INCREASED SALT APPETITE IN ADRENALECTOMIZED RATS

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Adrenalectomized rats are known to have a definitely increased salt need, inasmuch as the administration of large quantities of salt either greatly reduces or eliminates the symptoms of insufficiency, and actually increases the survival incidence (Rubin and Krick, 1933; Gaunt, Tobin and Gaunt, 1935; Kutz, McKeown and Selye, 1934). But is this need accompanied by an increased salt appetite, and will the adrenalectomized rat, if given free access to salt take sufficient quantity to keep itself alive and free from symptoms of insufficiency? In an effort to answer these questions the following experiments were undertaken.

METHODS. It was necessary for this purpose to devise a method by which salt could be given freely, under circumstances which made possible measurement of the actual amount ingested. It would have been simplest, of course, to present granular salt in a separate container. However, the small amount ingested daily and the comparatively large amount spilled or carried away on the paws definitely ruled out a quantitative measure by this method. For this reason salt was offered in solution in the drinking water. At the outset a 1 per cent salt solution was used because Rubin and Krick obtained their successful results from a solution of approximately this strength; but since, with only the salt solution available, the rat's intake would depend partly on the salt need and partly on the thirst for water, access was given at the same time to tap water presented in a second container. In this way the rat could satisfy its thirst and its salt appetite independently.

In the first series of experiments with the 1 per cent salt solution and water, the animals also received the usual amount of salt in the McCallum diet (approximately 0.145 gm. per day). Inasmuch as the normal rats did not distinguish between the salt solution and the water, a second series of experiments was started with the strength of the salt solution increased to 3 per cent and no salt given in the food. It was found then that the normal animals did differentiate very definitely between the 3 per cent salt solution and the water.

The rats were kept in individual cages containing a food cup, and two inverted graduated bottles, one with salt solution, the other with tap
water. The water and salt solutions were changed at the same time to avoid any difference in the freshness of the two liquids. The fluid intake was recorded daily and the body weight was recorded weekly.

To establish the effects produced by the salt solution two control groups of animals were adrenalectomized and kept under exactly the same conditions, except that one received only the salt contained in the food, while the other received no salt, either in the drinking water or in the food.

The adrenalectomy was done by the technique in which the surrounding fat, connective tissue and also about one-quarter inch of the pedicle are removed with the gland (Pencharz, Olmsted and Giragossintz, 1931; Firor and Grollman, 1933). In order to make certain that the effects produced depended specifically on adrenalectomy, a third group of control experiments was performed to determine the relation of gonadectomy and hypophysectomy to salt appetite.

RESULTS. Survival rate of adrenalectomized rats on a saltless diet and on a standard McCollum diet. Fifteen animals that had previously been on the standard McCollum diet were adrenalectomized and placed on a saltless diet. All of these animals immediately developed symptoms of insufficiency with a loss of weight, appetite, and death after an average of 11 days. None of the animals survived.

Twenty-six animals raised on the McCollum mixture were adrenalectomized and continued on this standard diet from which they received approximately 0.145 gram of salt per day. Sixteen of these animals died at an average interval of 17 days, while ten animals, or 39 per cent, gave signs of living their normal span of life, and were killed about forty-five days after adrenalectomy.

Increased survival rate of adrenalectomized rats with access to 1 per cent or 3 per cent salt solution and tap water. Thirteen animals on the regular McCollum diet given the choice of drinking 1 per cent salt solution or tap water, drank enough of the former to increase very markedly their chances of survival. Nine, or 69 per cent, showed all signs of living indefinitely and only four, or 31 per cent, died. This is a marked increase in the survival rate over that of the animals which received only the salt contained in the McCollum diet. Moreover the average duration of life of the animals that died was 19 days, which is greater than that of animals on either saltless diet or on only the McCollum mixture.

Five animals given the choice of 3 per cent salt solution or tap water showed a survival rate of 80 per cent. One animal lived 38 days, the others showed a normal gain in body weight and no signs of insufficiency except a slightly decreased appetite.

Further proof that the animals were actually kept alive by the salt which they ingested voluntarily, is shown by the effects produced on survival when the 1 per cent salt solution was removed leaving only tap
water available. The nine animals which gave every indication of living indefinitely on the 1 per cent salt solution were deprived of the salt solution at intervals ranging from 33 to 77 days after adrenalectomy but were still kept on the McCollum diet. (See the last two columns in table 1.) Eight out of the nine animals died after an average of 5.1 days with a range of variation of 4 to 7 days, while the ninth animal was still alive on the 36th day.

Amount of increase of salt intake in adrenalectomized rats. A marked effect produced by adrenalectomy on the salt appetite is shown very clearly in figure 1. It will be seen that before adrenalectomy the tap water averaged 20 cc. per day, the intake of 1 per cent salt solution only 10 cc. per day; and that almost immediately after adrenalectomy the intake of tap water began to decrease, while the intake of salt solution showed a sharp increase. Forty days after adrenalectomy, when the animal was killed, the salt solution intake had reached a level of 45 cc. per day and was still increasing while the water intake had decreased to less than 4 cc. per day.

The results of these experiments are summarized in table 1. It will be seen that the average daily intake of tap water decreased from 16.5 cc. for the 10 days before adrenalectomy to 3.4 cc. for the 20 to 30 day period after adrenalectomy, while the intake of the 1 per cent salt solution increased from 16.9 cc. for the 10 day pre-operative period to 27.6 cc. for the 20 to 30 day post-operative period. These daily averages of 27.6 cc. of salt solution and 3.4 cc. of tap water indicate definitely that the animals differentiated between these two fluids. However, before adrenalectomy the average daily intake was practically identical for tap water and for the 1 per cent salt solution (16.5 cc. as compared to 16.9 cc., respectively). This must mean that before operation the animals did not
differentiate between the two fluids. In keeping with this view is the
fact that some of the animals drank more water while others took more
salt solution, a fact which suggests that it was largely a matter of chance
which bottle was selected. It seems probable that had a definite distinc-
tion been made between these two fluids, the salt solution intake before
adrenalectomy would have been much lower, consequently the percentage
increase in the salt need after adrenalectomy would have been much
greater than was found in these experiments.

TABLE 1

Choice of 1 per cent salt solution or water (dry diet containing 1 per cent salt)

<table>
<thead>
<tr>
<th>RAT NO.</th>
<th>AVERAGE DAILY WATER INTAKE</th>
<th>AVERAGE DAILY INTAKE OF 1% SALT SOLUTION</th>
<th>AVERAGE DAILY SALT INTAKE FROM 1% SALT SOLUTION</th>
<th>TOTAL AVERAGE DAILY SALT INTAKE</th>
<th>AVERAGE TOTAL DAILY SALT INTAKE IN FOOD</th>
<th>BODY WEIGHT</th>
<th>AVERAGE DAILY SALT INTAKE PER KILOGRAM BODY WEIGHT</th>
<th>SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>days</td>
<td>cc, cc</td>
<td>gms, gms</td>
<td>gms, gms</td>
<td>gms, gms</td>
<td>gms, gms</td>
<td>gms, gms</td>
<td>gms, gms, cc.</td>
<td></td>
</tr>
<tr>
<td>1       78 10.4 4.7          10.8 33.3</td>
<td>0.108 0.332</td>
<td>0.120 0.110</td>
<td>0.228 0.442</td>
<td>165 173</td>
<td>1.38</td>
<td>2.55</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>2       78 15.1 19.9        19.9 19.9</td>
<td>0.190 0.120</td>
<td>0.120 0.120</td>
<td>0.310 0.120</td>
<td>150 141</td>
<td>2.13</td>
<td>16 D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3       78 14.9 11.9        11.9 0.119</td>
<td>0.120 0.120</td>
<td>0.230 0.125</td>
<td>0.120 0.125</td>
<td>145 135</td>
<td>1.65</td>
<td>16 D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4       88 20.3 4.8          35.1 44.6</td>
<td>0.351 0.446</td>
<td>0.121 0.096</td>
<td>0.470 0.522</td>
<td>214 230</td>
<td>1.67</td>
<td>2.13</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>5       88 16.6 1.6         16.6 21.4</td>
<td>0.160 0.214</td>
<td>0.100 0.183</td>
<td>0.220 0.267</td>
<td>188 207</td>
<td>1.70</td>
<td>1.77</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>6       87 19.4 1.4         19.4 19.3</td>
<td>0.097 0.193</td>
<td>0.143 0.110</td>
<td>0.210 0.300</td>
<td>220 222</td>
<td>0.95</td>
<td>1.30</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>7       89 12.2 1.9          37.7 26.7</td>
<td>0.377 0.267</td>
<td>0.120 0.110</td>
<td>0.497 0.377</td>
<td>170 181</td>
<td>2.92</td>
<td>2.08</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>8       83 22.6 3.6          8.9 33.0</td>
<td>0.059 0.350</td>
<td>0.120 0.110</td>
<td>0.209 0.400</td>
<td>170 180</td>
<td>1.23</td>
<td>2.55</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>9       83 23.0 4.5          9.1 27.0</td>
<td>0.090 0.270</td>
<td>0.120 0.110</td>
<td>0.211 0.380</td>
<td>182 195</td>
<td>1.16</td>
<td>1.95</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>10      89 23.0 4.5          9.1 27.0</td>
<td>0.090 0.270</td>
<td>0.120 0.110</td>
<td>0.211 0.380</td>
<td>182 195</td>
<td>1.16</td>
<td>1.95</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>11      82 9.2 3.1          19.3 19.0</td>
<td>0.100 0.190</td>
<td>0.100 0.090</td>
<td>0.200 0.290</td>
<td>151 168</td>
<td>1.94</td>
<td>1.75</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>12      73 30.0 6.9         9.7 25.5</td>
<td>0.060 0.255</td>
<td>0.180 0.099</td>
<td>0.220 0.354</td>
<td>234 215</td>
<td>0.94</td>
<td>1.64</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>13      84 3.6 1.2          57.4 34.5</td>
<td>0.374 0.241</td>
<td>0.120 0.110</td>
<td>0.494 0.351</td>
<td>217 205</td>
<td>2.28</td>
<td>1.71</td>
<td>16 D</td>
<td></td>
</tr>
<tr>
<td>Av.     89 15.5 14.9        16.9 27.0</td>
<td>0.169 0.279</td>
<td>0.123 0.110</td>
<td>0.301 0.388</td>
<td>181 183</td>
<td>1.65</td>
<td>1.98</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Killed.
† Died.

The failure of the rats before operation to distinguish between the tap
water and the 1 per cent salt solution may have been due either to the
fact that the salt solution was too weak or to the fact that the salt which
they received in the diet was sufficient to satisfy the salt need as well as
to dull the sensitivity of the salt appetite.

Because of this failure of the animals to differentiate definitely between
the 1 per cent salt solution and water before adrenalectomy, a 3 per cent
salt solution was substituted. This was not too concentrated to be measured
accurately in the water bottles used in these experiments, and it
was of sufficient strength that the five animals which had the choice of drinking it or tap water differentiated between the two before adrenalectomy as well as afterwards. A record from one of these animals is presented in figure 1. It will be seen that the intake of the 3 per cent salt solution increased from a level of less than 2 cc. per day before adrenalectomy to 20 cc. afterwards, while the water intake remained practically the same.

The results as summarized in table 2 show that before adrenalectomy the average daily water-intake was 23.0 cc. while the intake of 3 per cent salt solution was 2.2 cc. It will be noted that this marked difference in the consumption of salt solution and water was present in all five animals. The intake of the 3 per cent salt solution for the 20 to 30 day period after

### Table 2

<table>
<thead>
<tr>
<th>RAT NO.</th>
<th>AGE</th>
<th>AVERAGE DAILY TAP WATER INTAKE</th>
<th>AVERAGE DAILY INTAKE OF 3% SALT SOLUTION</th>
<th>AVERAGE DAILY SALT INTAKE FROM 3% SALT SOLUTION</th>
<th>BODY WEIGHT</th>
<th>AVERAGE DAILY SALT INTAKE PER KILOGRAM BODY WEIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10 days before adrenalectomy</td>
<td>20-30 days after adrenalectomy</td>
<td>10 days before adrenalectomy</td>
<td>20-30 days after adrenalectomy</td>
<td>10 days before adrenalectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>days</td>
<td>cc.</td>
<td>cc.</td>
<td>cc.</td>
<td>cc.</td>
</tr>
<tr>
<td>14</td>
<td>99</td>
<td>24.4</td>
<td>23.9</td>
<td>0.6</td>
<td>16.5</td>
<td>0.018</td>
</tr>
<tr>
<td>15</td>
<td>93</td>
<td>10.0</td>
<td>14.1</td>
<td>1.8</td>
<td>4.1</td>
<td>0.094</td>
</tr>
<tr>
<td>16</td>
<td>93</td>
<td>17.0</td>
<td>16.7</td>
<td>2.7</td>
<td>11.4</td>
<td>0.081</td>
</tr>
<tr>
<td>17</td>
<td>91</td>
<td>24.6</td>
<td>20.3</td>
<td>3.0</td>
<td>18.1</td>
<td>0.090</td>
</tr>
<tr>
<td>18</td>
<td>91</td>
<td>39.0</td>
<td>27.7</td>
<td>2.7</td>
<td>12.5</td>
<td>0.081</td>
</tr>
<tr>
<td>Av.</td>
<td>93</td>
<td>23.0</td>
<td>20.5</td>
<td>2.2</td>
<td>12.5</td>
<td>0.065</td>
</tr>
</tbody>
</table>

adrenalectomy was 12.5 cc., almost six times as high as the intake before. This, undoubtedly, is a much more correct estimate of the salt needs of the adrenalectomized animals than was obtained in the experiments with the 1 per cent salt solution.

**Effect of gonadectomy and hypophysectomy on salt appetite.** It was found that gonadectomy and hypophysectomy have no effect on salt appetite. The average daily intake of 3 per cent salt solution of four gonadectomized rats was 3.0 cc. for the 10 days before adrenalectomy and 3.9 cc. for the 20 to 30 days after; and for the six hypophysectomized rats it was 3.6 cc. before and 1.5 cc. afterwards, a decrease proportional to the general decrease in metabolism.

It may be assumed, then, that the increased salt appetite which follows adrenalectomy is specific for the deficiency created by the loss of the...
secretions of the adrenal gland. It is of interest that the atrophy of the adrenals found in the hypophysectomized rats was not associated with an increase in salt appetite.

Salt appetite of normal rats. In the above experiments it was shown that the amount of salt taken voluntarily by adrenalectomized rats gave an indication of their salt need. It seemed likely that the voluntary salt intake could also be a measure of the salt need of normal animals. It was of interest to know, then, how the salt need determined in this way compares with the salt that the animals receive in the standard McCollum diet.

This diet contains 1 per cent salt which according to the calculations of Wang (1925), of an average daily food intake of 14.5 gram in adult rats would mean an average daily salt intake of 0.145 gram or 0.659 gram per kilogram body weight.

Records taken on a group of nineteen normal animals on a saltless diet with a choice of either 3 per cent salt solution or tap water gave a daily voluntary salt intake of 0.123 gram or 0.577 gram per kilogram body weight, which is very nearly the same as the amount received in the McCollum diet. It was thus determined by a very different method that the salt present in the McCollum diet is an adequate amount for normal animals.

Discussion. The fact that the salt appetite of adrenalectomized rats has such a close relationship to the salt deficiency indicates that appetite may be used as a measure of the deficiencies produced by endocrine disturbances, or by pathological changes in other parts of the body.

It has been observed on the medical wards of the Johns Hopkins Hospital that patients with Addison's disease have spontaneously expressed a great appetite for foods rich in salt, particularly ham and herring. It is also known that during pregnancy, when the greatest changes take place in the entire endocrine system, appetites may also change considerably. Thus it may be that even in man a closer study of the appetite might throw more light on the actual needs and deficiencies present in such conditions as pregnancy or in acute or chronic disturbances of the endocrine system.

SUMMARY

1. The survival rate of thirteen animals adrenalectomized and put on a saltless diet was zero per cent and the average length of life after adrenalectomy was 11 days.

2. The survival rate of twenty-six animals adrenalectomized and continued on the standard McCollum diet (approximately 0.145 gram of salt per day) was 39 per cent and the average duration of life of the animals that died was 17 days.

3. Thirteen rats kept on the standard diet and given the choice of tap
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water or 1 per cent salt solution ingested a larger quantity of salt solution after adrenalectomy and their survival rate was increased to 69 per cent.

4. Five rats kept on a saltless diet but given the choice of a 3 per cent salt solution or tap water ingested six times as much salt solution after adrenalectomy and showed a survival rate of 80 per cent.

6. It was thus determined that the salt appetite is greatly increased by adrenalectomy and by virtue of this appetite the survival rate is also greatly increased.

7. The salt needs of the nineteen normal rats determined by the choice method on the 3 per cent salt solution was shown to be approximately the same as the amount calculated empirically by McCollum; that is, 0.577 gram per kilogram body weight per day as compared to 0.659 gram for the McCollum diet.

REFERENCES

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