Arterial Hypertension in Hemidecorticate Rats

By M. R. Covian and H. E. J. Houssay

Hemidecortication usually caused arterial hypertension in rats for one or two months. Sympatholytic drugs caused a transient reduction in blood pressure. Release of subcortical centers from the modulating action of the cerebral cortex seems to be the best explanation.

In preliminary reports it has been shown that removal of one cerebral hemisphere causes an increase of the arterial blood pressure in rats. In the present paper the characteristics of this hypertension, the effects of some drugs and the removal of the adrenals on it are presented.

Material and Methods

White male and female rats weighing 150-200 Gm. were used. The operation was performed under Nembutal anesthesia (4 mg. per 100 Gm. intraperitoneal). After a midline skin incision and opening of the skull, the cortical tissue on one side was sucked away with a small glass cannula using light suction. The dura was not sutured. Figure 1 shows the operation performed; all brain tissue to the thalamus and colliculi was removed. Control rats underwent all steps of the operation except removal of cortical tissue.

Arterial blood pressure was generally determined by the method of Williams, Harrison and Grollman; rats with blood pressure over 120 mm. Hg were considered hypertensive. In some rats blood pressure was determined directly through a polyethylene cannula introduced into the common carotid and connected to a mercury manometer, after the ether was turned off.

Bilateral adrenalectomy was performed in a one stage operation by a dorsal approach under ether anesthesia. Sodium chloride as a 2 per cent solution was given ad libitum.

Results

Effects on blood pressure. Seventy-two of 79 operated rats developed hypertension. The latency and duration of the hypertension was as follows: in 77 per cent of operated animals it appeared during the first 20 days (44 per cent in from 2 to 10 days and 33 per cent in from 11 to 20 days) and in 23 per cent it appeared in 21 to 30 days. The hypertension was not permanent, lasting no more than two months in 90 per cent of the rats and three months in the remaining 10 per cent.

Figure 2 shows in the first two columns the average blood pressure of all the 72 rats before operation (lined column) and after operation (dark column). The remaining pairs of columns are individual examples: the postoperative values being given in white columns. The frequency distribution of the hypertensive rats is given in table 1.

In figure 3 the full line shows the development of the hypertension in 20 hypertensive rats. It will be observed that blood pressure rose, progressively reaching a maximum in 20 to 35 days, but thereafter declined to control level by 90 days. That these effects are caused by hemidecortication and are not coincidental with the operative procedure is shown by the stability of blood pressure in 10 control rats (broken line).

In figure 4 the full line represents the development of the hypertension of one rat. Before the operation the blood pressure fluctuated between 115 and 118 mm. Hg; 18 days after the hemidecortication (indicated by an arrow) its value was 128 mm. Hg; from then on it rose, reaching a value of 180 mm. Hg 28 days after operation and maintaining its high values with oscillations. Fifty-seven days after operation the blood pressure was 150 mm. Hg; the direct blood pressure, without anesthesia, taken a short time later, gave a value of 145 mm. Hg. The blood pressure values of one of the control rats is indicated by the broken line; no significant change is observed after craniotomy alone.

The electrocardiogram revealed that 5 hemidecorticate rats had average heart rates of 473 per minute and 5 normal rats of the same.
HYPERTENSION IN HEMIDECORTICATE RATS

TABLE 1.—Magnitude of Hypertension

<table>
<thead>
<tr>
<th>mm. Hg</th>
<th>No. of rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>120-130</td>
<td>8</td>
</tr>
<tr>
<td>130-140</td>
<td>20</td>
</tr>
<tr>
<td>140-150</td>
<td>21</td>
</tr>
<tr>
<td>150-160</td>
<td>2</td>
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<tr>
<td>160-170</td>
<td>12</td>
</tr>
<tr>
<td>170-180</td>
<td>7</td>
</tr>
<tr>
<td>180-190</td>
<td>2</td>
</tr>
</tbody>
</table>

weight 399 per minute. The hemidecorticate rats showed more activity and excitability than the normal rats and had a marked hyperphagic reaction after fasting.4

Some Effects of Drugs. Dibenamine (10 mg./100 Gm.) was given by stomach tube to 5 hypertensive and 5 control rats. Figure 5 shows a temporary decline of arterial pressure approximately to normal levels. On the next day, the blood pressure rose again to 160 mm. Hg but administration of the same dose of Dibenamine again decreased it by 26 per cent. After the effect of the drug had passed, the blood pressure rose again. The blood pressure values and its changes in one of the rats of the group are represented in full line; it also shows redevelopment of hypertension after the effect of the Dibenamine has passed off.

The dotted lines show that Dibenamine caused much less reduction of pressure in 5 control rats.

Fourneau 933 was given intravenously (0.5 mg./100 Gm.) to 16 hypertensive rats causing a fall of blood pressure in all of them. Figure 6 shows the results obtained in one rat: starting from 148 mm. Hg the blood pressure fell to 100 mm. Hg (33 per cent) five minutes after the injection and to 90 mm. Hg (39 per cent) after 10 minutes. Thereafter, it began to rise, reaching 130 mm. Hg in 60 minutes and 140 in 90 minutes. This was the usual response; however, some rats showed a hypertensive reaction following the falling after the injection. The drug was also injected into six normal rats, causing a 33 per cent fall of blood pressure.

Tetraethylammonium bromide was given intravenously (0.5 mg./100 Gm.) to two rats and the blood pressure was taken from the common carotid. In one animal the blood pressure fell from 126 to 120 mm. Hg (4.7 per cent and in the other from 130 to 115 mm. Hg (11.5 per cent).

Hyderginc* was injected subcutaneously (0.3 mg./100 Gm.) into 4 hypertensive rats. Thirty minutes after the injection blood pressure decreased, reaching its maximum in 60 minutes and returning to normal 1.5 to 2 hours later. Two rats showed a hypertensive reaction before normalization. Figure 7 illustrates the

* Provided by Sandoz Chemical Company.
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In Fig. 3, average blood pressures of 20 hemidecorticate rats (full line) and 10 control rats (broken line) are shown. Arrow shows time of hemidecortication and craniotomy.

In Fig. 4, a hemidecorticate rat (full line) and its control (broken line) are compared. Dark line on right: direct blood pressure. Arrow shows moment of hemidecortication or craniotomy.

In Fig. 5, the effects of Dibenamine are illustrated. The blood pressure fell from 140 to 110 mm. Hg (21 per cent) in 30 minutes and kept this value up to 60 minutes. Thereafter it increased, reaching the value of 140 in 2.5 hours. In five normal rats the injection of hydergine caused no significant fall of the blood pressure.

In five hypertensive rats, bilateral adrenalectomy caused a permanent fall of the blood pressure beginning the day after the operation. Figure 8 illustrates the result obtained in one rat: blood pressure previous to the adrenalectomy was 140 mm. Hg; it fell to 100 after the operation and remained low values during the following months.

The depressing effect of total adrenalectomy on the blood pressure has also been observed in...
normal animals and in dogs and rats with renal hypertension.

**Discussion**

The results obtained would seem to indicate an increased activity of the sympathetic system and consequently an increase of the blood pressure following removal of one cerebral hemisphere in the rat.

In recent years many investigators have observed changes in the arterial blood pressure by electric stimulation of several areas of the cerebral cortex in animals and man. On the other hand, the hypothalamic representation of the sympathetic system is very well known and the relation between cerebral cortex and hypothalamus has been shown by Ward and McCulloch. Walker, Browne and McQueen* found no permanent changes in chronic neurogenic hypertension following hypothalamic lesions and Johnson and Browne, working in dogs with the same type of hypertension, observed no demonstrable effect when cortical ablations were performed.

The results reported suggest that subcortical cardiovascular centers are transiently modified by hemidecortication. Such an effect could be explained by some sort of "irritation" due to the operation or due to the removal of the modulating cerebral influence upon the subcortical structures. The rather long-lasting hypertension and the negative result of craniectomy are against the first explanation.

**Summary**

Arterial hypertension developed in 91.2 per cent of hemidecorticate rats in the course of the month following operation. It usually lasted no more than two months.

Administration of sympatholytic drugs to these hypertensive rats induced a transient fall of blood pressure to normal levels.

Bilateral adrenalectomy caused a permanent fall of the blood pressure.

This hypertension could be attributed to an increased activity of the sympathetic system following release of subcortical structures from the normal modulating action of the cerebral cortex.

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**References**

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