

PROLONGED SURVIVAL OF PRIMARY  
AND SECONDARY ALLOGRAFTS OBTAINED  
IN RATS WITH ANTILYMPHOCYTIC SERUM

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UDC 615.365.018.53.015.45:612.6.02

The effect of antilymphocytic serum on the duration of survival of alloplastic skin grafts was studied in rats. Antilymphocytic sera considerably prolong the survival of primary and secondary allografts. These antisera also cause a decrease in the titers of humoral antibodies.

In recent years antilymphocytic serum (ALS) has been extensively used as an immunosuppressive agent during organ and tissue transplantation [9, 12, 13, 15].

In investigations into the immunosuppressive action of ALS insufficient attention has been paid to the effect of antisera on secondary grafts, although this is a problem of considerable importance. The "hyperacute" rejections of grafted organs sometimes observed under clinical and experimental conditions are of the nature of rejection of secondary grafts [1, 5, 6, 8]. The possibility of preventing these "hyperacute" crises of graft rejections would be of the utmost importance in clinical practice. Moreover, there is an acute lack of information in the literature on the effect of ALS on the production of humoral antibodies, which are among the chief criteria used to assess the development of rejection crises [2, 3, 14].

In the investigation described below the effect of ALS was studied on the duration of survival of primary and secondary alloplastic skin grafts and on the dynamics of humoral antibody production. Besides the usual serological reactions, such as the cytotoxic test and the leucoagglutination and isohemagglutination reactions, the production of heterophilic hemagglutinins was also investigated in the allografted animals for, as experiments have shown [7, 10, 11], these reflect most adequately the level of the developing immunological conflicts.

#### EXPERIMENTAL METHOD

Heterologous ALS was obtained by immunizing chinchilla rabbits with cells of the mesenteric lymph glands of August rats by the method described earlier [4]. The resulting antisera, after absorption of hemagglutinins, possessed leucoagglutinating and lymphocytotoxic activity in titers of 1:512-1:1024.

To study the effect of ALS on the duration of survival of the primary and secondary allografts all the animals were divided into 4 groups. Group 1 included 23 rats undergoing alloplasty with skin grafts from female Wistar rats. Group 2 consisted of 23 rats undergoing repeated skin alloplasty 4-5 days after rejection of the primary allografts. Group 3 contained 25 rats which received intraperitoneal injections of ALS in a dose of 0.5 ml daily for the first 5 days after skin grafting. Group 4 consisted of 25 rats undergoing repeated skin grafting and ALS treatment.

The sera of the animals were tested for the presence of humoral antibodies on the 5th-6th day after rejection of the allografts.

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## EXPERIMENTAL RESULTS

A study of the duration of survival of the skin allografts showed that injection of ALS considerably prolonged survival of both primary and secondary allografts. The period of survival of the primary allografts without treatment of the animals with ALS was  $7.87 \pm 0.34$  days, compared with  $14.20 \pm 0.59$  days in the case of animals receiving ALS ( $P < 0.05$ ). The duration of survival was also considerably prolonged in animals treated with ALS after secondary alloplasty ( $5.6 \pm 0.25$  days without serum;  $11.2 \pm 0.41$  days in animals treated with ALS).

The animals of all groups were investigated for the presence of humoral antibodies 4-5 days after rejection of the skin allografts.

Analysis of the results showed that after rejection of the primary skin grafts the sera of most rats contained cytotoxins and leucoagglutinins in a titer of 1:32-1:64, and after rejection of the secondary grafts - in a titer of 1:256-1:512. Injection of ALS caused a sharp decrease in the titers of cytotoxins and leucoagglutinins after primary (1:2-1:4) and secondary (1:32-1:64) skin alloplasty.

The titers of agglutinins against the donor's erythrocytes were somewhat lower in the animals of groups 3 (1:2-1:4) and 4 (1:4-1:8) than in the rats of groups 1 (1:4-1:8) and 2 (1:32-1:128), i.e., in animals not treated with ALS.

The result of the study of titers of antibodies against heterologous erythrocytes (human group O, A, and B erythrocytes, rabbit, sheep, and dog erythrocytes) showed that antibodies were formed against all these heterologous erythrocytes after both primary and secondary alloplasty. The highest titer was observed after repeated skin grafting. Injection of ALS into the animals appreciably lowered the titers of heterophilic hemagglutinins. For instance, titers of heterohemagglutinins against human erythrocytes after injection of ALS into the animals of groups 1 and 3 were no higher than the titers of natural heterohemagglutinins found in the animals before skin grafting. The smallest decrease in titers of heterohemagglutinins after injection of ALS was observed in those against sheep and dog erythrocytes.

These experiments thus showed that ALS, if injected into animals after skin alloplasty, considerably prolongs the period of survival of the grafts. At the same time, the production of humoral antibodies such as cytotoxins, leucoagglutinins, isohemagglutinins, and heterophilic hemagglutinins, was reduced. ALS can also prolong the survival of secondary allografts. Investigation of the corresponding humoral antibodies under these circumstances revealed a marked decrease in their titers, and this must be borne in mind during detection of a rejection crisis on the basis of these serological indices.

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