The Water and Electrolyte Content of the Tissues in Hypertension

By Arthur Grollman, Ph.D., M.D.

with the technical assistance of Charles Campbell, Joe Mims and Floyd Rector

An analysis of the water and electrolyte content of various tissues of rats rendered hypertensive by a period of choline deficiency at the time of weaning indicates that no alterations are induced by this procedure. It is concluded that the hypertensive process, per se, is not necessarily accompanied by changes in the water and electrolyte content of tissues; where such changes are observed, they are probably secondary to parenchymal renal changes.

Several investigators have demonstrated an alteration in the water and electrolyte content of the tissues in hypertension. These results have been interpreted by some to indicate that the observed alterations, either directly or through some disturbance in adrenal cortical function, are responsible for the observed elevation in blood pressure. However, the above-mentioned studies have been performed on animals subjected to various manipulations of one and removal usually of the contralateral kidney. Despite the absence of any overt evidence of renal failure, one might consider the observed alterations as evidence of renal dysfunction rather than as part of the hypertensive process, per se. This possibility has been emphasized in particular by Ledingham who noted a tendency for the observed abnormalities to disappear with time following the application of a constricting band to one renal artery with removal of the contralateral kidney, despite the maintenance or accentuation of the elevation in blood pressure.

The present observations were made on rats rendered hypertensive by subjecting them at the time of weaning to a choline-free diet. This procedure, as shown by Hartcroft and Best, results in hypertension when the animals have grown to adult size. The smaller arteries of the kidneys of such animals reveal marked thickening and resemble closely those seen in human so-called essential hypertension of advanced degree. They manifest no evidence of renal excretory insufficiency and hence offer an excellent experimental material for the study of hypertension uncomplicated by more drastic manipulations or ablation of renal tissues.

METHODS

Rats reared in the laboratory were weaned at 20 days of age and placed on a choline-deficient diet for 10 days. They were then transferred to a normal stock diet for at least four months, after which time blood pressure determinations were made at bi-weekly intervals. When the blood pressure had become stabilized at levels of 150 to 190 mm. Hg, rats weighing 350 to 450 Gm. were sacrificed for analysis. Except for the observed elevation in blood pressure, the animals appeared entirely normal. Controls were rats of the same colony which had not been subjected to the choline-deficient diet. These were paired by sex and body weight (±5 Gm.) with the experimental group. The blood pressure of these controls varied between 90 and 110 mm. Hg.

Blood pressures were determined on the unanesthetized animal by the photoelectric tensometer of Kersten, Brosene, Abbondi, and SubbaRow. The tissues were prepared and analyzed as described in previous publications from this laboratory.

OBSERVATIONS

The results of the present study are summarized in table 1 which includes data on the water, sodium, potassium, magnesium and chloride contents of the brain, gut, heart (left ventricle), liver, skeletal muscle (thigh) and skin (abdomen) of groups of six hypertensive and an equal number of control rats. A comparison of the values and their standard deviations from the mean indicate clearly that within...
Tissue Water and Electrolytes in Hypertension

Table 1.—Water and Electrolyte Content of Normal and Hypertensive Rats

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Water (g/100g fat-free)</th>
<th>Sodium (mEq/kg wet tissue)</th>
<th>Potassium (mEq/kg wet tissue)</th>
<th>Magnesium (mEq/kg wet tissue)</th>
<th>Chloride (mEq/kg wet tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Hypertensive</td>
<td>Normal</td>
<td>Hypertensive</td>
<td>Normal</td>
</tr>
<tr>
<td>Brain</td>
<td>75.8±2.3</td>
<td>76.1±2.7</td>
<td>54.5±3.0</td>
<td>56.1±4.8</td>
<td>101.5±2.0</td>
</tr>
<tr>
<td>Gut</td>
<td>79.5±1.4</td>
<td>80.0±1.9</td>
<td>98.9±3.4</td>
<td>88.7±3.1</td>
<td>93.0±2.9</td>
</tr>
<tr>
<td>Heart</td>
<td>79.2±0.7</td>
<td>79.1±0.6</td>
<td>80.6±3.2</td>
<td>97.5±3.6</td>
<td>81.3±1.8</td>
</tr>
<tr>
<td>Liver</td>
<td>71.1±2.1</td>
<td>71.3±2.0</td>
<td>92.0±3.1</td>
<td>95.0±3.0</td>
<td>124.0±2.0</td>
</tr>
<tr>
<td>Skeletal</td>
<td>muscle</td>
<td>76.5±0.8</td>
<td>78.6±0.7</td>
<td>29.9±1.8</td>
<td>29.0±2.9</td>
</tr>
<tr>
<td>Skin</td>
<td>62.0±3.5</td>
<td>62.6±4.0</td>
<td>96.0±2.4</td>
<td>98.0±3.1</td>
<td>28.1±2.2</td>
</tr>
</tbody>
</table>

Values for water are expressed as grams per 100 grams of fat-free tissue; those for electrolytes, as milliequivalents per kilogram of fat-free, wet tissue except for brain which was not defatted. All values are averages of results obtained on six animals.

the limits of experimental error there is no difference in the composition between the normal tissues and those removed from the hypertensive animals.

Observations were also made on a second group of hypertensive animals which had been treated with a renal extract prepared by the method of Grollman, Williams and Harrison. These were analyzed with the expectation that the values obtained on the untreated hypertensive group would differ from those of the normotensive group. Despite the lowering of the blood pressure in the treated group, the composition of their tissues did not differ within the limits of experimental error from the normal and untreated hypertensive groups. This adds further confirmation of the independence of the composition of the tissues of the level of the arterial blood pressure.

Discussion

The present study demonstrates that hypertension may be induced in the rat without altering the distribution of water and electrolytes in the tissues. This finding is in sharp contrast to those of previous studies on the rat, dog and man. The discrepancy must be attributed to the different manner in which hypertension was induced in the different studies. The procedure used in the present investigation involved no manipulation of the kidney. Although accompanied by vascular alterations in this organ and hence presumably of renal origin, there was less damage to the parenchyma and no apparent loss of parenchymal renal tissue as in the case of the previous methods used in inducing hypertension. The conclusion, accordingly, would appear justified that the previously observed disturbances in water and electrolyte composition of tissues in hypertension are not an essential part of the hypertensive process, per se, but are secondary probably to the incidental renal damage incurred in inducing the disorder. That the kidney exerts an effect on the electrolyte content of the tissues is demonstrated by the movement of sodium and chloride from the extracellular to the intracellular spaces and of potassium in the opposite direction, following nephrectomy in the dog (unpublished observations). These alterations are noted in the days immediately following nephrectomy before hypertension appears.

Alterations in the water and electrolyte content of tissues may occur as a result of changes in the relative volumes of the intra- and extracellular phases. Unless this function is determined, it is impossible to conclude whether any observed moderate increases in sodium and chloride and decreases in potassium and magnesium contents are a result of actual migration of these ions between the cellular and extracellular phases, or whether they reflect simply an alteration in the relative volumes of the body compartments. As shown by Ledingham, the alterations in water, sodium and potassium which he observed in relatively acute experiments were explicable on the basis of an observed increase in extracellular fluid volume. In the present experiments, obviously, no such alterations in the extracellular fluid volume...
could have occurred, since no alteration in water and electrolyte content of the tissues resulted. In previous studies from this laboratory, an increase in extracellular fluid volume was noted in chronic hypertension in man as well as in the dog with chronic hypertension induced by the application of a figure-of-eight ligature to one kidney and excision of the contralateral kidney. Despite the absence of evident signs of renal excretory insufficiency it is not improbable that there was a greater interference with renal function in the patients and dogs used in these studies than in the rats rendered hypertensive by choline deficiency in early life.

It is not to be inferred from the present studies that marked alterations in water and electrolyte metabolism may not be an important finding in hypertension. Many such alterations have been demonstrated unequivocally in both the experimental animal and the human. The present studies, however, indicate that such changes play no basic or primary role in the pathogenesis of the disorder but merely reflect, probably, the renal disturbances which are frequent concomitants of the disorder.

**Summary**

The water, sodium, potassium, magnesium and chloride content of the brain, gut, heart, liver, skeletal muscle and skin were determined in a series of adult rats rendered hypertensive by subjecting them after weaning to a short period of choline deficiency. The results obtained did not differ from those obtained in a series of control normotensive animals. It is concluded that the changes in water and electrolyte content of the tissues observed by previous workers are not essential characteristics of the hypertensive state but are to be attributed rather to renal disturbances. There is little basis for the widely accepted notion that alterations in salt and water content of tissues either cause or reflect an essentially basic disturbance in hypertensive cardiovascular disease. Such alterations are probably only coincidental to disturbances in renal function which usually accompany the basic renal defect responsible for hypertensive disease.

**REFERENCES**

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