Letters to the Editor

Renal Autoregulation

In the paper "Autoregulation of Single Nephron Filtration Rate in the Presence and the Absence of Flow to the Macula Densa," which recently appeared in Circulation Research (34:836-842, 1974), Dr. Knox and his colleagues concluded that their study "... provides strong evidence that autoregulation of single nephron filtration rate is unaltered by interruption of tubule fluid to the macula densa." I suggest that the results as presented are not sufficient grounds to arrive at this conclusion.

First, it is quite unfortunate that the authors failed to provide measurements of renal blood flow or renal plasma flow in the rat. Even the para-aminohippuric acid clearances might have provided a satisfactory index of the changes in renal plasma flow. In any study evaluating the macula densa feedback hypothesis for the control of renal blood flow and glomerular filtration rate, it should be established that renal blood flow and glomerular filtration rate are closely coupled and that both exhibit the appropriate renal autoregulatory responses to a decrease in renal perfusion pressure. Second, it would have been very helpful to know more about the overall status of the experimental animals such as their hematocrits and whether they were being expanded during the course of the experiment. It would seem particularly important to establish the effects of bilateral carotid artery occlusion and vagal section on renal hemodynamics. Control recollection data in the absence of aortic constriction is not presented, and the responses following the release of aortic constriction and the reestablishment of control blood pressure are also missing. These data would have allowed one to evaluate whether the observations were manifestations of genuine autoregulatory responses. In addition, information concerning urine flow and sodium excretion at both arterial blood pressures would have allowed one to make additional comparisons between the data presented and the results obtained in our previous study with which the authors are in disagreement (Navar et al., J Clin Invest 53:516-525, 1974). Overall, since the anesthetized rat does not generally exhibit a high degree of autoregulatory efficiency, it might have been advantageous to examine this experimental preparation in greater detail and to document carefully its hemodynamic status. In the absence of a more complete examination, it is quite difficult to accept this study as definitive; several alternative explanations of the data exist.

The results from the dog experiments also cannot be accepted as firm evidence against the macula densa feedback hypothesis. The number of experiments presented is limited, and the degree of autoregulatory efficiency is quite variable with only four experiments demonstrating adequate autoregulation of glomerular filtration rate. The average hematocrit is quite high, and it is not clear if the animals exhibited characteristic changes in urine flow and sodium excretion with changes in blood pressure. Compared with the previous study with which the authors are in disagreement (Navar et al., J Clin Invest 53:516-525, 1974), the evidence presented in this study is somewhat scanty and fails to establish clearly that the authors can consistently obtain a high degree of autoregulatory efficiency in their experimental preparation. It would appear that this criterion would be important in any study that directs itself at the question concerning the mechanism of autoregulatory adjustments in renal vascular resistance.

Therefore, although it appears that the results presented by Dr. Knox and his colleagues are in disagreement with the concept that the distal feedback mechanism serves to control glomerular dynamics during alterations in blood pressure, I submit that firm conclusions regarding the existence of this mechanism should await more intensive and detailed experimental studies. The interested reader should carefully evaluate the bulk of the evidence both at the whole kidney level and at the single nephron level. In addition, the nature of the controversy is such that it can be resolved only by using experimental preparations that have been carefully evaluated with respect to their overall renal hemodynamic status and the characteristics of the autoregulatory responses being observed.

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REPLY TO THE ABOVE LETTER

Dr. Navar's letter in response to the paper "Autoregulation of Single Nephron Filtration Rate in the Presence and the Absence of Flow to the Macula Densa" basically requests additional information for comparison with his previously published studies in the dog. First, in regard to our studies in the rat, renal plasma flow measured by the clearance of para-aminohippuric acid averaged $12.1 \pm 1.4 \text{ ml/kg min}^{-1}$ in control periods and $11.5 \pm 1.2 \text{ ml/kg min}^{-1}$ following the reduction in perfu-
TABLE 1

Effect of Reduced Perfusion Pressure on Urine Flow and Sodium Excretion in Rats and Dogs

<table>
<thead>
<tr>
<th>Species</th>
<th>Urine flow</th>
<th>Fractional sodium excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Experimental</td>
</tr>
<tr>
<td>Dogs</td>
<td>0.16 ± 0.02</td>
<td>0.11 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>P</td>
<td>61 ± 13</td>
<td>44 ± 17</td>
</tr>
<tr>
<td>Rats</td>
<td>0.50 ± 0.15</td>
<td>0.24 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Values are means ± se. Urine flow is given in ml/min for dogs and μliters/kg min⁻¹ for rats.

The basic issue in these studies is whether autoregulation measured with collections from the distal nephrons, that is, in the presence of flow to the macula densa, differs from that measured with collections from the proximal nephrons, that is, in the absence of flow to the macula densa. Although both our studies and those of Dr. Navar's group report numerous data points for proximal tubule collections, it should be noted that our conclusions were based on 36 distal tubules studied both before and after reduction in perfusion pressure, whereas Dr. Navar's group investigated 15 tubules.

I stand by our conclusion that our study provides strong evidence that autoregulation of single nephron filtration rate is unaltered by interruption of tubule fluid flow to the macula densa.

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