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

Experimental results at final stage of observation	Series I		Series II		Total number of recipients	
	a	b	a	b	a	b
Survival of graft	4	1	27	7	31	8
Death of graft	4	9	3	20	7	29
Death of recipient with graft in good condition	1	–	–	3	1	3
Total . . .	9	10	30	30	39	40

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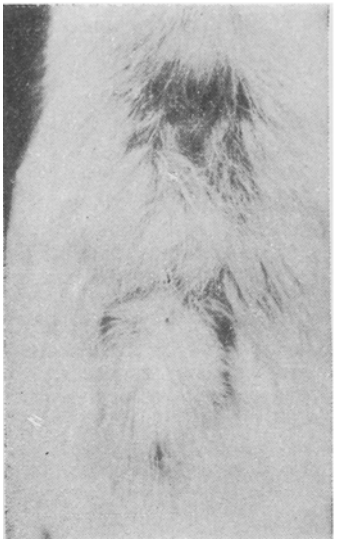

Fig. 1. Wistar rat. Second graft covered with thick, white hair. Borders of graft clearly visible. Thin hair covering a scar formed after death of the primary graft can be seen in the upper half of the photograph (period of observation 16 months).

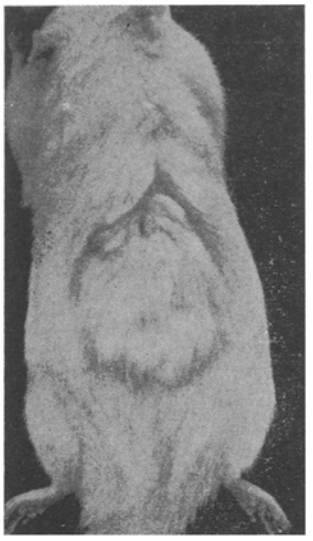

Fig. 2. Wistar rat. Graft has clearly defined borders and is covered with thick hair (11 months after operation).

was made repeatedly at intervals of 1-3 days. The skin grafts for transplantation were taken from August rats aged 7-10 days. Skin from one donor rat was grafted on two or, in very rare cases, three recipients.

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.

Fig. 3. Noninbred rat. Grafts covered with yellowish-white hair, clearly distinguishable against the background of the recipient's white hair (11 months after operation).

Series II.

Experiments were carried out on 60 recipients: 30 Wistar (male and female) and 30 noninbred (male) rats weighing 160-280 g. All the recipients received 25 combined injections of sodium amytal and donor's antigens: 20 injections before and 5 after transplantation. The interval between injections was 24 h.

Results of Skin Grafting on Wistar Rats. Permanent survival of the graft occurred in 28 of the 30 recipients. Death of the graft occurred in only one recipient, after 6 months. In the rest the grafts remained in a good condition throughout the period of observation. The grafts were covered with thick hair (Fig. 2). By September 30, 1967, the longest period of observation was 11 months.

Results of Skin Grafting on Noninbred Rats. Survival of the grafts occurred in 16 recipients, and in 7 of these (on September 30, 1967, period of observation 11 months) the grafts were in a good condition (Fig. 3). Three recipients died after 2 weeks with well preserved grafts, while the grafts on 6 recipients died between 3.5 and 7 months after operation.

The results of experiments of series I and II are given in Table 1.

Repeated injections of sodium amytal and donor's tissue antigens thus led to permanent survival of homografts in both groups of recipients. In some cases the grafts persisted until natural death of the recipients. An increase in the number of preliminary attacks on the immunogenetic system led to a corresponding increase in the number of permanently surviving grafts. If the same number of combined injections was given, the number of permanently surviving grafts in the Wistar rats was several times greater than in the noninbred rats. From the genetic standpoint, tissues of inbred August rats behave as foreign to a greater degree for noninbred rats than for Wistar rats. Possibly August rats differ from noninbred in having a larger number of strong loci of tissue incompatibility.

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