OVERCOMING TISSUE INCOMPATIBILITY IN RATS DURING SKIN HOMOGRAFTING

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Sodium amytal and supernatant obtained from homogenate of various donor organs were injected into noninbred and Wistar rats. In many cases permanent survival of a skin graft taken from inbred August rats was obtained even in the case of repeated grafting. Survival in Wistar rats was obtained in a high proportion of cases.

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In order to overcome incompatibility between recipient and homograft, Efimov [3] proposed a method of specific antigenic attack on the recipient's immunogenetic system by temporary, nonspecific suppression of its activity with immuno-depressive agents. The theoretical and experimental basis of the method of combined (specific and nonspecific) intervention was established by the work of Efimov and collaborators [2-5] and also of other investigators [6, 7]. As nonspecific inhibitors of the immunogenetic system, 6-mercaptopurine, prednisolone, and barbituric acid derivatives were used. Like most immunodepressive agents, barbituric acid derivatives disturb the processes of cell division and differentiation in reactive centers of lymphoid tissue [1].

The object of the present experiments was to study the effect of combined (specific and nonspecific) action on the immunogenetic system of two different noninbred groups of recipient rats and to obtain permanent survival of skin homografts in these animals taken from inbred rats.

EXPERIMENTAL METHOD

The recipients were 39 Wistar rats and 40 noninbred albino rats. The combined attack on the immunogenetic system of the recipients consisted of simultaneous subcutaneous injections of sodium amytal solution and of donor's tissue antigens. Sodium amytal was injected in doses of 1 ml of 0.5% solution per 100 g body weight for the noninbred rats and 0.8-0.9 ml per 100 g body weight for the Wistar rats. It produced pharmacological sleep lasting 3-4 h in the recipients. The donor's antigens were injected subcutaneously into the abdominal wall as supernatant of a homogenate in a volume of 5-6 ml per recipient. The homogenate was prepared from 45-55 g of a mixture of donor's organs (liver, spleen, kidney, brain, testes of adult inbred August rats) to 500 ml physiological saline. This combined attack on the recipients' immunogenetic system

### TABLE 1. Results of Skin Grafting Experiments on Wistar (a) and Noninbred (b) Rats

<table>
<thead>
<tr>
<th>Experimental results at final stage of observation</th>
<th>Series I</th>
<th>Series II</th>
<th>Total number of recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a b</td>
<td>a b</td>
<td>a  b</td>
</tr>
<tr>
<td>Survival of graft</td>
<td>4 1</td>
<td>27 7</td>
<td>31 8</td>
</tr>
<tr>
<td>Death of graft</td>
<td>4 9</td>
<td>3 20</td>
<td>7 29</td>
</tr>
<tr>
<td>Death of recipient with graft in good condition</td>
<td>1 -</td>
<td>- 3</td>
<td>1 3</td>
</tr>
<tr>
<td>Total ...</td>
<td>9 10</td>
<td>30 30</td>
<td>39 40</td>
</tr>
</tbody>
</table>

EXPERIMENTAL RESULTS

The recipients were divided into two series differing in the number of combined procedures, the interval between the procedures, and the number of homografts. In each series the recipients comprised two groups of rats: Wistar and noninbred. Skin was grafted on 20 recipients (10 Wistar and 10 noninbred rats) without preliminary treatment (control). All the grafts died after 9-18 days.

Series I.

The experiment was carried out on 19 recipients—9 Wistar (male and female) and 10 noninbred (male) rats weighing 100-150 g. All recipients underwent 20 combined attacks on their immunogenetic system together with two successive grafts: after the 10th and 20th attacks (in the case of recipients in which the first grafts died). The interval between successive attacks was 1-3 days.

Results of Skin Grafting in Wistar Rats. The first grafts survived on 3 recipients only. One of these recipients died 3 weeks later, when the graft was in a good condition, but the grafts of the other two recipients died after 10-11 months. Primary grafts on the remaining 6 recipients died after 1.5-2 weeks. After the 20th combined injection, a second graft was applied. Permanent survival of the second grafts occurred in 4 recipients. All 4 recipients survived until natural death, their grafts remaining in a good condition (Fig. 1). They remained under observation for 16-19 months.

Results of Skin Grafting on Noninbred Rats. Permanent survival occurred in only one recipient. This case was followed until natural death of the recipient 18 months later. Both primary and secondary grafts on all recipients died between 1.5 and 3 weeks after operation.

An increase in the number of attacks on the immunogenetic system of the recipients thus enabled intolerance to repeated skin grafting to be overcome, at least in Wistar rats.

To obtain permanent survival of homografts in a larger number of recipients, the number of combined procedures to which they were subjected was increased.