Adrenal Medullary Secretion During Hypoxia, Bleeding, and Rapid Intravenous Infusion

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With the technical assistance of Nora Chou, M.S.

Previous studies have indicated that reduced tissue oxygen supply due to hypoxia or to hemorrhagic hypotension may increase adrenal medullary secretion. Cannon and Hoskins studied asphyxiated cats by sampling inferior vena caval blood from an area just above the adrenal veins. These workers demonstrated inhibition of rabbit intestine contraction by vena caval blood during asphyxia, suggesting epinephrine release. Houssay and Molinelli anastomosed the left lumboadrenal vein of the dog to the jugular vein of another dog. Hypoxia in the donor animal produced tachycardia and increased systemic blood pressure in the recipient, suggesting increased adrenal medullary secretion. Baugh, Cornett, and Hatcher produced hypoxia in dogs by 6 per cent O₂ in N₂ breathing and observed an increase of cardiac output, stroke volume, heart rate, respiratory rate, and hematoctrit. These changes were prevented or moderated by adrenalectomy. Blood removed from intact anoxic dogs increased cardiac output significantly in assay dogs.

Watts and Watts and Bragg, employing a bio-assay method, found an increase of arterial blood epinephrine in bled dogs; epinephrine levels increased after bleeding 15 ml./Kg. and reached a maximum after bleeding 40 ml./Kg. Walker and associates, using a chemical method, observed augmentation ratios of 1.8 to 59.1 of adrenal vein catecholamines in dogs bled one-tenth to two-fifths of estimated blood volume.

Other studies have raised the possibility that impairment of tissue oxygenation during acute experimental anemia may increase adrenal medullary secretion. We have found an increase of cardiac output in dogs made hypervolemic and anemic by dextran infusion. Studies of Justus, Cornett, and Hatcher have suggested that a humoral substance is involved in the increased cardiac output of dogs made anemic with dextran.

The purpose of the present study was to measure the adrenal secretion of dogs during certain conditions associated with reduced oxygen transport, which might be expected to alter adrenal activity. Accordingly, adrenal secretion was studied during hypoxia, during hemorrhagic hypotension, and during dilution anemia associated with rapid intravenous infusion. The results, to be described later in the paper, confirm the observations cited before with regard to increased adrenal medullary secretion in hypoxia and bleeding. No evidence of increased adrenal medullary secretion during intravenous infusion of saline or Krebs’ solution was found.

Methods

The studies to be described were made upon 25 dogs weighing 18.6 to 29.1 Kg. The animals were anesthetized with sodium pentobarbital, 30 mg./Kg. intravenously. Mean blood pressure was obtained from the femoral artery by a mercury manometer. In hypoxic dogs only, cardiac outputs were measured by the direct Fick principle. Three-minute samples of expired air were collected in Douglas bags and analyzed in the Scholander 0.5 ml. gas analyzer. Midway during expired air collection, one-minute samples of blood were collected in heparinized syringes simultaneously from the pulmonary and femoral arteries. These blood samples were analyzed for O₂ in duplicate in the Van Slyke manometric apparatus. In the animals receiving

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saline infusions, cardiac outputs were measured by the indicator-dilution technique, using tricarboxy methane green as an indicator. Two and a half mg. of dye was injected into the pulmonary artery and sampled continuously from the aortic arch, using a constant withdrawal syringe. The optical density of aortic blood was recorded continuously by means of the withdrawal system described by Emanuel, Lacy, and Newman, using an infrared filter. This apparatus permits the separation of a portion of the dyed blood for calibration during recording of the curve by means of a double lumen stopcock, which also produces simultaneous electrical signals on the record to mark the period of withdrawal of the calibrating sample. The concentration of dye in the plasma of this sample was read at 800 m/λ in the Beckman DU spectrophotometer, using a sample obtained immediately before injection of dye as the control. The indicator curves were recorded with the Sanborn direct-writing recorder.

The mean height of the curve over the period of withdrawal of the calibrating sample was determined by planimetry; plasma flow was determined as described by Emanuelle, Lacy and Newman, and corrected to whole blood flow by means of hematocrit.

The effluent blood of the left adrenal gland was obtained by distal cannulation of the left lumbo-adrenal vein. The adrenoeaval vein was then ligated at its junction with the inferior vena cava. The animals were then heparinized with 2.5 mg. heparin/Kg. An additional similar amount of heparin was given midway during the experiments. Adrenal venous blood was collected simultaneously with measurement of cardiac outputs. In some animals, femoral arterial blood samples were obtained midway during the collection of adrenal venous blood samples. Blood was permitted to flow continuously from the left adrenal vein, and was not returned to the animal, so that the adrenal venous return would not be altered during periods of collection of adrenal venous blood samples. The volume of blood thus removed was replaced by donor blood.

The blood levels of norepinephrine-like substances (NEL) were measured by the method described by Helmer, using L-norepinephrine bitartrate as the standard. Measurements were made upon plasma and corrected to whole blood from the hematocrit. Since norepinephrine is more stable than epinephrine in a 0.001 N HCl solution, and the contractile effect of both amines on the aortic strip was found to be about the same, norepinephrine was used to make the standard solutions. Such solutions of various concentrations were used for comparative tests and for the estimation of the plasma levels of norepinephrine-like substances. The plasma samples, from heparinized blood, were kept refrigerated until time for the test. All determinations were done within eight hours after the blood samples were collected from the animals. The amount of plasma used varied from 0.1 to 3.0 ml., depending on the origin of the sample, its anticipated catecholamine level, and sensitivity of the individual aortic strip. The aortic strip was suspended in a muscle chamber containing 20 ml. of Krebs' bicarbonate solution.

In addition, the effects of angiotonin, serotonin, isopropynorepinephrine, dihydroxyphenylalanine (dopa), dihydroxyphenylalanine amine (dopamine), 3,4-dihydroxyphenylacetic acid (dopac), and 3,4-dihydroxymandelic acid upon the rabbit aortic strip were observed.

A total of 25 animals was studied. In 15 animals, hypoxia was produced by their breathing 7.1 per cent O₂ in N₂. In these animals, two control samples were obtained from the left adrenal vein before hypoxia; one sample was obtained during hypoxia, after 10 minutes of breathing the low oxygen mixture, and another was obtained 10 minutes after hypoxia. In later experiments, the control sample after hypoxia was obtained after a lapse of 20 minutes. In two animals, asphyxia was then produced by occlusion of the endotracheal tube for one to two minutes; two other animals were subjected to asphyxia without antecedent hypoxia. Adrenal vein samples were taken during asphyxia and again 10 minutes later. In five animals, four of which had been made previously hypoxic, the blood pressure was quickly lowered by bleeding 80 to 90 mm. Hg, and adrenal vein blood samples again taken. In 13 animals, including the aforementioned 5, the blood pressure was lowered to 40 to 50 mm. Hg by rapid bleeding, and adrenal vein blood samples again collected.

In seven animals, two control adrenal vein samples and cardiac outputs were measured; normal saline or Krebs' solution was then infused at approximately 100 ml per minute. After 1,125 to 1,600 ml. was infused, measurement of cardiac output was made and adrenal vein samples were collected during infusion. Cardiac output measurement and adrenal vein sampling were repeated after 10 to 15 minutes, at which time the pulmonary arterial pressure had returned to control levels.

In four additional animals, the left adrenal output of 17-hydroxycorticosteroids (17-OHCS) during hypoxia was measured. The technique of Nelson and Samuels was employed for 17-OHCS concentration. In five animals, the left adrenal output of 17-OHCS was determined during rapid infusion of normal saline. The measurements were made upon plasma, and corrected to whole blood from the hematocrit.

Because of our failure to observe a consistent

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Increase of cardiac output during hypoxia, the following studies were made. In five experiments, intact animals were subjected to hypoxia as described previously. Cardiac outputs were measured by the indicator-dilution method before, during, and after hypoxia. The cardiac outputs were again measured after the abdomen was opened as for adrenal cannulation in four animals, and in two of these the response of the cardiac output to hypoxia was again measured while the abdomen was open. In two additional animals, the response of the cardiac output to hypoxia was measured with the adrenal vein cannulated, but with the adrenal venous blood still entering the systemic circulation.

In all experiments the volume of blood removed for sampling was replaced by heparinized donor blood. In two animals, plasma pH was determined with and without hypoxia, using a Beckman pH meter.

Results

The rabbit aortic strip was found to contract in response to angiotonin and serotonin. Like Helmer, we found that Regitine did not prevent the contraction of the rabbit aortic strip produced by angiotonin. For these studies, angiotonin was used in amounts of 6 \( \mu \)g, and Regitine in amounts of 100 \( \mu \)g. Hence, this substance should not be confused with adrenal catecholamines. Serotonin is not known to be present in significant amounts in the adrenal gland. Precursors or metabolic products of epinephrine and norepinephrine must also be considered. The epinephrine and norepinephrine precursors, dopa, dopamine and its derivative, dopac, were found not to produce contractions. Dopac produced no contraction of the rabbit aortic strip when 20 or 100 \( \mu \)g was added to the bath. Dopa produced no contraction when 100 \( \mu \)g was added to the bath. Five \( \mu \)g of 3,4-dihydroxy-mandelic acid produced no contraction. Dopamine produced contraction only in amounts above 4 \( \mu \)g. Since this is less than one-eighth of the response produced by epinephrine or \( l \)-norepinephrine, this response was considered to be insignificant for our purposes. Iso-propynorepinephrine, also reported in the adrenal medulla, did not produce contraction of the rabbit aortic strip when 200 \( \mu \)g was added to the bath.

The remainder of the results are summarized in tables 1 to 5 and in figure 1. Table 1 indicates the effect of hypoxia upon adrenal output of norepinephrine-like substances (NEL). The table lists the results obtained in 11 animals subjected to hypoxia, and in 2 others subjected to asphyxia. Values of NEL output are expressed in \( \mu \)g. \( \times 10^{-5} \text{Kg./min.} \) as \( l \)-norepinephrine bitartrate. Not included in the table are the studies in four animals, one of which was inadvertently asphyxiated early during the experiment; thus, proper control levels were not obtained. In the remaining three although increased adrenal vein NEL output was observed

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**Table 1**

Effect of Hypoxia on Adrenal Medullary Secretion in Thirteen Dogs

<table>
<thead>
<tr>
<th></th>
<th>NEL* ( \mu )g./Kg./min. ( \times 10^{-5} )</th>
<th>Blood pressure† (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.46—17.1 (4.5)†</td>
<td>90—145 (128)</td>
</tr>
<tr>
<td>Second control</td>
<td>0.51—19.4 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Hypoxia</td>
<td>0.97—66.3 (14.3)</td>
<td>95—160 (135)</td>
</tr>
<tr>
<td>NEL augmentation ratio§</td>
<td>1.1—6.6 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.59—31.6 (7.0) *</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.9—7.9 (3.7) *</td>
<td></td>
</tr>
<tr>
<td>Asphyxia</td>
<td>5.2—12.1 (8.1) *</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.4—6.6 (3.5) *</td>
<td></td>
</tr>
</tbody>
</table>

*NEL = output of norepinephrine-like substances in \( \mu \)g./Kg./min. \( \times 10^{-5} \).
†Blood pressure = systemic arterial blood pressure, mm. Hg.
§Augmentation ratio = NEL output during hypoxia over mean control output.
||Figures for asphyxia represent only four animals.

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*Personal communication from Dr. Irvine H. Page.

Circulation Research, Volume IX, March 1961
FOWLER, SHABETAI, HOLMES

Adrenal medullary secretion during hypoxia and during bleeding.

during hypoxia, these levels did not return toward control levels after 10 minutes and it was concluded that the study was unsatisfactory. Control NEL outputs were from 0.46 to 19.4 × 10⁻² µg./Kg./min. In 10 of the 11 animals in table 1, an increase in adrenal NEL output was seen during hypoxia, with a decline in output 10 to 20 minutes after hypoxia. The only animal failing to show a significant increase was no. 115. This animal also showed very little increase in NEL output in response to bleeding, in contrast to the other animals. The NEL outputs during hypoxia in the remaining 10 animals were from 1.5 to 6.6 times the control levels. The four animals studied during asphyxia showed increase of adrenal NEL secretion during asphyxia comparable to that found during hypoxia. There was no consistent effect of hypoxia upon adrenal vein flow. Mean systemic blood pressure rose in each animal during the hypoxic periods. Femoral arterial NEL levels were measured in five of the animals listed in table 1. Control levels were from 6.3 to 18.6 µg./L. During hypoxia, three animals showed no change in femoral arterial NEL; in one animal the level increased from 6.3 to 13 µg./L, and in one the level increased from 11.6 to 36.8 µg./L.

In table 2 is indicated the effect of hypoxia upon cardiac output, systemic arterial oxygen saturation, and hematocrit in the same dogs listed in table 1. Only one animal exhibited an increase of cardiac output. In the others the cardiac output was unchanged or declined. The control systemic arterial saturations were near normal except in one animal, where the value was 78 per cent of capacity. During hypoxia, systemic arterial O₂ saturations were from 33 to 59 per cent of capacity. The hematocrits rose slightly in seven animals and were essentially unchanged in two.

Table 3 indicates the effect of bleeding upon adrenal NEL output. In each of five animals, lowering of blood pressure to 80 to 90 mm. Hg was associated with a striking increase of adrenal NEL secretion. The augmentation ratios following bleeding were from 2.8 to 7.4. Lowering of blood pressure to 40 to 50 mm. Hg was associated with a further increase of adrenal NEL secretion in these five animals, and with an increase in the remaining six animals listed in table 3. The remaining six animals were bled only once. Not included in the table are the results of two unsatisfactory bleeding experiments: one animal was asphyxiated early in the experiment; in the other, adrenal blood flow during shock was too small for a satisfactory sample. Augmentation ratios of adrenal NEL secretions in the animals bled to a pressure of 40 to 50 mm. Hg were from 1.8 to 17.0, as compared to control levels.

The response of one animal, dog no. 130, to hypoxia and to bleeding is shown in figure 1. This figure shows graphically the moderate increase of adrenal NEL secretion during hypoxia with an augmentation ratio of 4.2. During hypoxia, systemic arterial oxygen saturation fell to 40.3 per cent and cardiac output was essentially unchanged. After lowering blood pressure from 125 to 90 mm. Hg by bleeding, adrenal NEL secretion showed an augmentation ratio of 7.4 with a further increase to an augmentation ratio of 13.3 when
Table 2

<table>
<thead>
<tr>
<th>Effect of 7.1 Per Cent O₂ Breathing upon Cardiac Output and Systemic Arterial Oxygen Saturation of Eleven Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Hypoxia Control</td>
</tr>
<tr>
<td>Arterial O₂ saturation per cent capacity</td>
</tr>
<tr>
<td>78—85.4 (91.1) 33.3—59 (46.4) 78—92.8 (88.8)</td>
</tr>
<tr>
<td>Hematocrit</td>
</tr>
<tr>
<td>42—56 (47.9) 44.5—58 (50.9) 43—58 (49.8)</td>
</tr>
<tr>
<td>Cardiac output ml./Kg./min.</td>
</tr>
<tr>
<td>33—95 (75) 33—106 (68) 43—97 (69)</td>
</tr>
</tbody>
</table>

Figures in parentheses represent means.

blood pressure was lowered to 50 mm. Hg by additional bleeding.

Table 4 shows the effect of rapid infusion upon adrenal NEL output, cardiac output, hematocrit, and pulmonary arterial pressure. During the infusion, cardiac outputs were increased to more than twice control levels except in one animal. The hematocrits were greatly decreased, controls being 36 to 57, and values of 17 to 32 were found during the infusion. Hematocrits remained low 10 minutes after the infusion, but cardiac outputs had decreased to or toward control levels. Pulmonary arterial pressures increased by 5 to 28.5 cm. of water during the infusion, but had returned to control levels 10 minutes after the infusion. Adrenal vein NEL output decreased during the infusion, with values 14 to 50 per cent of control levels. Ten minutes after the infusion was discontinued, NEL output increased in four of the five animals; in two of the four, the NEL output returned to or above control levels.

Plasma pH was measured with and without hypoxia in two animals. In one, control pH was 7.46; pH was 7.45 during hypoxia. In the second, control pH was 7.40 and pH was 7.42 during hypoxia.

As shown in table 5, control values for 17-OHCS output were obtained in five dogs, and were from 0.44 to 1.08 µg./Kg./min. During hypoxia, there was no increase in 17-OHCS output in the four animals studied; in fact, three of the four animals showed a slight decrease in 17-OHCS output during hypoxia. During rapid saline infusion, hematocrits fell from initial values of 45 to 55 per cent to 17 to 30 per cent. Each of five animals showed an increase in 17-OHCS output during saline infusion; the increases were from 18.5 per cent to 92 per cent. During saline infusion, left adrenal flow increased from 77 per cent to 296 per cent (table 5).

In the five experiments in which hypoxia was produced in the intact animal, the cardiac output increased 9 to 52 per cent, average 30 per cent, during hypoxia, and fell 16 to 52 per cent, average 26 per cent, after hypoxia was discontinued. In four of these animals, the cardiac outputs declined 33 to 42 per cent when the abdomen was opened. No increase in cardiac output occurred during hypoxia in two of these animals following adrenal vein cannulation, although an increase had occurred in the animals when intact. No increase in cardiac output during hypoxia occurred in two other animals in which the adrenal veins were cannulated but not ligated.

Discussion

Specificity of the Method

The bio-assay method of adrenal NEL analysis used in this study cannot be considered specific for epinephrine and norepinephrine. The much higher levels of the substances assayed in adrenal venous blood than in simultaneously collected arterial blood indicate that most of the substances assayed arose in the adrenal gland. One can conclude that the method most likely measured epinephrine and norepinephrine under these circumstances, but does not differentiate the two.

Alteration of pH of the bath in which the rabbit aortic strip is suspended is known to affect smooth muscle contractility; a more alkaline pH tends to increase contractility, and a more acid pH tends to decrease con-
tractility. In two animals studied, plasma pH changes during hypoxia were not significant, so it appears doubtful that the increased contraction of the rabbit aortic strip observed during hypoxia could have been due to associated respiratory alkalosis.

Certain adrenal steroids are known to augment the contraction of rabbit aortic smooth muscle produced by norepinephrine. In our study, there was no evidence of increased secretion of 17-hydroxycorticosteroids during hypoxia; thus, it is unlikely that the increased contraction of the rabbit aortic strip, when tested with hypoxic adrenal venous plasma, was due to elaboration of adrenal cortical steroids. However, the secretion of other adrenal steroids was not measured, and this possibility cannot therefore be entirely dismissed.

The changes of hematocrit levels during rapid saline infusion indicate that considerable saline solution was present in the blood plasma at that time. Alterations in extracellular sodium and potassium are known to affect smooth muscle contractility: increase in extracellular sodium or decrease of extracellular potassium tends to lower contractility of smooth muscle in response to epinephrine. Thus, it is important to be certain that the apparent decrease of adrenal medullary secretion during rapid saline infusion did not result from an effect upon sodium and potassium concentrations in the bath. In four of the five animals studied during saline-induced hypervolemia, output of NEL tended to return to normal after pulmonary arterial pressure fell, although the hematocrit remained low. A comparison of hematocrits and adrenal NEL output during control, during saline-infusion period, and after infusion was of interest in two animals. In each animal hematocrit and NEL output fell strikingly during the saline-infusion period. After infusion, the hematocrits remained below those in saline-infusion period, yet NEL output had increased to above control level. Two animals infused with Krebs' solution of the same composition as the test bath also showed increased cardiac output with a fall in NEL output, indicating that the apparent decrease of NEL output was un-
related to alteration in the chemical composition of the bath. This suggested that the saline used in these experiments did not interfere with the analytical method.

**Hypoxia**

The response of adrenal medullary secretion to hypoxia confirms the work of Houssay and Molinelli,2 of Van Loo, Surtshin, and Katz,18 and of Baugh, Cornett, and Hatcher.3 Our study can be considered somewhat more specific than previous studies, however, since the previous studies employed an intact animal for assay, and thus did not exclude the possibility of other substances, such as angiotonin, being responsible for the observed rise in blood pressure. The failure of cardiac output to rise in our hypoxic animals was unexpected. The fact that the adrenal secretion of the left adrenal gland was not entering the systemic circulation could be a factor in the failure of the cardiac output to increase. However, in five experiments on intact animals, cardiac output rose during hypoxia; in two of these the cardiac output later failed to increase during hypoxia after the abdomen was opened, suggesting that the trauma of the abdominal operation, with possible splanchnic blood pooling, was responsible for the observed lack of cardiac output response to hypoxia. The increase of hematocrit during hypoxia was similar to that observed by Baugh, Cornett, and Hatcher.3 In contrast to the observations of Van Loo and co-workers,18 we observed increased adrenal medullary secretion during hypoxia during the period of increased systemic arterial pressure. Thus, the adrenal medullary response was not conditioned by a fall in systemic pressure in our studies. Since the studies of Van Loo and associates were performed during a shorter period of more severe and increasing hypoxia, their study was not strictly comparable to ours.

Our failure to find evidence of increased adrenal 17-OHCS output during hypoxia is in accord with the observations of Hale and associates,19 who noted no increase in 17-OHCS levels in venous plasma of men exposed to moderate hypoxia.

**Hemorrhage**

The increase in adrenal NEL output observed after bleeding confirms the observations of Walker and associates6 who employed a chemical fluorometric method. These authors observed augmentation ratios of 1.8 to 59.1 in adrenal catecholamine output when the blood pressure of dogs was lowered to 30 to 75 mm. Hg by hemorrhage. We observed augmentation ratios of 1.8 to 17.0 in dogs with blood pressure lowered to 40 to 50 mm. Hg by bleeding. Walker and associates6 observed a further increase of catecholamine output.
when animals were bled without lowering blood pressure, suggesting that the adrenal medullary secretion may be controlled by blood volume as well as by blood pressure.

**Infusion**

The observations of adrenal medullary secretion in relation to hypervolemia, anemia, and elevated cardiac output during rapid saline infusion are of interest. The increase of cardiac output in association with hypervolemic anemia produced by dextran infusion has been previously described in man and in animals. Studies of Justus, Cornett, and Hatcher suggested that a transferable humoral substance capable of increasing cardiac output was present in dextran-induced anemia. Their study suggested the possibility that epinephrine or norepinephrine could be, in part, responsible. We attempted to study this problem further by producing an increased cardiac output with hypervolemic anemia associated with rapid saline infusion. In our study, increased secretion of adrenal medullary substances was not associated with the increased cardiac output during rapid saline infusion. The cardiac outputs fell toward normal after the pulmonary arterial pressures declined, even though the animals were yet anemic, suggesting that increased filling pressure, rather than anemia, was largely responsible for the increased cardiac output in these animals. The decline of adrenal NEL output during saline-induced hypervolemia suggests that adrenal medullary secretion may fall during hypervolemia; this is in accord with Walker's hypothesis that blood volume may be an important factor in the control of adrenal medullary secretion.

**Summary**

This study reports the effect of hypoxia, of lowering blood pressure by bleeding, and of rapid infusion upon adrenal secretion in anesthetized dogs. Adrenal norepinephrine-like substances (NEL) were measured in adrenal venous blood by means of a bio-assay method, using the rabbit aortic strip. In 10 of 11 dogs breathing 7.1 per cent O₂ in N₂, the left adrenal NEL output was augmented 1.5 to 6.6 times control levels. The increased adrenal medullary secretion during hypoxia was not dependent upon a fall in systemic arterial blood pressure and was not associated with an increase of 17-hydroxycorticosteroid output. In five dogs bled to a blood pressure...
of 80 to 90 mm. Hg, left adrenal NEL output was augmented 2.9 to 7.4 times control levels. In 11 animals in which the blood pressure was lowered to 40 to 50 mm. Hg by bleeding, left adrenal NEL output was augmented 1.8 to 17 times control levels. Seven dogs were made anemic and hypervolemic by rapid infusion of 1,125 to 1,900 ml. normal saline or Krebs’ solution. Cardiac outputs were increased more than 200 per cent in six, and considerable dilution anemia was produced. However, left adrenal NEL outputs fell to values ranging from 14 to 50 per cent of control. During rapid infusions, output of adrenal 17-OHCS increased 18.5 to 92 per cent. It is concluded that increased adrenal medullary secretion did not participate in the increase of cardiac output observed in these seven animals.

Acknowledgment
The plasma analyses of adrenal 17-hydroxycorticosteroids in these experiments were performed under the supervision of Dr. Emile Werk, Chief of Metabolic Disease Section, Cincinnati Veterans Hospital, Cincinnati, Ohio.

The angiotonin used in these studies was kindly supplied as angiotensin, 5,000 units per mg., by Dr. Irvine H. Page, Cleveland Clinic, Cleveland, Ohio.

References
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