

EXPERIMENTAL THYROID HEMOGRAFTING DURING
INHIBITION OF THE RECIPIENT'S DEFENSIVE
REACTION BY IMMUNODEPRESSANTS

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The thyroid gland was homografted either freely (in rabbits) or on a vascular pedicle (in dogs). Comparison of the morphology of the grafts showed relatively weak round-cell infiltration and longer preservation of the follicular tissue in animals receiving 6-mercaptopurine alone or with hydrocortisone than in the control group and in the group receiving azothioprine. A study of the recipients' plasma protein fractions showed a statistically significant increase γ -globulin concentration in the control group and stabilization of their concentration in groups receiving immunodepressants.

An aspect of modern transplantation science which has so far received little study is the desirability of using immunodepressants and their effectiveness with transplantation of the endocrine glands. Data in the literature on this question are few in number and contradictory in nature [1, 5, 6].

The objects of the present investigation were to study histological changes in thyroid gland homografts and to compare the cellular reaction of incompatibility in connection with the administration of 6-mercaptopurine, azothioprine, and a combination of hydrocortisone and 6-mercaptopurine, and to study the dynamics of the recipients' plasma protein fractions. The γ -globulin fraction, which consists of antibodies, was studied with particular interest [3].

EXPERIMENTAL METHOD

Experiments were carried out on 47 rabbits and 12 dogs. Thyroidectomy on the recipients and transplantation were carried out at the same operation. The animals were grouped in pairs, and one lobe of the thyroid gland was exchanged between the partners. Transplantation in the dogs was carried out into the inguinal region by means of the ASTs-3 vascular suturing apparatus. Free intraocular transplantation was performed on the rabbits by the method described earlier [1].

The animals were distributed into groups. The rabbits of group 1 received 6-mercaptopurine after the operation (11 animals), those of group 2 received azothioprine (14 animals) in a dose of 0.005 g/kg body weight daily. Group 3 consisted of 11 rabbits and 12 dogs receiving as immunodepressants hydrocortisone and 6-mercaptopurine, each in a dose of 0.005 g/kg body weight. The animals received the immunodepressants for 20 days except in the case of premature death. The rabbits of the control group (10 animals) received no immunodepressants. On the day of the operation and 5, 10, 20, and 30 days thereafter the blood proteins were investigated and the ratio between the numbers of polymorphs and lymphocytes was studied. Electrophoretic fractionation of the proteins was used, and the fractions were determined refractometrically. At the end of the experiments the animals were killed, and histological sections of the grafts were examined under the microscope.

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TABLE 1. Concentration of Globulins (%) in Recipients' Plasma at Various Times of Investigation ($M \pm m$)

Immunode- pressant	Conc. of γ -globulins at various times (days) after operation				
	1	5	10	20	30
6-Mercaptopurine	19,0 \pm 1,01	18,8 \pm 1,3		16,5 \pm 1,3	
Azothioprine	15,8 \pm 0,8	17,0 \pm 0,55	16,23 \pm 1,4	15,8 \pm 1,6	
6-Mercaptopurine and hydrocortisone	15,5 \pm 1,0		14,8 \pm 0,6	15,2 \pm 1,3	
Control	15,7 \pm 0,6	20,4 \pm 0,9	16,1 \pm 0,1	17,4 \pm 0,6	14,3 \pm 1,1

EXPERIMENTAL RESULTS

The morphological investigation of the grafts during the first 7-8 days after transplantation revealed no significant differences between the different groups. The most characteristic feature of the structure of the grafts at these times was disintegration of the basic structural elements and their destruction, the numerous manifestations of which were described previously [1]. More than 10 days after transplantation, substantial changes were observed in the microstructure of the homografts. The zone of destruction was considerably smaller, and clusters of tiny young follicles with well differentiated thyrocytes were more frequently seen in the peripheral zone. In the intervals between the follicles regenerating pale cells appeared. Between the 10 and 20 days after grafting the peripheral zone was relatively well revascularized. Diffuse polymorphonuclear infiltration observed during the first days after the operation was replaced by homogeneous round-cell infiltration. Infiltrating cells were concentrated mainly in the perivascular zone. Comparison of the degree of infiltration in the various groups showed that it was least marked in the group receiving 6-mercaptopurine alone or in conjunction with hydrocortisone than in the control group or the group of animals receiving azothioprine and immunodepressants. This accounts for the more distinct prolonging effect of 6-mercaptopurine (up to 55 days compared with 20-25 days in the control group).

The microstructure of the thyroid homografts transplanted on an arterial pedicle characteristically showed well-preserved glandular elements during the first 3-6 days after the operation, massive infiltration of the gland parenchyma with polymorphs and lymphocytes after 8-14 days, and subsequent connective-tissue replacement of the graft, observed 20-25 days from the beginning of the experiment.

Determination of protein and protein fractions in the plasma of the experimental animals revealed a clearly marked tendency toward hypoproteinemia throughout the period of administration of the immunodepressants on account of a decrease in the albumen concentration while the globulins remained at a relatively stable level. The most characteristic changes in the globulin spectrum of the recipients' plasma were observed in the γ fraction (Table 1).

In all the experimental groups the γ -globulin concentration showed little change with time. The changes were not statistically significant. By contrast with the experimental groups, in the control the γ -globulin concentration rose by a statistically significant degree after the operation and remained high until the twentieth day, returning to normal by the end of the month in connection with completion of the connective-tissue replacement of the grafts.

The changes in the qualitative white blood indices in the recipients were essentially as follows: during the first days after the operation a moderate leukocytosis occurred on account of polymorphs with a decrease in the number of lymphocytes. From 10 to 15 days after the operation the leukocyte count in the peripheral blood fell to its initial values, whereas the lymphocyte count rose a little. Atrophic changes in the spleen were observed in the experiments using antimetabolites.

These experiments thus show that in rabbits receiving 6-mercaptopurine, alone or in combination with hydrocortisone, the tendency toward prolonged survival of thyroid gland homografts (up to 55 days) was most marked. The prolongation of survival of the thyroid homografts must be attributed to weakening of the humeral and cellular factors of the recipients' defensive reaction, as is shown by the slight degree of infiltration of the grafts, the decrease in number of leukocytes and lymphocytes, and stabilization of the γ -globulin indices of the recipients' plasma in the postoperative period.

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