Hemodynamic Effects of Angiotensin
in Normal and Environmentally Stressed Monkeys

By Ralph P. Forsyth, Ph.D., Barry I. Hoffbrand, B.M., M.R.C.P.,
and Kenneth L. Melmon, M.D.

SUMMARY
Simultaneous regional blood flow and resistance measurements were made in 21 organs in 11 supine unanesthetized rhesus monkeys before and during two different doses of intravenously infused angiotensin II or saline. Systemic arterial pressure and total peripheral resistance significantly increased at both infusion rates in the six experimental monkeys, compared with changes in five control monkeys; cardiac output decreased at the high dose level. Among major organs, the kidneys, skin, liver (hepatic artery), and mesentery had reductions in the fraction of cardiac output they received and, thus, the greatest increase in resistance and decrease in blood flow. No organ had a significant increase in its blood flow; however, skeletal muscle and bone were normally perfused due to increases in the fraction of cardiac output they received.

Four other monkeys received continuous intravenous angiotensin infusions at initially suppressor rates for periods of 26 to 30 days. There were steady increases of systemic arterial blood pressure due to a rise in total peripheral resistance which reached a plateau in about 5 days. Avoidance schedules or other environmental stresses in these angiotensin-infused monkeys produced much more marked pressor episodes than those which occur in noninfused monkeys. These observations support the hypothesis that small amounts of angiotensin can potentiate sympathetic mediated vasomotor activity.

Additional Indexing Words:
Distribution of cardiac output
Blood pressure
Cardiac output
Regional blood flow and resistance
Sympathetic nervous system
Total peripheral resistance
Hypertension

ALTHOUGH it is the most potent vasoconstrictor substance known, angiotensin plays an as yet uncertain role in circulatory control in both normal and pathological states. There have been many studies of the hemodynamic effects of infused angiotensin but only two,1 2 both in rats, in which its effect on blood flow to many organs has been measured simultaneously. We have investigated the changes in regional blood flow and resistance produced by acute infusions of angiotensin in conscious rhesus monkeys at two dose levels

From the Cardiovascular Research Institute and Division of Clinical Pharmacology, University of California, San Francisco Medical Center, San Francisco, California 94122.

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B. I. Hoffbrand was a San Francisco Bay Area Heart Association Senior Research Fellow; his current address is Whittington Hospital, London N. 19, England.

Address for reprints: Ralph P. Forsyth, Ph.D., Cardiovascular Research Institute, University of California, San Francisco Medical Center, San Francisco, California 94122.

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per animal. These changes are compared with the abnormalities in the distribution of cardiac output believed to occur in hypertension and hemorrhage, two conditions where the action of angiotensin has been implicated in man.

There is ample evidence that the sympathetic nervous system is involved in the pressor effects of angiotensin, particularly at low doses. Angiotensin can potentiate the effects of sympathetic nervous system activity and circulating catecholamines. McCubbin and Page have reported that long-term infusions of initially subpressor doses of angiotensin in dogs caused markedly enhanced pressor responses to both environmental stimuli and injected tyramine; they and their associates postulated that this action of angiotensin might be responsible for the enhanced pressor activity often noted in labile essential, as well as renal, hypertension. In a second series of experiments using the same primate preparation we have investigated the effects of initially subpressor angiotensin infusions in modifying hemodynamic responses to environmental stress. These effects were compared to those previously found in noninfused monkeys encountering the same stress situation.

Methods

Acute Hemodynamic and Regional Changes

Eleven male rhesus monkeys (Macaca mulatta) were anesthetized with sodium pentobarbital (30 mg/kg). Polyvinyl catheters were inserted into the abdominal aorta and vena cava via the iliac vessels, and in the left ventricle (LV) of the heart via the left common carotid artery. After recovering from this operation the monkeys were placed in primate restraining chairs modified to allow tilting inside sound-protected isolation booths. The catheters, brought out through the skin near the umbilicus to the outside of the booth, were flushed continuously with a lightly heparinized (5 USP units/ml) 0.9% NaCl solution at 1.0 ml/hr. All measurements and infusions could be performed without disturbing the monkeys.

The experiments were performed 6-9 days following surgery. The monkeys were tilted to a supine position 1-2 hr before the experiment began. Each of the six experimental monkeys (weighing from 3.4 to 6.1 kg) received a 20 to 40 min infusion through the venous catheter of either a low (0.015 to 0.0374 μg kg⁻¹ min⁻¹) or high (0.08 to 0.21 μg kg⁻¹ min⁻¹) dose of angiotensin (1-L-asparaginyl-5-L-valyl angiotensin octapeptide) (Hypertensin, Ciba). After the infusion and measurements were completed the monkeys were tilted to the normal upright position. The next morning the procedure was repeated with the dose levels changed, so that each monkey received either a low and a high dose (N = 3) or a high and a low dose (N = 3) on succeeding days. The other five monkeys (weighing from 4.1 to 4.7 kg) selected randomly, served as a control group. In the control group, the same procedures were used and the same measurements made except that saline, rather than angiotensin, was infused at a similar speed and volume.

Prior to and during the angiotensin infusion, arterial and LV end-diastolic pressures (LVEDP) were continuously measured with Statham P23Gb pressure transducers placed at midthoracic levels. Central venous pressure was similarly measured before and intermittently during the infusion. Cardiac output (CO) determinations were done in duplicate prior to (baseline) and near the end of the infusion period by the dye-dilution method of Hamilton, with indocyanine green injected into the LV, and a Waters X301 densitometer. All these measurements were recorded on a type R Beckman recorder. Samples of arterial blood were taken before each cardiac output measurement for hematocrit, pH, and blood gas determination, the latter measured by Radiometer microelectrodes at 38°C.

The distribution of cardiac output was determined after each cardiac output measurement using the labeled microsphere technique of Rudolph and Heyman. The validity and reliability of these measurements, as well as those for normal values in monkeys, have been reported. Each time a regional distribution measurement is made, a batch of 5,000-10,000 50 μ-diameter plastic microspheres labeled with either 125I, 51Cr, 85Sr, or 46Sc (varying from 0.5 to 1.5 x 10⁶ CPM) was injected over a 15-20 sec period into the LV. These spheres have been shown to mix well with blood in the LV and travel with the blood until trapped by tissue arterioles of the end organs. The number of spheres and, thus, the amount of radioactivity in each organ or tissue has been shown to be proportional to blood flow to it. The reliability of the distributional measurements is good for those organs that receive more than 1% of the output.

At the end of each experiment the animals were killed and dissected, and each of 21 organs plus remaining miscellaneous tissue was weighed to 0.1 g. Since each of the nuclides used has a characteristic gamma emission pattern within the
range of from 0 to 1,000 kev, the amount of gamma emission from each nuclide in each organ was calculated by using a scintillation counter and a pulse height analyzer. The percentage of cardiac output to each organ was the amount of each nuclide radioactivity in that organ, divided by the total body count (calculated by adding the radioactivity counted in the 21 organs and miscellaneous tissue) of that nuclide. The full details of the dissection procedure, of the tissue radioactivity counting, and of the mathematics involved in distinguishing a mixture of these gamma-emitting isotopes are to be found elsewhere. Blood flow was calculated as the dye-dilution CO \times \text{the fraction of CO received by each organ; resistance in each organ was the pressure gradient (Pa} - \text{Pv})/\text{flow.}

Changes in the fraction of cardiac output, blood flow, and resistance/100 g tissue in each organ for each monkey during the angiotensin or saline infusion period were expressed as a percentage of the appropriate baseline measurement. The changes at both low (N = 6) and high (N = 6) doses in each organ in the experimental group were compared to the changes found during both days 1 and 2 (N = 10) in the control group. Because of the skewed distribution of many of the regional variables, the regional statistical differences were evaluated with the nonparametric Mann-Whitney U test. Similarly, change scores for the systemic measurements for each of the infused monkeys at each dose level were compared by t-test for independent groups with the change scores in the 10 measurements in the five control monkeys. The numerous comparisons made with both the systemic and regional measurements increase the probability that some of the reported significant results may have occurred by chance.

**Chronic Hemodynamic Changes**

Four monkeys weighing from 4.5 to 5.8 kg were prepared, as previously described, with arterial and central venous catheters. After the surgery they were left sitting in their restraining chairs inside their isolation booths for the duration of the experimental period which lasted from 7 to 8 weeks. Timing apparatus was arranged so that a pump flushed 1 ml of 0.9% NaCl (which contained 5 USP units of heparin) through the arterial catheter once each hour; the blood pressure was then automatically recorded for 2 min on a Beckman type R recorder. The data presented represent averages of these hourly measurements. Infusions of saline or angiotensin II were continuously delivered at 1 ml/hr through the venous catheter. Cardiac output was determined as previously described, except that the dye was injected through the venous catheter.

The blood pressure and intermittent cardiac output values were measured for 7 to 10 days after surgery. Monkeys were then trained from 1 to 2 hr daily, for 6 to 10 days, on a 20-sec Sidman avoidance schedule. Each lever press on this type of schedule resets a 20-sec timer which, if allowed to complete its cycle, causes a noxious shock to be delivered to the monkey's tail electrode. We considered the monkey to be trained when he limited his shocks to 10 or fewer in an hour.

The monkeys were then allowed a 9 to 12 day postraining baseline period with no avoidance schedule. After this time the monkeys received a continuous infusion of 25 to 30 \( \mu \)g/kg/24 hr (17 to 21 ng/kg/min) of angiotensin II in a 0.9% NaCl solution through their central venous catheter in a volume of 1 ml/hr for 26 to 30 days. This dose level was chosen because it was near that given in some other studies of continuous angiotensin infusions and it was found not to have systemic effects over a 6-hr infusion period. After 11 to 15 days of the infusion the monkeys were subjected to a 20-sec Sidman avoidance schedule lasting 12 hr/day (from 2 to 8 AM and from 2 to 8 PM) for 15 days. Previous work with the same preparation has established the usual hemodynamic response to this type of schedule. Control monkeys sitting in their chairs but having no work schedule have very little change (except for the first few days after surgery) in their daily averaged systemic arterial pressure over a period up to 8 months.

**Results**

**Acute Hemodynamic and Regional Changes**

The systemic hemodynamic measurements for the five control and six angiotensin-infused monkeys are shown in table 1. The control animals showed little change throughout the experiment; their baseline arterial pressures, cardiac output, and pulse rate were higher than the angiotensin-infused monkeys. Compared with changes in the control group both angiotensin dose levels significantly increased systemic arterial pressures and total peripheral resistance. Cardiac output was decreased and LVEDP was increased at the high, but not the low, dose. There was no significant change in either group of arterial pCO\(_2\), pO\(_2\), pH, or hematocrit, which remained at normal levels throughout the experiments.

There was only one significant difference between the experimental and control groups in the first day's baseline distribution of...
Table 1

**Measurements in the Six Experimental and Five Control Monkeys**

<table>
<thead>
<tr>
<th></th>
<th><strong>Experimental group</strong></th>
<th><strong>Control group</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low dose baseline (N = 6)</td>
<td>During low dose (N = 6)</td>
</tr>
<tr>
<td></td>
<td><strong>Mean</strong></td>
<td><strong>sd</strong></td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>136</td>
<td>8</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>85</td>
<td>6</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)‡</td>
<td>111</td>
<td>9</td>
</tr>
<tr>
<td>Cardiac output (ml · min⁻¹ · kg⁻¹ body weight)</td>
<td>334</td>
<td>67</td>
</tr>
<tr>
<td>Total peripheral resistance (mm Hg · liter⁻¹ · min⁻¹ · kg body weight)</td>
<td>345</td>
<td>61</td>
</tr>
<tr>
<td>Pulse rate (beats/min)</td>
<td>162</td>
<td>25</td>
</tr>
<tr>
<td>Stroke volume (ml/kg body weight)</td>
<td>2.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td>8.6</td>
<td>6</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>-1</td>
<td>3</td>
</tr>
</tbody>
</table>

*Values for the experimental groups refer to the stated dose levels, whether or not the dose was given the first or second day. Both the first and second day values in the control group were used so that there are two measurements before and during the saline infusion for each of the five control monkeys.

†Changes significantly different (P < 0.01, t-test) from control group changes. See text for discussion of methods of calculation.

‡Electronically integrated.
## Table 2

*Total Body and Regional Circulatory Changes after Angiotensin Infusion in Six Monkeys*

<table>
<thead>
<tr>
<th></th>
<th>Absolute fraction of cardiac output at first day baseline</th>
<th>Percent cardiac output</th>
<th>Flow</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>sd</td>
<td>Mean</td>
<td>sd</td>
</tr>
<tr>
<td>Body (total)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>5.0</td>
<td>1.9</td>
<td>107</td>
<td>18</td>
</tr>
<tr>
<td>Brain</td>
<td>5.4</td>
<td>1.6</td>
<td>90</td>
<td>12</td>
</tr>
<tr>
<td>Kidney</td>
<td>15.5</td>
<td>4.5</td>
<td>77*</td>
<td>18</td>
</tr>
<tr>
<td>Skin</td>
<td>8.5</td>
<td>3.3</td>
<td>71†</td>
<td>16</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>19.7</td>
<td>7.2</td>
<td>146*</td>
<td>44</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>0.2</td>
<td>0.1</td>
<td>117</td>
<td>41</td>
</tr>
<tr>
<td>Chest wall</td>
<td>1.6</td>
<td>0.4</td>
<td>135†</td>
<td>31</td>
</tr>
<tr>
<td>Lung (bronchial artery)</td>
<td>0.9</td>
<td>0.9</td>
<td>81</td>
<td>26</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.2</td>
<td>0.1</td>
<td>104</td>
<td>51</td>
</tr>
<tr>
<td>Bone‡</td>
<td>12.5</td>
<td>2.9</td>
<td>130*</td>
<td>33</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>1.2</td>
<td>0.6</td>
<td>82</td>
<td>44</td>
</tr>
<tr>
<td>Fat</td>
<td>2.5</td>
<td>2.5</td>
<td>79†</td>
<td>17</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.2</td>
<td>0.1</td>
<td>38*</td>
<td>48</td>
</tr>
</tbody>
</table>

Values are expressed as a percent of baseline measurements; see text for discussion of methods of calculation.

*Significantly different from control changes (P < 0.05, Mann-Whitney U test).
†Significantly different from control changes (P < 0.01, Mann-Whitney U test).
‡Includes limb bone, skull, and spine.
Table 3

Regional Circulatory Changes after Angiotensin Infusion in Organs Comprising Total Liver Flow in Six Monkeys

<table>
<thead>
<tr>
<th></th>
<th>Absolute fraction of cardiac output at first day baseline</th>
<th>Percent cardiac output</th>
<th>Flow</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>sd</td>
<td>Low dose</td>
<td>Mean</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.0</td>
<td>0.3</td>
<td>107</td>
<td>29</td>
</tr>
<tr>
<td>Small intestine</td>
<td>2.7</td>
<td>1.1</td>
<td>101</td>
<td>30</td>
</tr>
<tr>
<td>Large intestine</td>
<td>3.1</td>
<td>0.5</td>
<td>81*</td>
<td>23</td>
</tr>
<tr>
<td>Cecum</td>
<td>0.5</td>
<td>0.3</td>
<td>86</td>
<td>36</td>
</tr>
<tr>
<td>Gastrointestinal organs†</td>
<td>3.2</td>
<td>1.4</td>
<td>93</td>
<td>26</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.9</td>
<td>2.2</td>
<td>104</td>
<td>18</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.6</td>
<td>0.5</td>
<td>86</td>
<td>14</td>
</tr>
<tr>
<td>Mesentery</td>
<td>1.3</td>
<td>0.4</td>
<td>54†</td>
<td>24</td>
</tr>
<tr>
<td>Portal vein organs§</td>
<td>13.1</td>
<td>3.1</td>
<td>89</td>
<td>20</td>
</tr>
<tr>
<td>Liver (hepatic artery)</td>
<td>8.2</td>
<td>3.7</td>
<td>70†</td>
<td>8</td>
</tr>
<tr>
<td>Total liver flow**</td>
<td>21.3</td>
<td>4.7</td>
<td>83*</td>
<td>18</td>
</tr>
</tbody>
</table>

Values are expressed as a percent of baseline measurements; see text for discussion of methods of calculation.

*Significantly different from controls (P < 0.05, Mann-Whitney U test).
†Significantly different from controls (P < 0.01, Mann-Whitney U test).
§Includes stomach, small and large intestines, and cecum.
††Includes gastrointestinal organs, spleen, pancreas, and mesentery.
**Includes portal vein and hepatic artery flow.
cardiac output in any of the organs measured; the percentage of the cardiac output to the hepatic artery was higher (x = 8.2%) in the angiotensin compared to the control (x = 3.8%) group. These measurements for the experimental group are shown in tables 2 and 3. There were no significant changes in the regional variables in the control group during the course of the experiment.16

Both levels of angiotensin caused significant reductions in the fraction of cardiac output and blood flow and a dose-related rise in resistance to the kidney, skin, liver (hepatic artery), mesentery, fat, and thyroid as shown in tables 2 and 3. Chest wall and bone received an increased fraction of the cardiac output at both dose levels, as did skeletal muscle at the low dose and the heart and diaphragm at the high dose. In eight organs (brain, lung [bronchial artery], adrenals, stomach, small intestine, cecum, spleen, and pancreas) there was little distributional change, the blood flow and resistance changing in proportion to the changes in cardiac output and total peripheral resistance. The absolute values of blood flow per 100 g tissue in seven major organs with the angiotensin infusions are shown in figure 1.

**Chronic Hemodynamic Changes**

The mean daily systemic arterial pressures and pulse rates of the four monkeys receiving the continuous angiotensin infusions and avoidance conditioning schedules are shown in figure 2. Over the 11-day infusion period, there were gradual increases of arterial pressures, and a fall in pulse rate which reached a plateau on the fifth day. At this time and during the remaining 10 days cardiac output values (measured every 3 days) were slightly lower (mean of 87% of baseline); total peripheral resistance rose to 129% of baseline values. Over the 11-day infusion periods systolic and diastolic pressures averaged 14 and 10 mm Hg, respectively, higher than the posttraining baseline period; pulse rate fell an average of 13 beats/min. Analyses of the mean diurnal cycles of the four monkeys showed that pressures and pulse rates were changed equally throughout the day.

When the avoidance schedules were initiated the monkeys had an acute rise in their pressures and pulse rate which gradually
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Mean daily systemic arterial blood pressure and pulse rate values measured hourly in four monkeys before and after receiving 25 to 30 µg/kg/24 hr intravenous angiotensin infusions and during 15 days of avoidance conditioning stress. Each day's value is the mean of 96 measurements. Co = the mean cardiac output measurements (ml·min⁻¹·kg⁻¹·body weight); TPR = total peripheral resistance, Ap (mm Hg)/cardiac output (in liters/min).

decreased, but remained elevated, over the 15-day period they worked on their schedules (fig. 2). This pressure rise was, initially, entirely due to a rise in cardiac output. By the end of the 15-day schedule period the cardiac output was similar to the values obtained during the latter part of the angiotensin infusion.

The pressor responses to the schedule in the angiotensin-infused monkeys are compared in Table 4 to those obtained previously in four monkeys working on identical schedules. The angiotensin-infused monkeys had a significantly greater pressor response to the schedule compared to the normal group which lasted throughout the entire 15-day period.

### Table 4

**Absolute Mean Hemodynamic Changes* During Fifteen Days of Avoidance Conditioning in Monkeys with and without Angiotensin Infusions**

<table>
<thead>
<tr>
<th></th>
<th>Days on schedule</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>sd</td>
<td>N</td>
</tr>
<tr>
<td>Systolic arterial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pressure (mm Hg)</td>
<td>C</td>
<td>9</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>24†</td>
<td>7</td>
</tr>
<tr>
<td>Diastolic arterial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pressure (mm Hg)</td>
<td>C</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>19†</td>
<td>6</td>
</tr>
<tr>
<td>Pulse rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(beats/min)</td>
<td>C</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>21</td>
<td>11</td>
</tr>
</tbody>
</table>

*Changes of the four experimental animals were compared to the mean of the last 3 days of their angiotensin infusion; the controls were compared to their posttraining baseline period.

†Significantly different from controls (P < 0.01, t-test).

Abbreviations: C = four saline-infused monkeys; E = four angiotensin-infused monkeys.
Although only a small rise of arterial pressure occurred during the angiotensin infusion it was clear that these monkeys had unusually marked pressor episodes to any environmental stress. An example of this is shown in figure 3, when the doors of the booths of an angiotensin-infused and a saline-infused monkey were both opened.

**Discussion**

The radioactive microsphere method has the advantage of allowing simultaneous serial measurements of blood flow to many different organs and tissues in animals who have not been exposed to recent anesthesia, surgery, or other traumatic experience. However, since continuous blood flow measurements in any one organ cannot be recorded with this technique early changes and compensations occurring during the infusions are missed. Thus, our data only reflect the steady state changes that occurred after 20 to 40 min of the infusion.

The systemic and regional cardiovascular responses we found during the angiotensin infusions confirm many previous studies, both in man and other animals. The pressor effect of intravenous angiotensin II is known to be due to an increased total peripheral resistance, rather than an augmentation of cardiac output.\textsuperscript{21-23} Recent reviews of blood flow changes have noted the disproportionate vasoconstriction (and, thus, reduced blood flow) found in the mesenteric, renal, and hepatic arteries and in the skin, while the skeletal muscle vascular bed usually remained relatively unaffected.\textsuperscript{23-26} We find that blood flow to the mesentery and hepatic artery is reduced more than that to other splanchnic organs. We also find that blood flow is relatively well maintained to the heart, skeletal muscle, diaphragm, chest wall, and bone.

Arterial blood levels of angiotensin have been shown to increase during hemorrhage in a variety of species although, apparently, not enough to have a direct effect on blood vessels.\textsuperscript{27} The angiotensin liberated could, however, be enough to potentiate sympathetic activity.\textsuperscript{7-9} Using the same preparation as in the present study we have found with acute hemorrhage a progressive increase in total peripheral resistance which is primarily due to increased resistance in the kidneys, skin, spleen, pancreas, and mesentery. Only the hepatic artery showed a significant decrease in

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*Figure 3*

Simultaneous arterial blood pressure recordings of two monkeys showing response to opening both booth doors (at the arrow). Top tracing shows a saline-infused monkey; lower tracing is a monkey infused with 30 μg/kg/24 hr angiotensin amide for 8 days. Numbers below each tracing indicate systolic and diastolic pressures and pulse rate, respectively.
resistance while there were nonsignificant changes in the heart, brain, adrenals, and skeletal muscle.\textsuperscript{28} Thus, except for the hepatic artery we find a pattern of redistribution occurring after hemorrhage which is similar to that which occurred during angiotensin infusion. This suggests that the redistribution of blood flow during hemorrhage may be partly due to the liberation of angiotensin.

Our results from the four monkeys receiving continuously intravenously infused angiotensin also support the suggestion of McCubbin and Page that the sensitizing pressor action of angiotensin to injected tyramine or psychological stress can act independently of its direct vasoconstrictor activity.\textsuperscript{10, 11} This sensitizing effect has been shown to be dependent on a functionally intact sympathetic nervous system.\textsuperscript{6, 11} Although our data do not necessarily have a direct bearing on the mechanisms operating in essential hypertension, they do suggest a chain of events in which humoral and neuronal factors could combine to lead to sustained hypertension. For example, it is thought that acute psychological stress evokes renal vasoconstriction.\textsuperscript{20, 29} If this stress were prolonged and severe enough there might be enough renin and then angiotensin formed to sensitize responses to further stress, creating the lability of blood pressure often seen in hypertensive and prehypertensive patients. The evidence that this unusual lability has been reported to occur both in animals subjected to long periods of environmental stress\textsuperscript{30, 31} and, as in the present study, in animals subjected to small chronically administered doses of angiotensin\textsuperscript{12} suggests support for this hypothesis.

Patients with essential hypertension have an increased total peripheral resistance which is reflected to some degree in every tissue in the body, except possibly skeletal muscle, and is unusually intense in the kidney.\textsuperscript{32} Since cardiac output is usually unchanged there is normal blood flow to most organs, an increase in skeletal muscle flow, and a decrease in renal flow.\textsuperscript{32} We found, particularly at the low dose of angiotensin infusion, qualitatively similar findings in regard to the resistance and blood flow changes to muscle and renal vascular beds. Although blood angiotensin levels in essential hypertension are not consistently elevated\textsuperscript{33} it is apparent that only modestly increased amounts of angiotensin could be important by sensitizing sympathetic function. However, this hypothesis cannot be directly tested until slightly elevated blood levels of angiotensin II can be reliably measured.

The four continuously infused monkeys in this study had a smaller pressor response than has been previously reported in studies in dogs\textsuperscript{12, 34} or rabbits\textsuperscript{6, 35, 36} given less or equal doses of angiotensin. Although there may be species differences in this response, it seems likely that the conditions of measurement were also important. In this study the monkeys were shielded from the usual laboratory noises and handling during the blood pressure measurements. As McCubbin et al. have reported, pressures were not elevated in their dogs when they were shielded from laboratory noise.\textsuperscript{12}

**Acknowledgment**

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**References**


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ANGIOTENSIN IN NORMAL AND STRESSED MONKEYS


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RALPH P. FORSYTH, BARRY I. HOFFBRAND and KENNETH L. MELMON

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