Antihypertensive Effect of Hypophysectomy in Dogs with Hypertension Following Bilateral Carotid Sinus Constriction

By Edward W. Hawthorne, M.D., Ph.D., and Mary Gaspar, M.S.

A chronic type of experimental hypertension has been produced in dogs by bilateral sinus area constriction. Hypophysectomy has a prolonged antihypertensive effect in dogs with persistent hypertension resulting from carotid sinus area constriction, while no decrease in mean arterial pressure is seen after hypophysectomy in normotensive control dogs. These findings suggest the possibility that altered hypophyseal function participates in the pathogenesis of this type of hypertension.

The bilateral carotid sinuses were constricted as described by Wakerlin1 using the plastic clamps described1,2 and generously supplied to us by Dr. Wakerlin.

After these dogs became hypertensive, they were hypophysectomized and observed for periods of varying lengths. Normotensive dogs, without prior carotid sinus constriction, were also hypophysectomized to observe the effect of complete hypophysectomy on their mean arterial pressure.

Preoperatively the dogs were given 25 mg. of cortisone intramuscularly. Brain shrinkage was obtained by administering intravenously 50 ml. of 30 per cent glucose solution approximately 20 to 30 min. prior to surgery. Hypophysectomy was accomplished via a left transtemporal approach, following (in part) the principles of Cushing.6 The surgical technic was modified in that the entire pituitary was removed under direct vision by suction rather than with Cushing forceps.

Glucose solution (30 per cent) was intravenously injected postoperatively to relieve increased intracranial pressure during the 24 hours immediately following surgery. Small maintenance doses of either prednisolone or cortisone (usually 12 mg. every third day, intramuscularly) were given. Postoperative therapy included antibiotics. Dogs invariably developed hypoglycemic shock—some died—following cessation of maintenance therapy. Occasionally, a dog was not given corticoids but was maintained in good clinical condition by adding a glucose supplement to his diet. Both the normotensive dogs (without bilateral carotid sinus constriction) and the carotid sinus hypertensive dogs were maintained postoperatively in the same manner. In some instances the dogs developed obesity postoperatively, suggesting hypothalamic damage. Such dogs were not included in the results.

Insulin sensitivity studies were also performed on some of the dogs before and after hypophy-
HAWTHORNE, GASPAR

FIG. 1 Top. A typical chronic rise of pressure.
FIG. 2 Middle. Typical changes in mean arterial pressure in a normotensive dog following hypophysectomy.
FIG. 3 Bottom. Fall in mean arterial pressure following hypophysectomy in dog number 22.

sectomy. The test dose of insulin, given intravenously, was 0.025 units/Kg.7

Throughout the period of study, the mean femoral arterial pressure was recorded by direct femoral artery puncture8 in the unanesthetized, lightly restrained animal two or more times a week.

The criteria for complete hypophysectomy were direct observation at operation, gross and micro-

scopic examination of the hypothalamic area of the brain and sella turcica region and microscopic appearances of the adrenals at autopsy.

RESULTS

Effect of Bilateral Carotid Sinus Constriction. Twenty-nine dogs received bilateral carotid sinus constriction. All but 3 developed a chronic and persistent hypertension by the third postoperative month. Sixteen (55 per cent) developed hypertension acutely, that is, within the first month after constriction.

In 10 of the dogs (34 per cent) the mean arterial pressure gradually rose to hypertensive levels over a period of 3 months (fig. 1, table 1).

One of the 3 dogs that did not have a hypertensive response to the carotid sinus area constriction was a "spontaneous hypertensive" (control mean arterial pressure averaged 154 mm. Hg). The other 2 remained normotensive for a period of 4 months after operation. At autopsy, it was found that in these animals the plastic clamps were loose and no constriction had occurred.

Effect of Hypophysectomy on Mean Arterial Pressure in Normotensive Dogs. Five normotensive dogs were hypophysectomized after a control period of one or more months. After hypophysectomy they received maintenance therapy similar to that administered to hypophysectomized dogs with carotid sinus area constriction. None showed a fall in mean arterial pressure below the control level following hypophysectomy (fig. 2).

Hypotensive Effect of Hypophysectomy. Table 2 shows the change in arterial pressure

TABLE 1.—Summary of Pressure Changes in Normal Dogs* Three Months After B.C.S.C.†

<table>
<thead>
<tr>
<th>Period of observation</th>
<th>Number of dogs</th>
<th>Mean ± S.D.</th>
<th>Average rise</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td>28</td>
<td>119 ± 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension‡</td>
<td>29</td>
<td>155 ± 30</td>
<td>+35</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* Average initial weight, 10 Kg.; range 7 to 14 Kg.
† Bilateral carotid sinus constriction.
‡ Third month post operative.
### Table 2.—Antihypertensive Effect of Hypophysectomy in Dogs with Carotid Sinus Hypertension

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Sex</th>
<th>Initial weight (Kg.)</th>
<th>Mean femoral artery pressure (mm. Hg)</th>
<th>Status of hypophysectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Average pressure last two months before hypophysectomy</td>
<td>Average pressure first month after hypophysectomy</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>8</td>
<td>121</td>
<td>156</td>
</tr>
<tr>
<td>21</td>
<td>M</td>
<td>8</td>
<td>120</td>
<td>150</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>9</td>
<td>119</td>
<td>154</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>8</td>
<td>109</td>
<td>159</td>
</tr>
<tr>
<td>25</td>
<td>F</td>
<td>9</td>
<td>111</td>
<td>151</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>7</td>
<td>120</td>
<td>183</td>
</tr>
</tbody>
</table>

Mean: 817 ± 2 S.D. 159 ± 42 124 ± 35

* Bilateral carotid sinus construction.

that followed hypophysectomy in 6 dogs with hypertension resulting from carotid sinus area constriction. All of these dogs showed a definite fall in pressure, in most instances to normotensive control levels. Figure 3 shows the typical pattern of change in the mean arterial pressure following hypophysectomy in dog number 22. The dog showing the least hypotensive response (no. 25) was found to have an incomplete hypophysectomy at autopsy.

### DISCUSSION

Our studies show that a chronic experimental hypertension can be produced by bilateral carotid sinus area constriction in dogs using special plastic clamps, confirming previous findings.¹

The finding that hypophysectomy has an antihypertensive effect on dogs with carotid sinus hypertension appears to be *bona fide*. This seems especially true in view of the lack of a blood pressure lowering effect from hypophysectomy in normal dogs. It might be said that a hypotensive effect from hypophysectomy in the normal dogs was prevented by the small maintenance doses of cortisone administered regularly post-operatively. It is to be stressed, however, that the hypertensive animals on similar post-operative therapy following hypophysectomy showed an average arterial blood pressure fall of 35 mm. Hg. The mean arterial pressure levels in dogs before and after hypophysectomy recorded by Goldblatt and associates⁵ showed no clear fall, without postoperative corticoid therapy. These studies suggest that there is an endocrine factor in the pathogenesis of the experimental hypertension which bilateral carotid sinus constriction produces in dogs and that this factor is in some way related to hypophysal function.

In view of our findings it will be interesting to observe the effects of administration of larger doses of corticoids and adrenocorticotropic hormones as a means of determining whether or not this blood pressure lowering effect of hypophysectomy is mediated solely by way of a decrease in adrenal cortical activity.

### ACKNOWLEDGMENT

Acknowledgment is made of the significant contributions to this study of Clarence S. Green, D.D.S., M.D. (Deceased); R. S. Simmons, M.D.; W. G. Pogue, M.D.; Mrs. E. Hawthorne, R.N.; Harry K. Thompson, B.S.

### REFERENCES


Antihypertensive Effect of Hypophysectomy in Dogs with Hypertension Following Bilateral Carotid Sinus Constriction

EDWARD W. HAWTHORNE and MARY GASPAR

_Circ Res._ 1959;7:705-708
doi: 10.1161/01.RES.7.5.705

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1959 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/7/5/705

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation Research_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation Research_ is online at:
http://circres.ahajournals.org/subscriptions/