

PROLONGING SURVIVAL OF SKIN HOMOGRAFTS IN RABBITS BY IMMUNIZATION WITH COMPETITIVE ANTIGENS

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Intensive immunization with tetanus toxoid, combined typhoid and paratyphoid vaccine, and homologous spleen tissue prolongs the survival of skin homografts in rabbits.

In 1964, Miller and associates [1] reported that the phenomenon of antigen competition could be used to inhibit transplantation immunity. Because this method points to new ways both for studying mechanisms of transplantation immunity and for developing methods of overcoming it, the present investigation was undertaken to test the validity of these workers' conclusion that intensive immunization with foreign antigens depresses transplantation immunity to homologous skin.

EXPERIMENTAL METHOD

Experiments were carried out on adult chinchilla rabbits of both sexes. The following antigens were used for immunization: tetanus toxoid, batch 206-4, purified and absorbed on aluminum hydroxide, prepared by the N. F. Gamaleya Institute of Epidemiology and Microbiology, AMN SSSR, which was injected in doses of 0.5 ml; typhoid-paratyphoid B divaccine, batch 43, chemically absorbed on calcium phosphate, prepared by the I. I. Mechnikov Moscow Institute of Vaccines and Sera, injected in doses of 1.5 ml; freeze-dried homologous spleen, injected in doses of 20 mg. All three antigens at once, or only two of the bacterial antigens were injected subcutaneously in the abdominal region. Injections began 24 h before grafting and continued until rejection of the grafts at intervals of three days or daily.

Whole-thickness skin homografts were transplanted by the usual method; in different experiments the size of the grafts varied from 11-16 cm².

The effects of different combinations and schemes of administration of the competitive antigens on transplantation immunity was judged from the duration of survival of the skin homografts.

TABLE 1. Effect of Nature of Competitive Antigens on Length of Survival of Homologous Skin Grafts

Antigen		—		Tetanus toxoid, divaccine, spleen		Tetanus toxoid, divaccine	
Group		1		2		3	
Mean dimensions of graft (in cm ²)		16,0		14,7		11,9	
Number of rabbits		6		6		6	
Rejection		began	complete	began	complete	began	complete
Statistical indices	M	12,3	15,5	17,3	22,8	20,7	21,5
	confidence limits	11,09 —13,51	13,74 —17,26	13,07 —21,53	16,37 —29,23	15,02 —26,38	16,78 —26,22
	P	—	—	0,05>P>0,02	0,05>P>0,02	0,02>P>0,01	0,05>P>0,02

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TABLE 2. Effect of Number of Injections of Competitive Antigens on Duration of Survival of Homologous Skin Grafts

Number of injections		0		4-10		16-20	
Scheme of injections		—		4-5 injections at intervals of 3 days, remainder daily		daily, or first two injections at interval of 3 days	
Group		1		2		3	
Mean dimensions of grafts (in cm ²)		16.0		13.7		12.7	
Number of rabbits		6		6		6	
Rejection		began	complete	began	complete	began	complete
Statistical indices	M	12.3	15.5	14.0	19.2	22.6	24.3
	confidence limits	11.09 to 13.51	13.74 to 17.26	12.00 to 16.00	12.55 to 25.85	19.32 to 25.85	20.98 to 27.62
	P	—	—	0.2 > P > 0.1	0.3 > P > 0.2	< 0.01	< 0.01

EXPERIMENTAL RESULTS

The object of the first series of experiments was to study the effect of the nature of the competitive antigens used on duration of survival of homologous skin grafts.

It will be seen from Table 1 that the first signs of rejection were observed in the control animals (group 1) on the 11th-14th day and rejection of the whole graft began on the 13th-18th day. Complete healing-epithelization of the wound with abundant growth of hair-usually occurred by the 50th-60th day after transplantation.

The first signs of rejection in the rabbits immunized with the antigen complex (group 2) was observed on the 11th-23rd day, and complete rejection took place on the 16th-30th day. Statistical analysis showed that this longer survival of the grafts was not due to random variations but was statistically significant. Epithelization in these animals likewise began earlier and was complete by the 42nd-58th day.

It must be emphasized that practically identical results were obtained when only two antigens instead of three, were used, and these antigens were bacterial (group 3). The first signs of rejection of the skin grafts were observed in these rabbits on the 13th-27th day and complete rejection began on the 17th-27th day. Comparison of the times of graft rejection by the animals of this group with those of the control group confirmed that the longer survival of the grafts was statistically significant.

The importance of the number of injections of competitive antigens and of the times at which they were given had next to be studied. For this purpose two schemes of immunization were tested: moderate and intensive.

The results in Table 2 show that with moderate immunization (group 2) rejection of the skin grafts was delayed only very slightly, and the difference was not statistically significant. On the other hand, intensive immunization (group 3) resulted in a statistically significant prolongation of survival of the skin homografts.

The results of these experiments thus showed that intensive immunization with an antigen complex consisting of three antigens or of two bacterial antigens only, caused inhibition of transplantation immunity and led to longer survival of skin homografts.

LITERATURE CITED

1. J. Miller, C. Martinez, and R. A. Good, Ann. New York Acad. Sci., 120, 270 (1964).