Cardiovascular Reactivity in Acute and Chronic Renal Hypertensive Dogs

By Irvine H. Page, M.D., Yoshihiro Kaneko, M.D., and James W. McCubbin, M.D.

Experimental renal hypertension might, in part, be due to heightened sensitivity or "augmented cardiovascular reactivity" which we defined as "the degree with which the heart and peripheral vascular system respond to quantitated stimuli." But its measurement in renal hypertensive animals by a number of investigators has yielded conflicting results for many reasons.

A distinction is often made between the stage of initiation of experimental renal hypertension and the stage after it has become established. It has been shown by McCubbin et al.2 that when arterial pressure rises during the initial stage, the carotid sinus baroreceptor resets so as to perpetuate a higher average level of blood pressure. Further, Reed et al.3 found differences in response to barbiturates and yohimbine during the initial stage compared with the chronic and suggested that the mechanisms of the hypertension differed, the former being humoral, the latter neural.

Subsequently, a number of studies have been made almost exclusively using anesthesia and under a variety of experimental conditions. We have re-examined the problem of whether heightened responsiveness to angiotensin, norepinephrine, tyramine, vasopressin, serotonin and, in the case of chronic renal hypertension, l,l-dimethyl-4-phenyl-piperazinium iodide (DMPP), phenylephrine, 3-hydroxy-phenyl ethanolamine and epinephrine occurs in the two different stages of renal hypertension in dogs with and without the use of pentobarbital. Vasoconstrictor responses of the pump-perfused hind limb have also been measured as an example of the effect of hypertension on an isolated vascular area. Finally, the responses during hypertension elicited by short term infusion of angiotensin were compared with those during the acute and chronic phases of renal experimental hypertension.

Methods

Adult mongrel dogs weighing from 10 to 16 kg were used in all experiments. When general anesthesia was employed, 30 mg/kg of pentobarbital were given iv. Mean arterial pressure was recorded from a cannulated femoral artery by a mercury manometer writing on a moving smoked paper. Test drugs were injected into a cannulated femoral vein. When unanesthetized dogs were used, local anesthesia was used for the cannulation procedures; the dogs lay quietly on their sides while being petted by an attendant to whom they were accustomed.

Acute renal hypertension was produced by partial constriction of one renal artery with a Goldblatt clamp and contralateral nephrectomy performed at the same time. Chronic renal hypertension was produced by the cellophane peri-nephritis method of Page.

In experiments involving perfusion of one hind limb, dogs were anesthetized with morphine (2 mg/kg/sc) followed by pentobarbital (15 mg/kg/iv). Both vagus-sympathetic-depressor trunks were cut. The aorta was tied just below the origin of the external iliac arteries and the right external iliac was cannulated in the caudal direction. With the aid of a constant output finger-type pump, the leg was perfused with the dog's own heparinized blood taken from a cannulated common carotid artery. The pump had a constant output during changes in resistance to flow ranging from 10 to 350 mm Hg. Since change in input pressure causes a small change in the output of pumps of this type, an electronically controlled reservoir with a volume of 10 ml was used in such manner that carotid arterial blood at atmospheric pressure was removed by the pump at a constant rate. A mercury manometer

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was connected into the perfusion circuit between the pump and the perfused leg, and changes in vascular resistance were reflected as changes in perfusion pressure and were recorded on a smoked paper simultaneously with systemic arterial pressure. By adjusting the output of the pump at the start of the experiment, perfusion pressure was made to approximate systemic pressure; flow rates varied between 50 and 85 ml/min in different experiments. Test drugs mixed in physiologic saline (total volume 0.2 to 0.3 ml) were injected through rubber tubing between reservoir and pump directly into the perfusion circuit. Drugs were: norepinephrine bitartrate (0.2 to 0.25 µg), angiotensin (octapeptide, 0.12 to 0.2 µg), serotonin creatinine sulfate (3 to 14 µg), tyramine (0.1 mg) and vasopressin (0.01 to 0.025 unit). An intact sympathetic innervation of the perfused leg was confirmed by presence of an active vasoconstrictor response to occlusion of the remaining unoccluded carotid artery and by reflex vasodilation accompanying the pressor response to norepinephrine given intravenously.

### Results

RESPONSIVENESS BEFORE AND AFTER PRODUCTION OF ACUTE RENAL HYPERTENSION

Following control tests of responsiveness, both before and after administration of pentobarbital, a Goldblatt clamp was tightened on one renal artery and the other kidney removed. When hypertension had been present for an average of eight days (range 2 to 14 days) the dogs were retested with the same dosages of vasoactive drugs under conditions as nearly identical as possible.

Significant changes in responsiveness to four pressor drugs were found (table 1). Response to norepinephrine was increased, and its duration prolonged both in the presence and absence of anesthesia. Response to epinephrine was also increased but not as markedly as that to norepinephrine. The pressor action of serotonin was enhanced, especially in the presence of anesthesia, and its depressor action was decreased. In contrast with the other pressor drugs, response to angiotensin was decreased, though the change in the presence of anesthesia was not significant. The most striking change in response was to tyramine which was markedly enhanced both with and without pentobarbital anesthesia. The duration of response was also prolonged in this group of dogs.

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**Table 1**

<table>
<thead>
<tr>
<th>Test drug</th>
<th>Control period</th>
<th>B.P.*</th>
<th>Days</th>
<th>Dose of drugs</th>
<th>B.P.*</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEP</td>
<td></td>
<td>160±30</td>
<td>1.5</td>
<td>0.25 unit</td>
<td>140±30</td>
<td>1.5</td>
</tr>
<tr>
<td>Angiotensin</td>
<td></td>
<td>160±30</td>
<td>1.5</td>
<td>0.25 unit</td>
<td>140±30</td>
<td>1.5</td>
</tr>
<tr>
<td>Serotonin</td>
<td></td>
<td>160±30</td>
<td>1.5</td>
<td>0.25 unit</td>
<td>140±30</td>
<td>1.5</td>
</tr>
<tr>
<td>Tyramine</td>
<td></td>
<td>160±30</td>
<td>1.5</td>
<td>0.25 unit</td>
<td>140±30</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Means of pressor-depressor responses followed by se of pressor response. 
#Not significant. 
+More ± standard error.
**TABLE 2**

<table>
<thead>
<tr>
<th>Test agent</th>
<th>Condition</th>
<th>No. of dogs</th>
<th>Weight of dogs, avg</th>
<th>Dose, avg</th>
<th>Control period</th>
<th>Chronic hypertensive phase</th>
<th>Significance of difference in response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B.P. avg</td>
<td>Response</td>
<td>B.P. avg</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>unanesth.</td>
<td>12</td>
<td>10.8</td>
<td>6.7</td>
<td>137 ± 3.9</td>
<td>28 ± 2.7</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>anesth.</td>
<td>9</td>
<td>12.2</td>
<td>3.0</td>
<td>140 ± 3.7</td>
<td>29 ± 4.3</td>
<td>153</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>unanesth.</td>
<td>6</td>
<td>11.8</td>
<td>2.9</td>
<td>149 ± 2.4</td>
<td>13 ± 0.9</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>anesth.</td>
<td>9</td>
<td>12.2</td>
<td>2.7</td>
<td>141 ± 3.7</td>
<td>19 ± 3.9</td>
<td>153</td>
</tr>
<tr>
<td>Angiotensin</td>
<td>unanesth.</td>
<td>12</td>
<td>10.8</td>
<td>0.55</td>
<td>137 ± 4.4</td>
<td>34 ± 4.9</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>anesth.</td>
<td>9</td>
<td>12.2</td>
<td>0.36</td>
<td>141 ± 3.6</td>
<td>19 ± 2.2</td>
<td>153</td>
</tr>
<tr>
<td>Serotonin</td>
<td>unanesth.</td>
<td>6</td>
<td>11.8</td>
<td>136</td>
<td>148 ± 2.9</td>
<td>13 ± 1.3</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>anesth.</td>
<td>9</td>
<td>12.2</td>
<td>129</td>
<td>141 ± 3.5</td>
<td>5 ± 4.3</td>
<td>153</td>
</tr>
<tr>
<td>Tyramine</td>
<td>unanesth.</td>
<td>6</td>
<td>11.8</td>
<td>500</td>
<td>149 ± 2.5</td>
<td>17 ± 3.0</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>anesth.</td>
<td>9</td>
<td>12.2</td>
<td>430</td>
<td>143 ± 3.5</td>
<td>19 ± 2.5</td>
<td>153</td>
</tr>
</tbody>
</table>

*Means of pressor-depressor response followed by se of pressor response.
†ns: not significant.
±Mean ± standard error.

**VARIABILITY**

Table 2. Responses in Chronic Phase of Experimental Renal Hypertension (measured in same dogs and with same doses).

To insure against variability in response and to avoid the possibility of great differences in control period, the same dogs were used for the control period and the experimental period. The test drug was injected intravenously at two or more times during each of four experiments. The only one changed significantly.

**HYPERRESPONSIVE RENAL HYPERTENSIVE DOGS**

Hypertension was produced by the perinephritis method of Paget and responsiveness to noradrenaline was measured after hypertension had been produced for several weeks. Because no significant differences were noted between the groups of animals, the experiments were extended to include hypertension produced by other methods of renal hypertension. The data on the chronic renal hypertensive dogs are summarized in Table 1.
was constant, and the injections were made both before and after induction of anesthesia with pentobarbital. The conditions under which the tests were made were kept as nearly constant as possible.

The responses to epinephrine and serotonin showed the greatest variability but, on the whole, changes were relatively minor and, in essentially all cases of change in response, the average change was a slight decrease following induction of hypertension, both in anesthetized and unanesthetized dogs, even though the intervals between some tests were very long, being over three months in one instance.

Similar experiments were done on additional normal, sham operated and chronic hypertensive dogs and 10 anesthetized ones and all the data then grouped and means and standard errors determined for two measurements. These data show very little difference in the mean response to any of the five pressor drugs either in the anesthetized or unanesthetized dogs, even though the average interval between tests was long, being 55 days for the unanesthetized and 36 days for the anesthetized dogs.

Next, the effect of sham operation on responsiveness to the same five pressor drugs was measured. After control tests, one kidney was removed and a Goldblatt clamp placed on the renal artery of the opposite kidney but not tightened. An average of four and one-half days after operation, responses were re-measured, before and after induction of anesthesia with pentobarbitol, and the tests were repeated in the same manner several months after operation. The mean values of responses to all drugs were not significantly different either at the early or the late test.

With this information that the average values for pressor responses to different drugs can be counted upon to remain reasonably constant over long periods of time, even after sham operation for production of hypertension accompanied by unilateral nephrectomy, and in both the presence and the absence of general anesthesia, we felt justified in comparing responses before and after development of hypertension.

**EFFECT OF ANGIOTENSIN INFUSION ON PRESSOR RESPONSIVENESS BEFORE AND THEN DURING ACUTE AND CHRONIC RENAL HYPERTENSION**

The effect of hypertension produced by infusion of angiotensin on pressor responsiveness was compared with the effect produced by renal artery constriction and contralateral nephrectomy. During control measurements, angiotensin was infused into anesthetized dogs at an average rate of 0.15 μg/kg/min. After approximately 20 min when arterial pressure had stabilized at an average of 170 mm Hg, having risen from an average resting level of 141 mm Hg, responses to norepinephrine and tyramine were measured and compared with the preinfusion values (table 3). Responses to norepinephrine were not changed significantly; those to tyramine were more than doubled.

In the same group of dogs, during the acute phase of renal hypertension (3 to 14 days after constriction of a renal artery and contralateral nephrectomy) mean arterial pressures averaged 189 mm Hg. The preinfusion responses to single injections of both norepinephrine and tyramine were increased as in the previous group of dogs with acute renal hypertension. Infusion of angiotensin now failed to cause further change in response to either norepinephrine or tyramine.

In five dogs in which chronic hypertension was elicited, infusion of angiotensin caused an increase in response to tyramine but did not modify response to norepinephrine. The total increase in response to tyramine was the same during acute renal hypertension as during chronic renal hypertension plus infusion of angiotensin.

**RESPONSIVENESS OF A PERFUSED HIND LIMB OF NORMOTENSIVE COMPARED WITH ACUTE AND CHRONIC RENAL HYPERTENSIVE DOGS**

A. Acute Renal Hypertension

Eight dogs were tested at from 2 to 12 days (average five and one-half days) after application of a clamp to one renal artery and removal of the opposite kidney. Arterial pressures at this time ranged from 173 to 211 mm Hg (average 192 mm Hg). The vasoconstrictor
response of the perfused leg to angiotensin injected into the arterial circulation was markedly reduced (table 4) when compared with normotensive controls and sham-operated controls, but response to norepinephrine was not changed significantly. The pressor response to serotonin was much increased and the depressor response was reduced, while response to tyramine was unchanged. Sham operation did not change the normal responsiveness.

B. Chronic Renal Hypertension

Thirteen dogs with mean arterial pressures ranging from 191 to 232 mm Hg (average 211 mm Hg) at the time of the experiment, were tested from 25 to 110 days (average 58 days) after wrapping one kidney in cellophane and removing the other, and in three dogs after constricting one renal artery and removing the other kidney.

In contrast with dogs with acute renal hypertension, where the response to angiotensin was reduced, responses of the perfused hind limb of dogs with chronic renal hypertension were normal (table 4). No differences in responsiveness were observed between dogs made chronically hypertensive by cellophane perinephritis and those made hypertensive by constricting one renal artery and nephrectomy.

C. Hypertension Due to Infusion of Angiotensin

Since a selective and marked decrease in the pressor response to angiotensin was found in dogs with acute renal hypertension and in their perfused legs, it was assumed that the decrease was related to an increased amount of circulating endogenous angiotensin. Accordingly, a comparison was made with normal dogs made hypertensive by infusing angiotensin. During the hypertension caused by the infusion there was striking decrease of the vasoconstrictor response to superimposed injections of angiotensin (table 5); the much smaller responses were like those seen in the group of dogs with acute renal hypertension. Response to norepinephrine, on the other hand, was not significantly changed in the perfused hind limb. Response to another polypeptide, vasopressin, was reduced like that to angiotensin.
Responses to Norepinephrine, Angiotensin, Serotonin and Tyramine in the Perfused Leg of Renal Hypertensive Dogs

<table>
<thead>
<tr>
<th></th>
<th>No. of dogs</th>
<th>Weight of dogs avg</th>
<th>Systemic pressure avg</th>
<th>Rate of perfusion, ml/min</th>
<th>Perfusion pressure avg</th>
<th>Dose, μg</th>
<th>Response†</th>
<th>Norepinephrine response‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>13</td>
<td>12.5</td>
<td>145 ± 4.1</td>
<td>60</td>
<td>138 ± 3.9</td>
<td>0.24</td>
<td>26–4 ± 4.2</td>
<td></td>
</tr>
<tr>
<td>Sham-operated</td>
<td>3</td>
<td>12.4</td>
<td>145 ± 8.4</td>
<td>65</td>
<td>151 ± 7.5</td>
<td>0.25</td>
<td>31–2 ± 2.5</td>
<td></td>
</tr>
<tr>
<td>Operated</td>
<td>2</td>
<td>12.4</td>
<td>150 ± 9.0</td>
<td>63</td>
<td>148 ± 6.5</td>
<td>0.25</td>
<td>32–3 ± 13</td>
<td></td>
</tr>
<tr>
<td>Acute renal hypertensive</td>
<td>8</td>
<td>13.4</td>
<td>192 ± 5.9</td>
<td>61</td>
<td>213 ± 7.5</td>
<td>0.24</td>
<td>ns†</td>
<td></td>
</tr>
<tr>
<td>Chronic renal hypertensive</td>
<td>13</td>
<td>11.6</td>
<td>208 ± 4.8</td>
<td>64</td>
<td>216 ± 7.4</td>
<td>0.24</td>
<td>ns†</td>
<td></td>
</tr>
</tbody>
</table>

*Pressor-depressor response followed by se of pressor response.
†ns: not significant.
‡Mean ± standard error.

Discussion

Because of widely divergent results of measurements of vascular responsiveness in different animals before and after eliciting renal hypertension, we have re-examined the problem in dogs during both the acute and chronic phases of hypertension and with and without pentobarbital anesthesia. Only a few studies had previously been done on dogs, most having been done on rats or rabbits. The numerous studies on these latter two species are not reviewed here. In six dogs Verney and Vogt5 found no change in response to epinephrine but an irregular increase in pressor response to tyramine. There was no difference in response to epinephrine, histamine, barium chloride, renin and angiotensin in a larger number of chronic renal hypertensive dogs anesthetized with pentobarbital in the study of Page and Taylor.6

The experiments we now report show that an increase in responsiveness to norepinephrine, epinephrine, tyramine and serotonin, either with or without pentobarbital anesthesia, occurred regularly during the first days after renal hypertension was elicited. In contrast, response to angiotensin was reduced. If acute renal hypertension is, in part, due to increase in renin secretion and angiotensin formation, the following two mechanisms might be set in operation: 1) Angiotensin receptors are partially saturated so that endogenous angiotensin no longer has as much pressor effect. 2) Angiotensin increases the pressor effectiveness of endogenous norepinephrine† so accounting for the increased response to tyramine which depends in the main for its own action on norepinephrine release. These mechanisms might explain the increases in response to tyramine and decrease to angiotensin but not the observed increase to endogenous norepinephrine, epinephrine and the pressor effect of serotonin. We can speculate that during the acute phase of renal hypertension there is an increase of humoral stimulation and decrease of neural tone with resultant supersensitivity. It is the sort of increased responsiveness to a variety of pressor substances that Page and Taylor8 found when ganglion-blocking agents such as tetraethylammonium chloride were given. We have for some time hoped that we might find a normally occurring agent that regulates ganglion transmission and therefore indirectly the responsiveness of blood vessels.

The increased response to norepinephrine during the chronic phase was so small that a large number of experiments was necessary to make sure of it at all. If there is any increase, it is so small that it can be ruled out as an
important mechanism in the genesis of the chronic hypertension in these dogs. There was no heightening of response to serotonin, DMPP, 3-hydroxyphenylethanolamine and angiotensin. Tyramine remained the only substance showing increased responsiveness. On this basis, there is little to suggest that during chronic renal hypertension the responses to chemical stimulation are abnormal. The exception of tyramine may well be due to a small rise in angiotensin formation increasing the effectiveness of endogenous norepinephrine, so contributing to an elevated neural tone as an important part of the mechanism maintaining increased peripheral resistance.7

One of the major difficulties that has plagued all experiments in which cardiovascular reactivity has been measured is the variability of the responses due not only to the kind and depth of anesthesia but to spontaneously occurring change. We believe the variability in part is due to the fact that the degree of participation of the components of the mechanisms controlling arterial pressure levels are often not the same even though blood pressure levels are identical.8 For this reason the test drug is not necessarily acting on the same mechanism. Being aware of this, we took unusual precautions to insure that the variability was not greater than the supposed effect of the test drugs. For example, certain types of preparations, such as the perfused hind quarters of rats, were so variable in our hands as to be unreliable for detecting relatively small changes in reactivity.

To bring the results a little closer to the problem of the mechanism of experimental renal hypertension, arterial hypertension was produced by infusing angiotensin and the control responses were compared with those following the production of acute and then chronic hypertension, usually in the same dogs. During the acute phase, angiotensin infusion failed to cause further increase in response to the already elevated response to single injections of norepinephrine and tyramine. During the chronic phase, infusion of angiotensin caused an increased response to tyramine but did not alter response to norepinephrine. Since the total increase in response to tyramine was the same during acute renal hypertension as during chronic hypertension, plus the infused angiotensin, it is reasonable to suggest that much less angiotensin was present in the blood during chronic renal hypertension. During the acute phase, angiotensin is already present; addition of more of it would not be expected to cause further increase in response to either norepinephrine or tyramine.

Lastly, an isolated vascular bed, the dog's hind limb, was perfused with blood and the responses to angiotensin and norepinephrine were compared before and after production of acute hypertension by a clamp on one renal artery. The response to angiotensin was
Effects of Angiotensin Infusion into Perfused Leg and Body of Normal Dogs

<table>
<thead>
<tr>
<th>Test agent</th>
<th>No. of dogs</th>
<th>Weight of dogs, kg</th>
<th>Rate of infusion, μg/kg/min</th>
<th>Rate of perfusion, ml/min</th>
<th>Control Pressure*, mm Hg</th>
<th>Control Response*, mm Hg</th>
<th>During Infusion Pressure*, mm Hg</th>
<th>During Infusion Response*, mm Hg</th>
<th>Significance of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>7</td>
<td>12.6</td>
<td>0.83</td>
<td>66</td>
<td>145 ± 4.0</td>
<td>34 ± 3.1</td>
<td>203 ± 3.8</td>
<td>26 ± 2.8</td>
<td>ns</td>
</tr>
<tr>
<td>Angiotensin</td>
<td>6</td>
<td>12.8</td>
<td>0.94</td>
<td>65</td>
<td>145 ± 4.8</td>
<td>29 ± 2.7</td>
<td>215 ± 4.6</td>
<td>5 ± 3.2</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>5</td>
<td>12.8</td>
<td>1.08</td>
<td>65</td>
<td>154 ± 3.0</td>
<td>30 ± 2.7</td>
<td>205 ± 4.8</td>
<td>12 ± 2.4</td>
<td>P &lt; 0.025</td>
</tr>
</tbody>
</table>

*Mean ± standard error.

ns: not significant.

When the chronic phase of hypertension developed, i.e., after an average of 58 days, responses to angiotensin and norepinephrine of perfused leg vessels were normal, as they were also in intact animals with chronic renal hypertension. If the decrease in response to angiotensin of the blood vessels of the perfused leg was due to exposure to blood-borne endogenous angiotensin during the acute phase of hypertension, then the same decrease should be produced in normal dogs by perfusing them with angiotensin. This proved to be true. A high degree of specificity to angiotensin, however, cannot be assumed because we also found that the responses to vasopressin were decreased. The vasopressor responses to angiotensin, norepinephrine, epinephrine, serotonin, and angiotensin seem to form a consistent pattern composed of the varied phases of experimental renal hypertension and the hypertension elicited by infusion of angiotensin. They suggest that during the acute phase of hypertension increased quantities of endogenous angiotensin are present. During the chronic phase the increased humoral tone of the blood vessels due to exposure to blood-borne endogenous angiotensin during the acute phase of hypertension probably changed the response to serotonin in peripheral resistance vessels.

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*TABLE 5*
CARDIOVASCULAR REACTIVITY seems relatively more dependent on neural control.

Summary

Both before and after pentobarbital anesthesia, cardiovascular responsiveness to norepinephrine, epinephrine and serotonin was increased and that to angiotensin was decreased when experimental renal hypertension was first elicited. Response to tyramine was strikingly enhanced.

Several weeks later, during the chronic phase of hypertension, there was a slight and scarcely significant heightened response to norepinephrine, a clearly increased response to tyramine, and no change in that to serotonin, dimethylphenylpiperazinium iodide, and 3-hydroxy-phenyl-ethanolamine HCl.

Study of the problem of variability of responsiveness showed relatively little difference in mean response to any of five pressor drugs with or without anesthesia and after sham operation.

Hypertension produced by infusion of angiotensin into normal anesthetized dogs did not change the response to norepinephrine but more than doubled that to tyramine. When acute renal hypertension was produced in the same dogs, angiotensin infusion failed to cause further change in response to either substance. Infusion of angiotensin into dogs with chronic renal hypertension caused increased response to tyramine but not to norepinephrine.

The perfused hind legs of dogs with acute renal hypertension showed clearly reduced responses to angiotensin with no concurrent change in responses to norepinephrine. The pressor response to serotonin was increased while that to tyramine was unchanged. During chronic hypertension responses were like the normal values.

Hypertension caused by infusion of angiotensin decreased greatly the vasoconstrictor response to superimposed injections of angiotensin into the perfused leg circuit while norepinephrine responses were unchanged. Response to another peptide, vasopressin, was reduced like that to angiotensin.

These studies suggest that during acute renal hypertension increased quantities of angiotensin are present and that there is a decrease in neural tone. The finding that during the chronic phase of hypertension, the response to tyramine alone remained elevated, suggests the presence of small amounts of angiotensin, i.e., enough to increase the pressor effectiveness of endogenous norepinephrine released by tyramine. During the chronic phase of hypertension, peripheral resistance appears relatively more dependent on neural control.

References

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