The Effects of Angiotensin on Pulmonary Circulation and Ventricular Function

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Although the discovery of angiotensin (angiotonin or hypertensin) was reported independently in 1939 by Page and Helmer in this country and by Braun-Menendez and co-workers in Argentina, its structure was not described until 1956 and its active principle not synthesized until 1957. Angiotensin is known to exist in at least two forms, angiotensin I and angiotensin II. While the decapeptide angiotensin I does not have vasocostrictor properties, the octapeptide, angiotensin II, formed by action of the converting enzyme on angiotensin I, is an extremely powerful vasoconstricting agent.3, 4

Circulatory effects of synthetic angiotensin in animals have been extensively studied by Page and his associates and other investigators.5-7 Many workers have reported the hemodynamic effects of various angiotensin preparations in normotensive subjects.8-14 However, there has been scanty information in the literature regarding the effects of angiotensin on pulmonary circulation and ventricular function in man. It is the purpose of this paper to report these effects of angiotensin II in 16 normotensive patients. Data of hemodynamic studies in eight anesthetized dogs were also included for delineation of some of the findings in human studies.*

Clinical Material and Method

Human Studies

Sixteen patients with normal systemic and pulmonary artery pressures were studied. There were 11 males and five females whose ages ranged from 17 to 60 years. None of these patients had clinical or physiologic evidence of aortic stenosis, mitral valvular disease, or intracardiac shunts.

Right heart catheterization was performed in the usual manner. The methods of determining the cardiac output and recording blood pressures have been previously reported in detail,16 and the technic of inscribing indicator-dilution curves and measuring the total and “central” blood volumes has also been described elsewhere.17 The cardiac output determined by the dilution curves was used for the calculation of “central” blood volume. The indicators (iodinated I131 human serum albumin or Indocyanine Green, or both) were injected into the main pulmonary artery and the dilution curves recorded from the femoral artery. The pressures were measured by Statham transducers and carrier amplifier connected to a Sanborn Polyscope Cardiette, and the mean pressures were obtained by electrical integration.

The formulas used to derive resistances and ventricular work against pressures were modified from the paper by Gorlin and Gorlin.18 Mean pulmonary wedge (considered as left ventricular end-diastolic) and right ventricular end-diastolic pressures were used respectively in the calculation of left and right ventricular work against pressure. The cardiac output determined by the Fick procedure was used for the calculation of vascular resistance and ventricular work against pressure. In patients with aortic insufficiency the calculated left ventricular work against pressure would be less than the actual value.

When the patient’s condition was stable, pres-
sures were recorded from the right atrium and right ventricle. Subsequently, measurements of cardiac output (both by the Fick procedure and indicator-dilution curves) and of femoral arterial, pulmonary arterial, and pulmonary wedge pressures were made.

Angiotensin* diluted in 5 per cent dextrose in water was injected through an antecubital vein at the rate of 0.015 to 0.135 microgram per kilogram of body weight per minute, depending upon the rise of the systemic blood pressure, which was monitored continuously by direct intra-arterial recording. During infusion one or more cardiac output determinations were made, followed immediately by recording femoral arterial, pulmonary arterial, and pulmonary wedge pressures, and sometimes by measurement of right ventricular and right atrial pressures.

**Animal Studies**

Eight adult mongrel dogs were kept lightly anesthetized by separate small injections of intravenous thiopental. With chest open and intermittent positive pressure respiration, a cardiac catheter was introduced into each of the following sites: (a) right atrium or right ventricle, (b) main pulmonary artery, (c) pulmonary wedge position, (d) pulmonary veins, and (e) left atrium. Following the insertion of various catheters, which were securely anchored with stay sutures, the chest was tightly closed and spontaneous respiration started.

A polyethylene tube was then introduced into the abdominal aorta via a femoral artery for arterial blood sampling and pressure recording. The position of the cardiac catheters was frequently checked by pressure recordings.

Cardiac output in the dogs was determined by indicator-dilution curves by use of the dye Indocyanine Green. After each determination of the cardiac output, the blood drawn in a syringe mounted on the Colson Constant-Flow System was reinfused into the dogs, so that the blood loss was kept minimal.

Intracardiac and intravascular pressures were measured in the same manner as that described in human studies. In most instances, pulmonary arterial and right ventricular pressures were recorded alternately on the same channel. The formula for calculating left ventricular stroke work was similar to that employed in human studies except that the left atrial mean pressure was substituted for the left ventricular diastolic pressure.

In a series of five dogs, following control studies, a rapid infusion of heparinized blood was given through a cardiac catheter into the right side of the heart by means of a reservoir. Similar to the experimental studies designed by Sarnoff and Berglund,10 the amount of blood infused and the pressures in both atria could be varied over wide ranges by changing height of the reservoir. The initial amount of blood infused was about 15 ml./Kg. and increased to approximately 60 ml./Kg. in different stages. Studies were repeated within 5 minutes of the completion of each infusion. After the effects of rapid infusion of known volume of blood had been studied, a "phlebotomy" to remove rapidly slightly less than the total volume of blood infused was accomplished by simply lowering the reservoir. When the circulatory state had stabilized, pressure and flow measurements were again made and the figures used as the second control values. Subsequently, angiotensin (1 to 2 µg./Kg./min.) was infused into an external jugular vein. During the administration of angiotensin solution, rapid blood infusion was again given in

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*Hypertensin II (CIBA), Courtesy of Dr. William E. Wagner, CIBA Pharmaceutical Products, Inc., Summit, New Jersey.
the same manner as previously described. Determination of cardiac output and measurements of pressures were carried out repeatedly during angiotensin infusion with or without rapid blood infusion. Table 3 shows the values of various parameters in a given dog by averaging two or more determinations obtained during a certain circulatory state, (i.e., blood or angiotensin infusion).

In another three dogs pressure and flow measurements were first made during a control period as well as during angiotensin infusion, with graded doses ranging from 0.1 µg./Kg./min. to 5 µg./Kg./min. In two of these dogs, after angiotensin infusion was discontinued, single or multiple doses of hexamethonium (5 to 10 mg.) were given intravenously to lower the systemic arterial pressure. When the systolic pressure reached a level slightly less than 50 mm. Hg the angiotensin infusion was recommenced. In each case systemic and pulmonary arterial pressures were again recorded.

Results
Human Studies
The results are summarized in tables 1 and 2.

During angiotensin infusion there were statistically significant increases in femoral arterial, pulmonary wedge, and pulmonary arterial pressures. No statistically significant change was observed in cardiac output, heart rate, and stroke volume. For the whole group, there was a parallel increase in oxygen consumption and in the arteriovenous oxygen difference. However, significant increase in oxygen consumption, i.e., more than 13 per cent of the control value, was noted in only six patients. The cause of this increase was not apparent.

Total systemic, total pulmonary, and pulmonary vascular resistances and the left ventricular work against pressure were all statistically increased. In most cases, however, the magnitude of increase in the pulmonary vascular resistance was small.

In seven patients in whom right ventricular pressure was measured, there was a consistent rise in both systolic and diastolic pressures directly proportional to the magnitude of elevation of pulmonary artery pressure. In six of these seven patients the right ventricular work against pressure was also increased.

In most instances there was a slight prolongation in the mean transit time from the pul-

Table 1
Effects of Angiotensin on Rate of Blood Flow and Blood Volume

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of subjects</th>
<th>Average during control period (A)</th>
<th>Average during angiotensin infusion (B)</th>
<th>Average difference (B-A) ± SE</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fick procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\dot{V}_o$ (ml./M.²/min.)</td>
<td>16</td>
<td>138.5</td>
<td>147.8</td>
<td>$9.3 \pm 3.3$</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>$C_{ao}-C_{v0}$ (ml./L.)</td>
<td>16</td>
<td>38.9</td>
<td>49.5</td>
<td>$10.6 \pm 4.4$</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>CI (L./M.²/min.)</td>
<td>15</td>
<td>3.80</td>
<td>3.26</td>
<td>$-0.54 \pm 0.24$</td>
<td>NS</td>
</tr>
<tr>
<td>HR (beats/min.)</td>
<td>16</td>
<td>85</td>
<td>76</td>
<td>$-9 \pm 4.7$</td>
<td>NS</td>
</tr>
<tr>
<td>SI</td>
<td>15</td>
<td>45</td>
<td>46</td>
<td>$1 \pm 2.8$</td>
<td>NS</td>
</tr>
<tr>
<td>Indicator-dilution curve</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI (L./M.²/min.)</td>
<td>16</td>
<td>3.80</td>
<td>3.40</td>
<td>$-0.40 \pm 0.24$</td>
<td>NS</td>
</tr>
<tr>
<td>$T_m$ (sec.)</td>
<td>16</td>
<td>13.2</td>
<td>15.3</td>
<td>$2.1 \pm 0.74$</td>
<td>0.01 &lt; p &lt; 0.02</td>
</tr>
<tr>
<td>$T_s$ (sec.)</td>
<td>16</td>
<td>18.3</td>
<td>25.0</td>
<td>$6.7 \pm 0.83$</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>&quot;CBV&quot; (ml./M.²)</td>
<td>16</td>
<td>798</td>
<td>801</td>
<td>$-12 \pm 10.1$</td>
<td></td>
</tr>
<tr>
<td>TBV (ml./M.²)</td>
<td>12</td>
<td>2500</td>
<td>2745</td>
<td>$-5 \pm 27.8$</td>
<td>NS</td>
</tr>
</tbody>
</table>

$\dot{V}_o$, oxygen consumption; $C_{ao}-C_{v0}$, arteriovenous difference; CI, cardiac index; HR, heart rate; SI, stroke index; $T_m$, mean transit time from pulmonary artery to femoral artery; $T_s$, circulation time from femoral artery to femoral artery; "CBV", "central" blood volume or dilution volume from pulmonary artery to femoral artery; TBV, total blood volume; SE, standard error of mean; p indicates the probability that difference as large as that observed will occur by chance—a difference with a chance probability of 0.05 or less is considered to be significant; NS, not significant.
Femoral arterial pressure tracings recorded during the control period (upper half) and during angiotensin infusion (lower half) in three patients. Note the prolongation of the upstroke time and the appearance of an anacrotic notch.

Femoral artery to the femoral artery, although the total and "central" blood volumes and arterial oxygen saturation usually remained unchanged. In all but one case there was a prolongation in the circulation time as measured by intervals between the peak of primary circulation and that of recirculation of indicator-dilution curves (fig. 1).

The increase in the femoral arterial, pulmonary wedge, and pulmonary arterial pressures usually occurred within 2 minutes of the start of intravenous injection of angiotensin and
reached its maximum within 5 minutes of infusion.

During angiotensin infusion in nine of the 16 patients there was a significant increase in the upstroke time of the femoral arterial pressure tracing associated with the presence of an anacrotic notch close to the top (fig. 2). In the remaining seven patients no such change in the contour of femoral arterial pressure tracings was observed. There was no alteration in the pressure distribution through the cardiac cycle.

In some cases a graded increase in the dose of angiotensin produced further elevation of
Effects of Angiotensin on Systemic and Pulmonary Blood Pressures and Resistances and Ventricular Work

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of subjects</th>
<th>Average during control period (A)</th>
<th>Average during angiotensin infusion (B)</th>
<th>Average difference (B-A) ± SE</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressures (mm. Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S/D</td>
<td>16</td>
<td>123/67</td>
<td>166/92</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>16</td>
<td>87</td>
<td>119</td>
<td>32 ± 4.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RV</td>
<td>7</td>
<td>23/4</td>
<td>36/8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>PA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S/D</td>
<td>16</td>
<td>22/8</td>
<td>33/13</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>16</td>
<td>12</td>
<td>20</td>
<td>8 ± 1.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&quot;PC&quot;m</td>
<td>16</td>
<td>7</td>
<td>13</td>
<td>6 ± 1.3</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Resistances (dynes·sec·cm⁻⁴)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSR</td>
<td>15</td>
<td>1155</td>
<td>1916</td>
<td>761 ± 154</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TPR</td>
<td>15</td>
<td>161</td>
<td>312</td>
<td>151 ± 22</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PVR</td>
<td>15</td>
<td>73</td>
<td>127</td>
<td>54 ± 14.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Stroke work against pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Gm/M/beat/M²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV</td>
<td>15</td>
<td>56</td>
<td>76</td>
<td>20 ± 5.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RV</td>
<td>7</td>
<td>8</td>
<td>15</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

FA, femoral artery; S/D, systolic/diastolic; RV, right ventricle; PA, pulmonary artery; "PC"m, pulmonary wedge; TSR, total systemic; TPR, total pulmonary; PVR, pulmonary vascular; LV, left ventricle.

the femoral arterial and pulmonary wedge pressures, but relatively small increment in the pulmonary arterial and right ventricular pressures. With a carefully regulated infusion the elevated systemic arterial pressure could be satisfactorily maintained over a period of an hour or more. Following cessation of angiotensin infusion, both the femoral arterial and pulmonary arterial pressures returned to control values within 2 or 3 minutes.

Figures 3 and 4 show a positive correlation between the increment in the stroke work against pressure and that in the diastolic pressure of the respective ventricle. In half of the cases the pulmonary wedge pressure rose above 12 mm. Hg and in three cases to 20 mm. Hg or higher during infusion of angiotensin, yet there was still an increase in the stroke work against pressure in each case. The change in the right ventricular work against pressure in a smaller number of cases also showed the same trend, even when the right ventricular diastolic pressure rose to 10 mm. Hg or greater.

Animal Studies

The results are summarized in table 3. Continuous recording of the pressures showed that
Simultaneous recordings of femoral arterial (FA), right ventricular (RV), left atrial (LA), pulmonary wedge ("PC"), and pulmonary venous (PV) pressures, and electrocardiogram (ECG) in a dog before and during angiotensin infusion. For about 20 seconds during the control periods the systolic and diastolic pressures were recorded. Subsequently, FA, LA, "PC", and PV mean pressures were obtained by electrical integration. Note a rise in all the pressures within 1 minute of the start of the angiotensin infusion (1 μg./Kg./min.). During the second minute there was a maximal rise in LA, PV, and "PC" and RV diastolic pressures. Subsequently, the FA pressure rose steadily to a plateau while there was a sustained and moderate rise in both left and right ventricular diastolic pressures.

Figure 5

Within 1 minute after the angiotensin infusion was started there was a uniform rise in pressures in the systemic circuit, pulmonary circuit, and all four cardiac chambers. In the next minute there was usually a rise in the left ventricular diastolic (represented by mean left atrial, pulmonary venous, and pulmonary wedge) and right ventricular diastolic pressures (fig. 5). The magnitude of the elevation in the left ventricular diastolic pressure was variable in different animals. Subsequently, the systemic arterial pressure rose steadily to a plateau, whereas a sustained and moderate rise in both left and right ventricular diastolic pressures was observed.

The increase in the systemic arterial pressure could be satisfactorily maintained as long as the constant infusion of angiotensin was continued. The optimal dose of angiotensin was found to be approximately 1 μg./Kg./min., which was 8 to 60 times the dose given to patients. Further increase of the dose (2 to 5 μg./Kg./min.) did not appreciably augment the systemic arterial pressure or left ventricular stroke work, although there was usually a further rise in left atrial and pulmonary arterial pressures.

Within 1 or 2 minutes following the cessation of angiotensin infusion all the pressures returned to control level, and in some instances the systemic arterial pressure was even lower than the control value. It was possible, however, to increase the systemic arterial pressure again if angiotensin infusion was resumed.

In two dogs severe systemic hypotension (i.e., femoral arterial systolic pressure less than 50 mm. Hg) produced by single or multiple intravenous injections of hexamethonium was satisfactorily counteracted by angiotensin infusion, although the magnitude of rise in systemic arterial pressure was not as high as...
that observed with infusion of angiotensin alone (fig. 6).

As shown in table 3, rapid blood infusion caused an increase in cardiac output, stroke volume, left atrial and pulmonary arterial pressures, and left ventricular stroke work. The average pressure gradient from the pulmonary artery to the left atrium was widened. There was a slowing in heart rate but no appreciable change in the systemic arterial pressure. In contrast, angiotensin infusion produced an increase in systemic arterial pressure and left ventricular stroke work, but no change in cardiac output, stroke volume, and heart rate. A slight increase in both left atrial and pulmonary arterial pressures was observed, but compared with the control value there was no appreciable change in the average pressure gradient from the pulmonary artery to the left atrium.

When both blood and angiotensin were infused simultaneously, the effects were additive, manifested particularly by the increase in left ventricular stroke work and left atrial and pulmonary arterial pressures. Representative left and right ventricular function curves during blood infusion with or without angiotensin are depicted in figure 7.

Discussion

Angiotensin infused intravenously to both men and dogs is a very powerful pressor agent. It produces a prompt increase in total systemic resistance and systemic arterial pressure, most likely as a result of systemic arteriole constriction.

During angiotensin infusion the consistent rise in the pulmonary wedge or left atrial pressure reflects a rise in the left ventricular diastolic or filling pressure. The increased left ventricular filling pressure accompanied by the alteration of systemic arterial pressure tracing, which was characterized by a prolonged upstroke time and the presence of an anacrotic notch, strongly suggests an increase in the "left ventricular" resistance. Such changes are frequently observed in patients with aortic stenosis.

It should be pointed out that in human studies, although there was a direct relation-
Table 3

Hemodynamic Effects of Angiotensin or Rapid Blood Infusion, or Both, in Dogs*

<table>
<thead>
<tr>
<th>Periods of study</th>
<th>No. of dogs</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml./beat)</th>
<th>Mean pressures (mm. Hg)</th>
<th>Left ventricular stroke work (Gm./M./beat)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>M</td>
<td></td>
<td>Femoral arterial R</td>
<td>Pulmonary arterial R</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>1.18-1.94</td>
<td>1.50</td>
<td>140-190</td>
<td>158</td>
<td>8-10</td>
</tr>
<tr>
<td>Blood infusion</td>
<td>5</td>
<td>1.53-3.62</td>
<td>2.56</td>
<td>90-153</td>
<td>121</td>
<td>17-32</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>0.50-1.98</td>
<td>1.35</td>
<td>100-160</td>
<td>138</td>
<td>3-17</td>
</tr>
<tr>
<td>Angiotensin</td>
<td>5</td>
<td>0.95-1.76</td>
<td>1.51</td>
<td>120-195</td>
<td>147</td>
<td>5-14</td>
</tr>
<tr>
<td>Angiotensin plus</td>
<td>4</td>
<td>2.06-4.18</td>
<td>2.90</td>
<td>120-154</td>
<td>138</td>
<td>15-31</td>
</tr>
</tbody>
</table>

*The values of various parameters in a given dog were the average of two or more determinations obtained during a certain circulatory state. R, range; M, mean.

It is reasonable to assume that similar results probably would have been obtained in man if ventricular function could be obtained during these two circulatory states. Nevertheless, the bulk of evidence indicates that during angiotensin infusion, the left ventricle responded to angiotensin almost as if it were a normal ventricle, and could therefore be taken as the normal ventricle by which to judge the effects of the other agents. In this study, angiotensin alone or in combination with other agents was not effective in raising arterial pressure.

At the time there was no means to measure the pulmonary arterial and left atrial pressures in all subjects; therefore, it was not possible to correlate changes in right ventricular pressure with left atrial pressure. At the same time, it was not possible to measure right atrial pressure with left ventricular pressure. Nevertheless, the bulk of evidence indicates that during angiotensin infusion, the left ventricle responded to angiotensin almost as if it were a normal ventricle, and could therefore be taken as the normal ventricle by which to judge the effects of the other agents. In this study, angiotensin alone or in combination with other agents was not effective in raising arterial pressure.
EFFECTS OF ANGIOTENSIN

Figure 7
Left and right ventricular function curves during blood infusion with or without angiotensin after step-wise elevation of the reservoir. The respective ventricular stroke work was plotted against atrial mean pressure during each circulatory state. With angiotensin administration the ventricular function curves were shifted above and to the left of those without angiotensin. These changes indicated that more external work was performed at any given filling pressure with angiotensin infusion than without.

In most human subjects, and in all dogs, the increase in pulmonary arterial pressure appeared to be passive and secondary to the rise in left ventricular diastolic pressure, since there was little or inconsistent change in the pulmonary artery to left atrial (pulmonary wedge) pressure gradient. Similar observations were reported by Nelson and associates,12 and by Sancetta,14 when other preparations of angiotensin were used. The possibility of constriction of pulmonary veins probably can be ruled out, inasmuch as in dogs the changes in pulmonary wedge and left atrial pressures were identical.

Since the "central" blood volume in the patients of this series did not change significantly, the increase in pulmonary vascular pressures was probably not related to redistribution of blood volume from the peripheral to the pulmonary circulation.

Our unpublished observation21 showed that in most patients with mitral valvular lesion angiotensin produced a consistent increase in both left atrial and pulmonary arterial pressures accompanied by a decrease in the true pulmonary blood volume. These findings strongly suggest that active vasoconstriction of the pulmonary vascular bed may occur in patients with mitral valvular disease. No comparable data were obtained in patients included in this series.

The prolongation of the total circulation time from femoral artery to femoral artery was more striking than that of the mean transit time from the pulmonary artery to the femoral artery. This difference strongly
suggests that slower circulation did occur in the systemic circuit probably as a result of acute systemic vasoconstriction and hypertension.

It would appear that in man the optimal dose of angiotensin infused intravenously is about 0.05 to 0.10 μg./Kg./min. Larger doses may cause severe headache and general discomfort, which were present in two of our patients. We have not observed some of the unpleasant manifestations, such as chilly sensation, piloerection, and difficulty in urination, frequently encountered during methoxamine (Vasoxyl) infusion. Furthermore, it also has the advantage over methoxamine in that the hypertensive effects can be repeatedly induced and terminated within a matter of several minutes.

As shown by other workers, angiotensin has been used effectively in the treatment of hypotension and shock in various disease states. It was found to be six to 10 times as potent as norepinephrine.13 Furthermore, from our animal studies it is apparent that marked hypotension induced by the administration of a ganglion-blocking agent (i.e., hexamethonium) can be promptly counteracted by intravenous infusion of angiotensin. Therefore, there is a potential use of this vasopressor agent in the practice of anesthesiaology, since in some instances it is urgent to raise promptly and effectively the systemic blood pressure that has been lowered by a ganglion-blocking agent for the purpose of a specific surgical procedure.

Summary and Conclusions

The effects of angiotensin (Hypertensin II CIBA) given by intravenous infusion on pulmonary circulation and ventricular function were studied in 16 normotensive patients and eight anesthetized dogs.

During angiotensin infusion the following changes were observed: (a) an increase in pressures in both systemic and pulmonary circuits and four cardiac chambers, and variable change in pulmonary artery-pulmonary wedge (or left atrial) pressure gradient; (b) slightly decreased or unchanged cardiac output and stroke volume; (c) significantly increased total systemic and total pulmonary resistances; (d) significant increase in stroke work of both ventricles; (e) significant prolongation in the circulation time from femoral artery to femoral artery and slight prolongation in mean transit time from pulmonary artery or right heart to the femoral artery and, (f) no significant alteration in total or "central" blood volume.

It is concluded that (a) angiotensin is a very powerful vasopressor agent and has its action primarily on the systemic circulation; (b) in the compensated human and canine hearts it also increases myocardial contractility and ventricular function; and (c) in patients without mitral valvular lesions or intracardiac shunts the hemodynamic changes in the pulmonary circulation are mostly secondary.

Acknowledgment

We wish to express our thanks and appreciation to Dr. Arthur Dutton, Assistant Professor of Radiation Biology and Scientist (Statistics), Atomic Energy Project, University of Rochester, for his help on the statistical aspect of this study. We are indebted to Drs. Gerald Glick, Frank W. Lovejoy, Jr., Michael R. McCreasie, Celia Oakley, Clay Phillips, Jr., and Bernard F. Schreiner for their participation in the study.

References


It is a sound rule rarely to diagnose conditions that occur rarely.—Sir Thomas Lewis.

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