period. In these collections, an oil block 4-5 tubular diameters in length was placed distal to the site of puncture, and collections were made without the application of negative pressure in the pipette. The entire volume of collected tubular fluid was added to 10 ml of Aquasol counting solution and counted to at least 10,000 counts. Superficial nephron glomerular filtration rate was calculated as the specific activity of tubular fluid collected per minute divided by the specific activity of plasma per μliter. After the final clearance period, India ink was injected and total glomerular counts were determined so that mean nephron glomerular filtration rate could be calculated.

All values are expressed as means ± SE. Student’s t-test was used for the statistical comparison of groups whenever it was applicable.

Results

CHANGES IN GLOMERULAR FILTRATION RATE AND RENAL BLOOD FLOW AFTER PROGRESSIVE SURGICAL ABLATION

Four weeks after surgery, there was a marked increase in renal mass due to compensatory growth in both group B rats (50% ablation) and group C rats (75% ablation) (Table 1). The weight of the left kidney in group B rats (1.79 ± 0.07 g) was 78% of the weight of both kidneys in group A rats (2.26 ± 0.09 g) (P < 0.01). Despite extensive surgical ablation in group C rats, the remnant kidney weighed 1.46 ± 0.05 g, which was 65% of the control kidney weights (P < 0.01). The final weight of the remnant kidney was significantly greater than the weight of a single control kidney (1.13 ± 0.06 g) (P < 0.01). Total glomerular count in group A rats was 70,105 ± 2,118. There was no difference between the mean number of glomeruli in one control kidney (34,025 ± 1,368) and the value found in the single hypertrophied kidney in group B. The total number of glomeruli in the remnant kidney of group C rats was 14,408 ± 1,898 or 42% of that in a control kidney and 21% of the number of glomeruli in a control rat with both kidneys present (P < 0.01).

Whole rat glomerular filtration rate was 68% of the control value (1,144 ± 48 μliters/min 100 g⁻¹ body weight) in group B. In group C, glomerular filtration rate was 559 ± 40 μliters/min 100 g⁻¹, 49% of control. Mean nephron glomerular filtration rate demonstrated a dramatic and progressive increase following surgical ablation (Fig. 1). The mean nephron glomerular filtration rate rose from a control value of 46.5 ± 2.4 μliters/min to 73.2 ± 4.9 μliters/min after 50% ablation and to 113.8 ± 9.2 μliters/min after 75% ablation. These changes indicated a 57% and a 145% increase in mean nephron glomerular filtration rate in groups B and C, respectively.

The adaptive response in renal blood flow exceeded the compensatory changes in glomerular filtration rate. Although glomerular filtration rate was reduced to 68% of the control value after unilateral nephrectomy and to 49% after 75%

| TABLE 1 Changes in Renal Function and Blood Flow after Partial Ablation |
|-----------------------------|-----------------------------|-----------------------------|
|                             | Group A (Sham operated)     | Group B (50% Nephrectomy)   | Group C (75% Nephrectomy)   |
| No. of rats                | 8                           | 7                           | 7                           |
| Body weight (g)            | 279 ± 15                    | 305 ± 6.2                   | 297 ± 18                    |
| Total weight of kidney mass (g) | 2.26 ± 0.09                | 1.79 ± 0.07*                | 1.46 ± 0.05*                |
| Total glomerular count     | 70,105 ± 2,118              | 33,508 ± 1,447*             | 14,408 ± 1,898*             |
| Cmin (μliters/min 100g⁻¹ body weight) | 1,144 ± 48                 | 775 ± 40*                   | 559 ± 40*                   |
| Cmin (μliters/min g⁻¹ kidney weight) | 1,415 ± 53                 | 1,378 ± 95                  | 1,136 ± 103†                |
| Mean nephron glomerular filtration rate (μliters/min) | 46.5 ± 2.4                 | 73.2 ± 4.9*                 | 113.8 ± 9.2*                |
| Renal blood flow (μliters/min 100g⁻¹ body weight) | 5,290 ± 195                 | 4,307 ± 295†                | 3,577 ± 412*                |
| Mean glomerular blood flow (μliters/min) | 6,561 ± 254                 | 7,661 ± 566                 | 7,229 ± 644                 |
| Filtration fraction (Cmin/RPF) | 0.39 ± 0.02                 | 0.35 ± 0.04                 | 0.29 ± 0.03†                |

All values are expressed as means ± SE. Cmin = inulin clearance and RPF = renal plasma flow.

*P < 0.01 compared with group A.
†P < 0.05 compared with group A.
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ablation, total renal blood flow was 81% of control (5,290 ± 195 μl/min/100 g⁻¹ body weight) in group B and 68% of control in group C. The increase in renal blood flow per gram kidney weight in both experimental groups compared with the control value was not significant. Mean glomerular blood flow was 215.2 ± 10.1 nl/min in group A, 404.2 ± 25.7 nl/min in group B, and 724.3 ± 57.2 nl/min in group C (Fig. 1). Since the adaptive increase in blood flow was greater than the change in glomerular filtration rate, the filtration fraction of the whole kidney fell progressively among the three groups from 0.39 ± 0.02 in controls to 0.35 ± 0.04 in group B and to 0.29 ± 0.03 in group C (P < 0.05).

DISTRIBUTION OF INTRAHEPATIC BLOOD FLOW AFTER PROGRESSIVE SURGICAL ABLATION

Relative changes in proportional blood flow to each of the renal zones were determined using radioactive microspheres (Table 2). There was no change in the proportional blood flow to any zone in the group A rats. In contrast, in both group B and group C there was approximately a 20% fall in the distribution of blood flow to the outer cortex and an increase in the midcortical area. Blood flow to the deep cortex was unchanged in both experimental groups.

Since total renal blood flow and its relative distribution were known for each cortical zone studied, blood flow per gram of tissue in each zone could be calculated (Table 2). Estimated in this way, blood flow in the outer cortex (zone A) increased approximately 61% after 50% ablation and 22% after 75% ablation. In groups B and C, blood flow in the midcortical area (zone B) increased approximately 100% over control. In zone C, an increase in blood flow of 31% in group B and 78% in group C occurred.

The zonal hypertrophy index for each zone in group B and C rats is shown in Table 3. The glomerular density in each zone fell approximately 25% in group B and 60% in group C. Since the relative change in glomerular density among the three renal zones in each experimental group was similar, compensatory growth occurred symmetrically throughout the kidney.

COMPARISON OF SUPERFICIAL NEPHRON GLOMERULAR FILTRATION RATE AND MEAN NEPHRON GLOMERULAR FILTRATION RATE AFTER SURGICAL ABLATION

These experiments were performed because the mean nephron glomerular filtration rate in group C rats measured in the clearance studies (113.8 ± 9.2 nl/min) differed significantly from superfi-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Changes in Cortical Blood Flow following Partial Ablation</th>
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<tr>
<td></td>
<td>Group A (Sham operated)</td>
</tr>
<tr>
<td>Change in proportional flow (²⁹ Ce⁶² Sr)</td>
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</tr>
<tr>
<td>Zone A (superficial cortex)</td>
<td>0.99 ± 0.02</td>
</tr>
<tr>
<td>Zone B (midcortex)</td>
<td>0.97 ± 0.03</td>
</tr>
<tr>
<td>Zone C (deep cortex)</td>
<td>0.99 ± 0.01</td>
</tr>
<tr>
<td>Zonal blood flow (nl/min g⁻¹)</td>
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<tr>
<td>Zone A (superficial cortex)</td>
<td>10,781</td>
</tr>
<tr>
<td>Zone B (midcortex)</td>
<td>6,691</td>
</tr>
<tr>
<td>Zone C (deep cortex)</td>
<td>3,395</td>
</tr>
</tbody>
</table>

Values for changes in proportional flow are means ± se; zonal blood flow was calculated as described in Methods.

*P < 0.01 compared with group A.
†P < 0.05 compared with group A.

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TABLE 3

<table>
<thead>
<tr>
<th>Zone</th>
<th>Group B (50% nephrectomy)</th>
<th>Zone B</th>
<th>Zone C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.749 ± 0.072</td>
<td>0.848 ± 0.038</td>
<td>0.718 ± 0.045</td>
</tr>
<tr>
<td></td>
<td>0.351 ± 0.031</td>
<td>0.469 ± 0.050</td>
<td>0.473 ± 0.025</td>
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</tbody>
</table>

Values are means ± se for six rats. Zonal hypertrophy index = (total number of glomeruli/g zone in experimental kidney)/(total number of glomeruli/g zone in control kidney).

The zonal hypertrophy index was determined by micropuncture (75 nliters/min) in similarly prepared rats studied previously (2).

A comparison of single kidney values from rats studied by clearance methods alone with rats prepared for micropuncture analysis showed that the preparation for micropuncture studies resulted in a reduction in the glomerular filtration rate in all groups and that the reduction was most marked in group C rats (Fig. 2). Glomerular filtration rate was reduced 9% in group A, 13% in group B, and 36% in group C. These data suggest that the procedures of open laparotomy and fixation of the left kidney result in a modest, nonsignificant decline in renal function in normal rats and rats subjected to unilateral nephrectomy. Despite very careful handling of the remnant kidney of group C rats and fluid replacement for surgical losses, a marked decrease in overall function occurred during preparation for micropuncture study.

The mean values for simultaneously determined superficial nephron glomerular filtration rate and mean nephron glomerular filtration rate in each of the three groups after preparation for micropuncture are shown in Table 4. The lower levels of mean nephron glomerular filtration rate in these rats (Table 4) compared with the measurements made during clearance experiments (Table 1) reflect the changes in overall renal function incurred as a result of preparation for micropuncture analysis. The ratio of superficial nephron glomerular filtration rate to mean nephron glomerular filtration rate was 0.73 ± 0.05 in control rats, and it increased to 1.00 ± 0.09 in group C rats. Because of alterations in renal function due to the experimental manipulations, it was not possible to evaluate changes in distribution of nephron function in the remnant kidney.

Discussion

Removal of renal tissue stimulates prompt functional and anatomical adaptation in the remaining renal parenchyma. A recent investigation (1) has demonstrated that there is no apparent limitation to the compensatory growth, since the increase in mass correlates directly with the amount of tissue excised. After accounting for the rate of normal growth, compensatory changes result in a 50% increase in mass after removal of one kidney and a 140% increase following 75% nephrectomy (1). From a comparison of the changes in whole rat glomerular filtration rate found in the present study with those previously reported (1), it is apparent that the values in groups A and B are similar but that the glomerular filtration rate in group C is slightly greater. This difference in group C can be accounted for by a lesser degree of surgical ablation (14,408 ± 1,898 remaining glomeruli) in this study compared with that in the earlier study (10,650 ± 1,982 remaining glomeruli). The present study demonstrated that the functional adaptation in glomerular filtration rate is similar to the compensatory changes in renal mass. When changes in mean nephron glomerular filtration rate were compared, there was a 60% increase in mean nephron glomerular filtration rate after a 50% nephrectomy and a 150% increase after removal of 75% of the kidney tissue. The more pronounced increments in renal blood flow,
however, provided an important new finding. Mean glomerular blood flow increased 90% after unilateral nephrectomy and 240% following 75% nephrectomy. Thus, it is apparent that following progressive renal ablation the adaptive changes in renal blood flow exceed those in filtration rate and result in a fall in filtration fraction. A similar fall in filtration fraction has previously been demonstrated in man during chronic renal insufficiency (7). Recently, Allison and associates (8) have demonstrated a reduction in filtration fraction due to a disproportionate fall in glomerular filtration rate in relationship to changes in renal blood flow in two experimental models of glomerulonephritis in the rat.

Several investigators have reported values for mean glomerular plasma or blood flow in the rat using a variety of techniques. Brenner et al. (9) measured glomerular capillary plasma flow in superficial glomeruli of Sprague-Dawley rats by the micropuncture technique and reported a control value of 97 nliters/min. Morgan (10), using complete collection of efferent arteriolar blood from superficial glomeruli in Sprague-Dawley rats, found a postglomerular blood flow of 180 nliters/min. Calculated mean glomerular blood flow from the sum of the postglomerular blood flow and the measured superficial nephron glomerular filtration rate provided a value of 215 nliters/min. Kallskog and associates (11), using 15μm microspheres, estimated mean glomerular blood flow to be 230 nliters/min in the outer cortex of the rat and 200 nliters/min in the juxtamedullary glomeruli. These data are quite similar to the mean glomerular blood flow of 215 ± 10 nliters/min in group A rats calculated in the present study. The zonal blood flow observed in group A rats in the present study corresponds to values reported by Wallin et al. (12) using a similar method.

The marked increase in renal blood flow in the hypertrophied tissue was characterized by a redistribution of intrarenal blood flow. Proportional blood flow decreased in the outer cortex and increased in deeper cortical areas. Carriere and associates (13) used 85Kr disappearance curves and silicone rubber vascular casts to evaluate renal blood flow distribution in the partially infarcted kidney of the dog. Although they did not demonstrate a change in cortical distribution between the remnant kidney and control, they noted an increased volume of the outer cortex in the hypertrophied kidney associated with a more rapid appearance and disappearance of krypton in the medullary area and pointed out that such changes could have obscured a change in blood flow distribution. An important technical advantage of the present experiments was the use of two injections of labeled microspheres, one administered before and the other after compensatory growth had occurred. By this method, blood flow distribution to the renal cortex was evaluated in a way that was not influenced by changes in cortical volume or contour. Consideration of these factors is important because of the marked increase in tubular mass that occurs during compensatory growth.

The renal hemodynamic changes observed in the present study suggest a marked vasodilation associated with compensatory adaptation, especially in deep cortical areas. Although medullary blood flow derives from juxtamedullary nephrons, it was not

<table>
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<th>TABLE 4</th>
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<tr>
<td>Comparison of Simultaneous Measurements of Mean Nephron Glomerular Filtration Rate and Superficial Nephron Glomerular Filtration Rate in Rats Prepared for Micropuncture Analysis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Group A (Control [6])</th>
<th>Group B (50% Nephrectomy [10])</th>
<th>Group C (75% Nephrectomy [8])</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (μliters/min 100 g~1 body weight per kidney)</td>
<td>519 ± 45</td>
<td>675 ± 55*</td>
<td>357 ± 39†</td>
</tr>
<tr>
<td>Superficial nephron glomerular filtration rate (nliters/min)</td>
<td>31.3 ± 2.0</td>
<td>49.3 ± 5.7*</td>
<td>74.2 ± 5.2†</td>
</tr>
<tr>
<td>Mean nephron glomerular filtration rate (nliters/min)</td>
<td>43.5 ± 1.8‡</td>
<td>63.1 ± 5.0*</td>
<td>75.8 ± 5.6†</td>
</tr>
<tr>
<td>Ratio of superficial nephron glomerular filtration rate to mean nephron glomerular filtration rate</td>
<td>0.73 ± 0.05</td>
<td>0.79 ± 0.07</td>
<td>1.00 ± 0.09</td>
</tr>
</tbody>
</table>

Values represent means ± se. Number of rats is given in brackets. The mean value for superficial nephron glomerular filtration rate represents the average of four or five separate determinations in six rats, and the value of mean nephron glomerular filtration rate represents the average of ten determinations in six rats.

*P < 0.05 for comparison with group A.
†P < 0.05 for comparison with group B.
‡P < 0.05 for comparison of mean nephron glomerular filtration rate with superficial nephron glomerular filtration rate for group A.

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possible to quantify absolute medullary perfusion. However, based on present data it seems likely that, in association with compensatory hypertrophy, the ratio of superficial mean glomerular blood flow to juxtamedullary mean glomerular blood flow falls below 1.0, in the control state, similar rates of perfusion are found in both cortical areas (11). Such changes in renal vascular resistance may be an important factor in establishing the profound changes in the tubular reabsorption of water and electrolytes which occur in response to loss of renal mass.

Although the increase in renal blood flow was most prominent in the midcortical and deep cortical areas, the increase in renal mass estimated from the zonal hypertrophy index was symmetrical throughout the cortex. McNay and Miyazaki (14) have made similar, but indirect, observations in the dog following unilateral nephrectomy.

Micropuncture experiments were performed to measure superficial nephron glomerular filtration rate in superficial nephrons of the remnant kidney for several reasons. First, estimation of nephron glomerular filtration rate by conventional micropuncture techniques provides a confirmation for the method used to measure mean nephron glomerular filtration rate. This correlation was felt to be important because of the assumption that glomeruli containing India ink represent functional structures. Second, it was important to confirm the marked changes in mean nephron glomerular filtration rate observed in the remnant kidney, because the increment rise in glomerular filtration rate appeared to occur without a finite limitation. In a previous study, superficial nephron glomerular filtration rate increased to a maximum of about 70–75 nliters/min after unilateral nephrectomy, but no further increase was found after more extensive ablation (2). Third, an experimental model characterized by a onefold increase in filtered load has important applications in the study of mechanisms involved in electrolyte transport by the proximal tubule. As previously noted, special care was taken to prepare the rats used in the micropuncture study in a similar way to that used in the clearance studies, except for the exposure and fixation of the left kidney for micropuncture.

The amount of tissue surgically removed in group C rats was the same in both clearance and micropuncture studies. The total number of remaining glomeruli was 14,408 ± 1,898 in the clearance experiments and 13,204 ± 1,662 in the micropuncture studies (P > 0.05).

Preparation of the experimental left kidney resulted in small, nonsignificant reductions in whole kidney and mean nephron glomerular filtration rate in group A and group B rats. The ratio of superficial nephron glomerular filtration rate to mean nephron glomerular filtration rate in both groups averaged approximately 0.75. A previous study (15) has shown that under normal nondiuretic conditions there is a gradual increase in nephron glomerular filtration rate between superficial and juxtamedullary nephrons in control rats. Using sodium ferrocyanide to measure nephron glomerular filtration rate, the filtration rate was 29.7 ± 1.3 nliters/min in superficial, 32.7 ± 1.7 nliters/min in midcortical, and 40.1 ± 1.9 nliters/min in juxtamedullary glomeruli. Therefore, these data show that in control rats preparations required for micropuncture do not significantly influence renal function and thus provide validation for our estimate of mean nephron glomerular filtration rate. In contrast, there was a marked reduction of approximately 35% in the glomerular filtration rate of the remnant kidney in group C. Although renal blood flow was not measured in these experiments, it is possible that the manipulations used to prepare the remnant kidney for micropuncture reduced the renal vasodilation observed in clearance studies and resulted in a fall in glomerular filtration rate. The superficial nephron glomerular filtration rate measured in group C was reduced in proportion to the change in overall glomerular filtration rate and corresponded to the value previously reported in the same model during micropuncture studies (2). Since these observations indicated that marked alterations in renal function had occurred in the remnant kidney during preparation for micropuncture, no attempt was made to interpret changes in the distribution of superficial nephron glomerular filtration rate. Several previous micropuncture studies of a segmentally diseased kidney (16, 17) have also reported superficial nephron glomerular filtration rate values in the range of 70 to 80 nliters/min.

Another previous study (18) has shown that the kidney is capable of adjusting the fractional excretion of water and electrolytes inversely to reductions in glomerular filtration rate so that homeostasis is maintained unless severe renal insufficiency occurs. The results of the present study suggest that marked alterations in the filtered load of water and solutes to the remaining nephrons occur following loss of renal mass and that changes in renal hemodynamics play an important role in compensatory adaptation. These changes are characterized by a renal cortical vasodilation that results in markedly increased mean nephron blood flow and a change in blood flow distribution.
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Circ Res. 1975;36:286-293
doi: 10.1161/01.RES.36.2.286

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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