The Effect of Adrenal Grafting on Transplanted Lymphatic Leukemia in Rats*

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It is a well established fact that the adrenal cortical hormone exerts a depressing influence on the lymphoid tissue. A previous report from this laboratory showed that removal of the adrenals renders a rat far more susceptible to a transplantable lymphatic leukemia (1) and that treatment with the cortical hormone increases resistance to the disease (2). In the present investigation, the effect of auto- and homoplastic grafts of the adrenals on the resistance of rats to leukemia has been determined.

EXPERIMENTS

The rats used for these experiments were from a subline of the Wistar Institute strain and were approximately 8 weeks old. Inoculations were made about 2 weeks after the operative procedure.

GROUP 1.—These experiments were designed to test the effect of autografting. The adrenals of 49 rats were removed, cut in half, and the four halves reimplanted in the abdominal cavity. This proved to be ineffective in that 91.8 per cent of such animals proved susceptible to transplanted leukemia, while the 30 controls gave 80 per cent positive results.

GROUP 2.—In this group of experiments 47 rats were adrenalectomized, and one adrenal was returned to the abdominal cavity, and the other grafted into the spleen. The 50 control rats gave 94 per cent leukemia, while the grafted ones gave 85.1 per cent, a difference not mathematically significant.

GROUP 3.—The 241 rats used in this group of experiments were treated in the following way:

A.—Seventeen rats were subjected to adrenalectomy and 2 weeks later inoculated intraperitoneally with a suspension of leukemia cells. These rats proved susceptible in 100 per cent.

B.—The adrenals were removed from 65 rats, each adrenal was cut in half, and the halves were reintroduced into the abdominal cavity, with the addition of two adrenals from another rat. Ten days to 2 weeks later these animals were inoculated with leukemia cells. Only 26.1 per cent proved susceptible.

C.—Two adrenals were halved and both inoculated into the abdomen of each of 73 intact rats. Ten days to 2 weeks later the animals were inoculated with leukemia. Of these, 57.5 per cent proved susceptible, as compared with an 82.5 per cent susceptibility among the 86 controls.

GROUP 4.—These experiments were planned to show the effect of subcutaneous introduction of two additional adrenals into 34 intact rats, as compared with the susceptibility of 33 controls. The adrenal-grafted animals were rendered definitely more resistant, showing only 44.1 per cent susceptibility, as compared with 87.8 per cent in the controls. This result indicated that adrenals grafted subcutaneously are just as effective as the intra-abdominal grafts tested in group 3.

The results from the above experiments are brought together in Table 1. It will be seen from the first experiment that removal and reimplantation of the adrenals in the abdominal cavity does not affect resistance. The results are not modified when one of the grafts is introduced into the spleen, where active growth of the adrenal grafts has been noted. Simple adrenalectomy markedly reduced resistance—a finding which confirms an earlier observation (1). The removal of the adrenals and the reimplantation in the abdomen with the addition of two adrenals from other rats resulted in very definite augmentation of resistance. While the introduction of two adrenals into the abdominal cavity of intact rats increased susceptibility to a significant degree, it was not increased to the extent observed in the foregoing group. The additional adrenals implanted subcutaneously gave results comparable to those with the grafts in the abdominal cavity.

DISCUSSION

The interpretation of the reported results is not entirely clear. Certainly, a definite increase of resistance to a transplanted lymphatic leukemia re-
sulted from the implantation of two extra adrenals, whether these were added to either an intact rat or one that had undergone adrenalectomy and autografting. Autografting alone, into either the abdominal cavity or the abdominal cavity and spleen, had little or no effect; but autografting combined with homotransplantation had the most pronounced effect in inducing resistance of any of the procedures used. The figures were significantly different from those obtained from intact rats with adrenals grafted in the abdomen but not from intact rats with adrenals grafted subcutaneously. However, it is doubtful whether the greater effectiveness of combined auto- and homografting should be emphasized. In general, reduction in leukemia incidence may be attributed to the presence of additional adrenal glands, presumably through increased hormonal control. This is in line with our previous experiments with adrenal cortical extracts and preparations of pituitary adrenotropic hormones. It is known that a degree of resistance to this transplanted leukemia may be induced by the injection of normal homologous living cells (3–5), but it is believed that the number of cells in the adrenal homografts is insufficient to induce this nonspecific type of resistance (6). In judging the degree of effectiveness of the various procedures, it should be noted that not only quantitative hormonal relationships but also the phenomena of transplantation are involved.

The idea suggests itself that different degrees of incompatibility among grafted adrenals and host, or other uncontrolled variables, may enter the picture. Jaffe (7) demonstrated that autoplastic grafts of adrenals in the abdominal wall take and grow to a fairly large size. Even small grafts in adrenalectomized animals maintain life, and larger ones enable such animals to remain in good condition indefinitely. Homoplastic grafts take, but they degenerate after a few months. More recently, Everett (8) found that autografts of adrenals are successful, but only about 25 per cent of the grafts among litter mates take, and homografts among nonlitter mates rarely succeed. While there was no information in our experiments on the relation of the rats to each other, it is judged that the stock is genetically fairly uniform, because it shows such a high susceptibility to transplants of a tumor arising in the stock. In any case, there appeared to be

### TABLE 1

<table>
<thead>
<tr>
<th>Group 1:</th>
<th>No. of rats</th>
<th>No. with leukemia</th>
<th>Per cent leukemia</th>
<th>Average days survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenalectomized and autograft of glands returned to abdomen</td>
<td>49</td>
<td>45</td>
<td>91.8</td>
<td>9.3</td>
</tr>
<tr>
<td>Intact controls</td>
<td>30</td>
<td>24</td>
<td>80.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Group 2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenalectomized—autograft, one in abdomen and one in spleen</td>
<td>47</td>
<td>40</td>
<td>85.1</td>
<td>8.7</td>
</tr>
<tr>
<td>Intact controls</td>
<td>50</td>
<td>47</td>
<td>94.0</td>
<td>10.7</td>
</tr>
<tr>
<td>Group 3:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Adrenalectomized</td>
<td>17</td>
<td>17</td>
<td>100.0</td>
<td>7.8</td>
</tr>
<tr>
<td>B. Adrenalectomized—one and two additional adrenals from another rat grafted in abdomen</td>
<td>65</td>
<td>17</td>
<td>28.1</td>
<td>10.3</td>
</tr>
<tr>
<td>C. Intact rats—two adrenals grafted in abdomen</td>
<td>73</td>
<td>42</td>
<td>57.5</td>
<td>11.2</td>
</tr>
<tr>
<td>D. Intact controls</td>
<td>86</td>
<td>71</td>
<td>82.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Group 4:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact rats—2 adrenals grafted subcutaneously</td>
<td>34</td>
<td>15</td>
<td>44.1</td>
<td>12.0</td>
</tr>
<tr>
<td>Intact controls</td>
<td>33</td>
<td>29</td>
<td>87.8</td>
<td>8.7</td>
</tr>
</tbody>
</table>

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SUMMARY

Rats in which the adrenals were removed and reimplemented intraperitoneally, with two additional adrenals from another rat, showed a definite increase in resistance (73.9 per cent) to a transplanted lymphatic leukemia over that of control animals (17.5 per cent). The removal and reimplantation of the adrenals, one in the abdominal cavity and one in the spleen, without the addition of homoplastic adrenals, failed to induce any significant increase in resistance. The introduction of two homoplastic adrenals into intact rats reduced susceptibility to inoculated leukemia to 57.5 per cent, as compared to 82.5 per cent for the controls; and in a second
experiment to 44.1 per cent, as compared to 87.8 in the controls. The simple removal of the adrenals resulted in a 100 per cent susceptibility to leukemia, a finding which confirms an earlier observation.

REFERENCES
5. STURM, E. Induced Resistance to a Transplantable Lymphatic Leukemia in Rats. Cancer Research, 1:627-28, 1941.
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