Resetting of renal blood autoregulation during acute blood pressure reduction in hypertensive rats

BJARNE M. IVERSEN, FRED IVAN KVAM, KNUT MATRE, AND JARLE OFSTAD
Renal Research Group, Medical Department A, University of Bergen, N-5021 Bergen, Norway

Iversen, Bjarne M., Fred Ivan Kvam, Knut Matre, and Jarle Ofstad. Resetting of renal blood autoregulation during acute blood pressure reduction in hypertensive rats. Am. J. Physiol. 275 (Regulatory Integrative Comp. Physiol. 44): R343–R349, 1998.—Decrease in systemic blood pressure, duration of pressure decrease, and change in the activity of the renin or the sympathetic nervous system may represent mechanisms involved in resetting the renal blood flow (RBF) autoregulation found in hypertensive rats. Autoregulation of RBF, plasma renin concentration (PRC), and the time needed for resetting to take place were studied in the nonclipped kidney before and after removal of the clipped kidney of two-kidney, one-clip (2K1C) hypertensive rats and before and after mechanical reduction of the renal arterial pressure (RAP) for 10 min in the spontaneously hypertensive rat (SHR) and in the nondocked kidney of 2K1C hypertensive rats with and without renal denervation. Mean arterial pressure (MAP) fell from 147 to 107 mmHg 30 min after removal of the clipped kidney, and the lower pressure limit of RBF autoregulation decreased from 113 to 90 mmHg (P < 0.01); PRC fell. Mechanical reductions of RAP from 161 to 120 mmHg in the nondocked kidney for 10 min did not change RBF, but at 120 mmHg, the lower pressure limit of RBF autoregulation was reduced from 115 mmHg before pressure reduction to 96 mmHg afterwards (P < 0.02). In SHR, similar pressure reduction for 10 min decreased the lower pressure limit of RBF autoregulation from 106 to 86 mmHg (P < 0.01). PRC was unchanged in both models, and denervation did not change RBF autoregulation. When RAP was reduced below the lower pressure limit of RBF autoregulation, RBF decreased ~20%; the lower pressure limit of RBF autoregulation remained unchanged. In normotensive Wistar-Kyoto rats, pressure reduction did not change the range of RBF autoregulation. These results indicate that acute normalization of the pressure range of RBF autoregulation in hypertensive rats is dependent on the degree of pressure reduction of RAP, whereas renal innervation and PRC do not play a major role. We propose that the mechanism of resetting is due to afterstretch of noncontractile elements of the vessel wall or is caused by pure myogenic mechanisms. An effect of intrarenal angiotensin cannot be excluded.

When the systemic blood pressure changes acutely, renal blood flow (RBF), glomerular filtration rate (GFR), and the glomerular capillary pressure remain constant within a wide range of pressure changes. This regulatory function is named renal autoregulation, and the systemic blood pressure can be considered to represent its set point. The resistance changes involved are mostly localized to afferent arterioles (19).

When the deviation from the set point of a system regulating acute and transitory variations becomes more or less permanent, the system usually adapts to the new condition by altering its set point so that the regulatory capacity is kept intact. A familiar example is the resetting of the baroreceptor control of the systemic blood pressure that takes place during the development of hypertension (11). Correspondingly, the inflection point of autoregulation of RBF is reset to a higher perfusion pressure in spontaneously hypertensive rats (SHR) and in two-kidney, one-clip (2K1C) hypertensive rats (13, 16). On the other hand, the lower pressure limit of autoregulation can be reduced when the arterial pressure is lowered due to antihypertensive treatment (16). Characteristically, the capacity of the afferent arteriole to dilate is increased at lower pressures after the set point is acutely reset (16).

When the perfusion pressure chronically increases or drops outside the pressure limits of RBF autoregulation, the flow and capillary pressure will change until the regulatory system adjusts to cope with the new situation or another system has taken over. Even at permanent pressure changes within the pressure range of autoregulation, superimposed transitory pressure variations may be insufficiently compensated for until autoregulation is reset. The time necessary for resetting autoregulation is therefore important. Apart from protecting the tissue fed by the involved vessels from functional consequences of acute capillary pressure and blood flow variations, autoregulation also prevents or delays tissue damage (2). In the kidney, the glomerular damage seems well correlated to an increase of the glomerular capillary pressure (21). The time factor of resetting may therefore be important for the development of hypertensive renal damage and also for electrolyte excretion. It should be added that previous studies from our laboratory have observed the reduction of RBF autoregulation to lower pressure levels after converting enzyme inhibition for 1 wk (16).

One possible mediator of resetting is the renal nerves. Renal nerves do not seem to be involved in autoregulation of RBF in euolemic normotensive rats or in the dog (15, 20). However, in 40-wk-old severely hypertensive SHR with moderately advanced glomerulosclerosis, RBF autoregulation is abolished by cycloxygenase inhibition in innervated, but not in denervated, kidneys (15). Furthermore, resetting of the RBF autoregulation curve to the right has been observed after 10 min of sympathetic nerve stimulation (bilateral carotid artery occlusion) and systemic pressure increase in awake normotensive dogs (24). A similar acute resetting of blood flow in the pial arteries in normotensive rats has been demonstrated by induction of systemic hypertension by norepinephrine (23). In this study, we therefore also investigated the resetting of RBF autoregulation in SHR before and after acute denervation.

When the systemic pressure in the rat is decreased to the lower pressure limit of RBF autoregulation and
below, there is a substantial increase of the renin secretion and the afferent nerve traffic (6, 7). This raises the question of whether resetting of RBF autoregulation is modulated by renal nerves or plasma renin or whether the pressure reduction is within the normal pressure range of autoregulation or below this range.

Our working hypothesis is that resetting of RBF autoregulation is strictly dependent on the level of systemic blood pressure per se. To test this hypothesis, we examined the following three aspects of RBF autoregulation in hypertensive models: we examined (1) the time necessary for resetting and (2) the role of renal nerves, and we made experiments to determine (3) whether resetting is different when pressures are reduced within the normal range of autoregulation or below this range.

In both models, RAP was reduced by an aortic clamp; in the 2K1C hypertensive model, the systemic blood pressure was also reduced by removal of the clamped kidney, a procedure that induces a concomitant reductio of the plasma renin concentration (PRC).

METHODS

Animals. A total of 73 experiments was performed in SHR and 2K1C hypertensive Wistar rats and in Wistar and Wistar-Kyoto rats (WKY) as their normotensive controls. The rats were obtained from Møllegård Breeding Center (Skensved, Denmark). The rats were kept three in each cage and were fed standard rat chow.

The experiments were performed in accordance with, and under the approval of, the Norwegian State Board for Biological Experiments.

Hypertensive models. SHR were 12 wk of age with a fixed high blood pressure. Their body weight was 250–280 g. The 2K1C hypertensive model was induced in 8-wk-old rats by placing a silver clip with an internal diameter of 0.2 mm on the right renal artery. The left nonclipped kidney was used for RBF measurements 4–5 wk after clipping.

Denervation. With use of a microscope with ×50 magnification, all visible nerves to the kidney were sectioned. The renal artery was isolated, and the adventitia was stripped carefully along the renal artery and vein.

Hemodynamic study. The rats were deprived of food overnight before the experiment but were allowed free access to water. They were anesthetized by an intraperitoneal injection of pentobarbital sodium (50 mg/kg body wt). After tracheotomy, catheters (PE-50) were introduced into the aorta via the left femoral and the left carotid arteries for sampling and blood pressure measurement. The aortic pressure was assumed to be equal to the renal arterial pressure (RAP). Arterial blood (0.1 ml) was taken for each measurement of PRC. A PE-50 catheter was introduced into a femoral vein for infusion of 5% bovine serum albumin in Ringer solution at a rate of 3 ml/h to keep the hematocrit constant. In the first group, the blood pressure was lowered by removal of the clamped kidney in 2K1C hypertensive rats. In the 2K1C hypertensive rats, the screw clamp was placed between the clipped kidney and compared with unilateral nephrectomized normotensive Wistar rats as controls (n = 6). In two other groups (n = 14) of the 2K1C hypertensive model and in two groups (n = 15) of SHR, RAP was reduced acutely to ~120 mmHg for a period of 10 min by aortic constriction. In each model, autoregulation was examined with intact innervation to the kidney (n = 14) and immediately after denervation.

Recordings of RBF autoregulation were carried out before and immediately after the period of pressure reduction with further reduction of the perfusion pressure without release of the clamp. In WKY rats (n = 12), the perfusion pressure was reduced 20% compared with control pressure. Arterial blood samples for measurements of renin concentration were taken before and 10 min after reduction of the perfusion pressure but before the examinations of RBF autoregulatory capacity. The sampled volume was 0.1 ml, which was substituted with albumin solution.

In a third group of SHR (n = 7), RAP was lowered to ~90 mmHg for 10 min by aortic constriction. This pressure is below the lower pressure limit of autoregulation in SHR. RBF autoregulation was recorded before and immediately after the period of low pressure, but the clamp was released shortly before the second recording was done. This part of the study was carried out to examine the effect of reduced RBF and low perfusion pressure on resetting. The control group in this part of the study was SHR (n = 7) in which the perfusion pressure was kept at ~120 mmHg, i.e., above the lower pressure limit and without any change in RBF.

In a fourth group of SHR (n = 6), we examined spontaneous resetting of RBF autoregulation. Blood pressure reductions were done in the rats during a 1-h period.

PRC. PRC was measured by the ANG 1-trapping method of Poulsen and Jørgensen (22). The antibody used was ANG I coupled to gamma globulin with carboimidate. Plasma from rats with high angiotensinogen levels was used as substrate. The antiserum was kindly provided by K. Poulsen (Copenhagen, Denmark).

Data Analysis

Lower pressure limit of autoregulation. The lower pressure limit of RBF autoregulation was defined as the last perfusion pressure that reduced RBF. Resetting of RBF autoregulation was defined as the change in lower pressure limit induced by different procedures.

RVR. Renal vascular resistance (RVR) was calculated at control pressure and at the lower pressure limit of RBF autoregulation in all groups. The percent reduction in RVR during pressure reduction within the autoregulatory range was calculated in all groups.

Statistical methods. The results were expressed as means ± SE. Differences between groups were assessed by one-way analysis of variance when this was appropriate. Where a
RESULTS

Effect of clip removal on RBF autoregulation in 2K1C hypertensive rats. Mean arterial pressure (MAP) fell rapidly after removal of the clipped kidney and became stable after 30 min. RBF in the nondipped kidney increased slightly (5.0 \pm 0.5 to 5.7 \pm 0.6 ml/min\cdot\text{kidney}^{-1}) (P < 0.05). The lower pressure limit of RBF autoregulation was reduced but still higher than the value 30 min after unilateral nephrectomy (91 \pm 3 vs. 81 \pm 4 mmHg) (P < 0.02) in normotensive control rats (Fig. 1). PRC fell from 260 \pm 20 to 62 \pm 16 ng ANG I/ml after removal of the clipped kidney (P < 0.02).

Effect of mechanical reduction of RAP on RBF autoregulation in nondipped kidney of 2K1C hypertensive rats and in kidneys from SHR and WKY. During mechanical reduction of RAP for 10 min from 155 \pm 4 to 124 \pm 2 mmHg (P < 0.01), RBF in the nondipped kidney did not change significantly. Studies of the flow-pressure relationship when RAP was reduced from 124 mmHg showed that the pressure range of RBF autoregulation was shifted to the left and the lower pressure limit was reduced from 115 \pm 9 to 96 \pm 9 mmHg (Fig. 2). In SHR, reduction of RAP from 156 \pm 4 to 120 \pm 2 mmHg for 10 min did not change RBF. However, the flow-pressure relationship when RAP was reduced from 120 mmHg showed that the range of RBF autoregulation was shifted to the left and the lower pressure limit was reduced from 106 \pm 5 to 86 \pm 4 mmHg (Fig. 2). In WKY, reduction of RAP from 104 \pm 4 to 94 \pm 4 mmHg for 10 min did not change RBF. When the flow-pressure relationship was studied after a 10-min reduction of RAP in WKY, the range of RBF autoregulation did not shift to the left and the lower pressure limit remained unaltered: 81 \pm 4 vs. 78 \pm 5 mmHg (not significant) (Fig. 3). In Fig. 4, the change in lower pressure limit of RBF autoregulation is shown in 2K1C hypertensive, SHR, and normotensive WKY rats.

Effect of renal innervation on RBF autoregulation and PRC in 2K1C hypertensive rats, SHR, and WKY. RBF increased significantly after renal denervation in the nondipped kidney of 2K1C hypertensive rats and in kidneys from SHR and WKY as shown in Fig. 5.

There was no effect of denervation on the range of RBF autoregulation either at control pressure (Fig. 6A) or at reduced pressure (Fig. 6B) in 2K1C hypertensive rats, SHR, or WKY. Reduction of RAP in the denervated, nondipped kidney of 2K1C hypertensive rats and SHR from control MAP to \approx 120 mmHg did not change RBF, but the pressure range of RBF autoregulation was significantly shifted to the left as the lower pressure limit of autoregulation was reduced from 121 \pm 9 to 96 \pm 6 mmHg (P < 0.01) in 2K1C hypertensive rats and from 104 \pm 4 to 89 \pm 2 mmHg in SHR. RAP reduction of 10–20% in the denervated WKY rats did not change the lower pressure limit (Fig. 6B).

In 2K1C hypertensive rats, PRC was 189 \pm 11 before and 146 \pm 31 ng ANG I/ml after pressure reduction (not significant) and fell to 125 \pm 36 ng ANG I/ml (P < 0.05) after denervation. During pressure reduction in denervated rats, PRC was unchanged (140 \pm 52 ng ANG I/ml) (P > 0.10).

In SHR, PRC was 112 \pm 22 before and 160 \pm 16 ng ANG I/ml after pressure reduction (not significant). After denervation, PRC fell to 70 \pm 32 ng ANG I/ml (P < 0.05) but was unchanged during pressure reduction (90 \pm 28 ng ANG I/ml).

In WKY, PRC was 120 \pm 18 before and 158 \pm 38 ng ANG I/ml after pressure reduction (not significant). After denervation, PRC fell to 41 \pm 14 ng ANG I/ml (P < 0.02). During pressure reduction in denervated kidneys, PRC was unchanged at 36 \pm 12 ng ANG I/ml (not significant).

RBF autoregulation in SHR after lowering RAP to values above (120 mmHg) or below (90 mmHg) lower pressure limit of autoregulation. These experiments were done in two groups of SHR. In the first group, MAP was 184 \pm 9 mmHg, the lower pressure limit of autoregulation was 120 \pm 4 mmHg, and RBF was 6.2 ml/min\cdot\text{kidney}^{-1}. In this group, RAP was reduced to 122 \pm 3 mmHg for 10 min. When the clamp was released, MAP increased to 182 \pm 8 mmHg but RBF was unchanged. When RBF autoregulation was reexamined immediately afterward, the lower pressure limit of autoregulation was significantly lowered (106 \pm 2 mmHg; P < 0.02).

In the second group, RAP was 193 \pm 6 mmHg, the lower pressure limit of autoregulation was 122 \pm 5 mmHg, and RBF was 5.2 \pm 0.8 ml/min\cdot\text{kidney}^{-1}. In this group, RAP was reduced to 90 \pm 5 mmHg for 10 min, i.e., an RAP significantly below the lower limit of autoregulation. In this group, RBF fell to 2.4 \pm 0.8 ml/min\cdot\text{kidney}^{-1}. After release of the aortic constriction, RAP rapidly returned to 187 \pm 6 mmHg, but RBF remained low (4.6 \pm 0.7 ml/min\cdot\text{kidney}^{-1}). However, when RBF autoregulation was reexamined immediately afterward, the pressure range was unchanged.
with a lower pressure limit of 118 ± 5 mmHg, not significantly different from what was obtained before pressure reduction. The change in the lower pressure limit of autoregulation when the RAP was reduced to 90 or 120 mmHg was 4 ± 2 and 18 ± 4 mmHg, respectively (P < 0.01).

Examination for spontaneous change in RBF autoregulation in SHR. RBF autoregulation was examined two times in six innervated SHR, with a 1-h interval in between. The systemic blood pressure did not change, and the lower pressure limit of RBF autoregulation was 107 ± 6 before and 109 ± 7 mmHg afterward (not significant).

Calculation of maximal reduction in RVR during RBF autoregulation. As shown in Table 1, the maximal reduction of RVR in percent of control value was not significantly altered in SHR or in nonclipped kidney of 2K1C after the pressure was reduced to 120 mmHg for 10 min (P > 0.10). In the WKY in which the lower pressure limit of autoregulation was not shifted to the
DISCUSSION

The main observation that emerges from this study is that the RBF autoregulation can be reset in hypertensive rats by reduction of the systemic blood pressure per se. The time course of the readjustment in autoregulatory mechanisms is \( <10 \text{ min} \) when the blood pressure is acutely lowered within the pressure range of autoregulation. Obviously resetting is not an instantaneous process; if so, resetting would have occurred pari passu with the stepwise reduction of the blood pressure. The observation of a difference between the lower pressure limits indicates that resetting either did not take place or was not fulfilled during the stepwise reduction of the blood pressure in the control groups. The repeatability of autoregulation at constant systemic blood pressures indicates that spontaneous variation in RBF autoregulation cannot explain the decrease in lower pressure limit that was observed in our study.

Our observations in this study correspond with the time needed to reset the baroreceptor-mediated systemic pressure control in response to sustained change in mean blood pressure. By analogy, resetting of the renal autoregulation thus seems to be of physiological importance first by stabilizing the solute load presented to the relatively slowly adaptable enzyme systems of the tubular cells (5), and second by countering the deleterious effect of increased glomerular capillary pressure when the perfusion pressure is acutely increased (2).

The observations in the 2K1C hypertensive groups were similar to those in SHR. The lower pressure limit in the group with the clamped kidney removed was similar to that observed in rats with mechanical reduction of RAP; this demonstrates that resetting also can be induced by a slow, gradual reduction of the systemic blood pressure and to the same degree after an acute pressure reduction. The present study confirms our earlier observation that the capacity to reduce the renal resistance is kept unaltered after resetting has taken place in both SHR and 2K1C and that resetting does not seem to be strain specific (13, 16). The lack of resetting in normotensive WKY suggests that resetting toward lower pressures occurs only when autoregulation has been reset to pressures higher than normal. These observations are also supported by a constant change in RVR before and after resetting in hypertensive rats.

Table 1. Maximal reduction of renal vascular resistance in percent of control value during RBF autoregulation

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>( P )</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2K1C hypertensive rats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clipped kidney removed</td>
<td>28 ± 2</td>
<td>NS</td>
<td>25 ± 3</td>
</tr>
<tr>
<td>Reduced RAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Innervated kidney</td>
<td>21 ± 2</td>
<td>NS</td>
<td>26 ± 4</td>
</tr>
<tr>
<td>Denervated kidney</td>
<td>24 ± 3</td>
<td>NS</td>
<td>22 ± 3</td>
</tr>
<tr>
<td><strong>SHR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced RAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Innervated kidney</td>
<td>31 ± 4</td>
<td>NS</td>
<td>31 ± 3</td>
</tr>
<tr>
<td>Denervated kidney</td>
<td>28 ± 2</td>
<td>NS</td>
<td>24 ± 3</td>
</tr>
<tr>
<td><strong>WKY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced RAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Innervated kidney</td>
<td>20 ± 3</td>
<td>( P &lt; 0.05 )</td>
<td>15 ± 2</td>
</tr>
<tr>
<td>Denervated kidney</td>
<td>25 ± 2</td>
<td>( P &lt; 0.02 )</td>
<td>11 ± 2</td>
</tr>
</tbody>
</table>

Values are means ± SE. RBF, renal blood flow; RAP, renal arterial pressure; 2K1C, 2-kidney, 1-clip; SHR, spontaneously hypertensive rats; WKY, Wistar-Kyoto rats; NS, not significant.
sive models but not in the normotensive controls. This finding confirms our earlier observations in WKY when the systemic blood pressure was reduced with captopril (16).

Although autoregulation of RBF has been shown to be reset by sympathetic nerve stimulation, it is not clear whether this is due to a direct effect or is secondary to the systemic blood pressure increase (24). The RBF increase after denervation in our study indicates the presence of a sympathetic nerve tone in both models. However, the lower pressure limit and the capacity to reset this limit were not influenced by acute renal denervation. Possibly the reduction of RVR after denervation was mainly localized to the efferent arteriole, which is assumed to play only a minor role in autoregulation of RBF (12). Thus the renal nerves did not seem to participate in the resetting of RBF autoregulation in the present study.

In all groups, a reduction in renal perfusion pressure within the pressure range of autoregulation had no significant effect on PRC. As expected, removal of the clamped kidney in the 2K1C hypertensive animals induced a substantial drop of the PRC. A small but significant reduction of PRC was observed after denervation. This supports earlier observations in SHR (16) and normotensive rats (1) when treated with converting enzyme inhibition. These observations suggest that the capacity to autoregulate RBF and reset the range of RBF autoregulation is not related to PRC. These findings do not, however, permit the conclusion that the renin-angiotensin system does not participate in the resetting of renal autoregulation. Although our studies seem to rule out an effect at systemic levels, it is possible that the resetting depends on the renal tissue concentration of ANG. Our study did not address this possibility, which is likely to be complex because of intrarenal compartmentalization of ANG (8). The earlier observations in SHR (16) treated with converting enzyme inhibitors should also be interpreted with care because a considerable amount of ANG II may be present in the renal tissue even when high doses of the converting enzyme inhibitor are used. Cupples (4) reported that ANG influences the resetting of RBF autoregulation after prolonged reductions of the perfusion pressure below the lower limit of autoregulation. At such low pressures the renin secretion rate is substantially increased. Thus the role of ANG in resetting of autoregulation may vary according to conditions.

The lack of resetting of RBF autoregulation when the perfusion pressure was lowered for 10 min below the lower pressure limit of autoregulation in hypertensive animals was unexpected. This finding may suggest that the tubuloglomerular feedback (TGF) mechanism is not a major mediator in this resetting. There is good evidence that the TGF mechanism is attenuated pari passu with reduction of the renal perfusion pressure (25). In our study, the substantial reduction of RBF in the groups in which the pressure was reduced below the lower pressure limit certainly was accompanied by a corresponding reduction of GFR, i.e., an additional contribution to reduce the TGF response. The lack of resetting when the TGF-mediated dilation of the afferent arteriole was maximal indicates only a minor, if any, role for TGF in the process of resetting in our study. Selen and Persson (26) have reported sensitization of TGF after prolonged renal pressure reduction. This was observed after the systemic pressure was normalized, and it is thus unlikely that this mechanism can explain our findings. Reduction of RAP to a level substantially below the lower pressure limit of RBF autoregulation using the microsphere method has also been shown to have no effect on afferent arteriolar diameter (unpublished observations). In addition, resetting of autoregulation has also been reported in other organs without a TGF-like mechanism (9). However, only a study with simultaneous measurement of TGF and resetting can produce a definite answer to this question.

The resetting observed in our study implicates the acquisition of an increased dilatory capacity of the resistance vessels obtained during the 10-min exposure to reduced perfusion pressure. One possible explanation of this is “afterstretch” of the resistance vessel walls. Afterstretch is well known from diameter measurements in isolated arteries and is characterized by a slow minor increase of the vessel circumference after an initial rapid dilation when the stretch is applied (3). The explanation of afterstretch is not clear but is possibly linked to the noncontractile components of the vessels. In our study, resetting was observed only in connection with long-standing hypertension and may have been related to such structural changes in the vessel wall. There is good evidence that increased extramuscular tissue is a feature in the remodeling of the vessel wall induced by hypertension (10, 17, 18). According to Mulvany (18), the morphology of the individual smooth muscle vessel cell as well as the wall stress per smooth muscle cell seems to remain normal in SHR, i.e., similar to the smooth vessel cell in the normotensive controls that did not present resetting. This complies with the notion that afterstretch is not due to special features of the smooth vessel cells.

In conclusion, this work supports our hypothesis that resetting of RBF autoregulation is observed in hypertensive rats when the pressure is lowered for 10 min within the pressure range of autoregulation. Resetting was not observed in the normotensive controls and could not be found when the RAP was reduced below the lower pressure limit of RBF autoregulation. Renal nerves, circulating ANG, and possibly also the macula densa mechanism do not seem to play a decisive role in this phenomenon. Afterstretch of the noncontractile elements in the vessel wall is a possible, although hypothetical, explanation. A mediating effect of intrarenal ANG cannot be excluded. A fundamental reservation is that our studies only involved acute pressure reductions. Resetting during chronic pressure alterations may involve other mechanisms. Resetting during pressure increase can obviously not be explained by afterstretch.
Perspectives

The broad implication of these findings is that systemic blood pressure represents the set point for RBF autoregulation and that normal blood pressure represents the minimal set point pressure. There seems to be an absolute lower limit of RBF autoregulation that cannot be surpassed by further lowering of the blood pressure, at least in the normotensive rat. The structural modulation and remodeling of the resistance vessels may thus play an important role in the functional adjustment of the range of RBF autoregulation in hypertensive animals. Interruption of smooth muscle and the noncontractile components in the resistance vessels during change in systemic blood pressure would probably provide an important area of research that might have an impact on the understanding of how RBF and GFR are regulated in hypertensive animals. Interrelationship between smooth muscle cells and the noncontractile components in the resistance vessels may thus play an important role in the functional modulation and remodeling of the resistance vessels during change in systemic blood pressure, at least in the normotensive rat.

The authors thank Heidi Monsen and Tone Husby for excellent technical assistance.

Address for reprint requests: B. M. Iversen, Medical Dept. A, N-5021 Haukeland Sykehus, Norway.

Received 24 October 1997; accepted in final form 31 March 1998.

REFERENCES


