THE EFFECT OF THYMECTOMY AND THE INJECTION OF LARGE DOSES OF CORTISONE ON THE SURVIVAL OF THYROID HOMOGRAFTS IN MICE OF PURE STRAINS

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At the present time there are adequate reasons for considering that the process of homograft destruction is related to the penetration of immunologically active lymphocytes into the grafts [3, 9]. Several research workers have shown that retardation and even suppression of the reaction which destroys skin grafts can be achieved by a drastic curtailment of lymphopoiesis and this is attainable either by removal of the thymus gland from the recipient of the graft [5, 8, 10, 11], or by the injection of large doses of cortisone [6], or as a result of other agents [1, 7, 12].

In this particular research project we have studied the "fate" of thyroid homografts in mice which have suffered thymectomy and have received large doses of cortisone. In contrast to the situation involving skin grafts, transplantation of the thyroid gland not only enables the research worker to follow the morphological process of dissolution, but also permits the measurement of the functional activity in the transplanted organ.

EXPERIMENTAL METHODS

The experiments were conducted on 40 male mice hybrids of the CBA and $C_{57}Bl$ strains weighing 16 g. The animals were divided into 3 groups. Group I mice had their thymus glands removed [4] and one week later they underwent thyroidectomy followed by simultaneous homotransplantation of the thyroid gland. Group II mice received homoplastic transplants of thyroid glands from donor animals without the removal of their own and beginning one day after the operation they were given 5 injections of cortisone at a dosage of 125 mg/kg at daily intervals. Group III mice only underwent thyroid homotransplantation and these served as controls. The thyroid glands were transplanted subcutaneously above the sternum without their vascular anastomosis. Male mice of the Balb strain; weighing 16g, were used as donors. Mice were killed at 5, 10, 20, and 40 days after transplantation of the thyroid glands. Some of the mice received 0.1 microcuries of sodium iodide^{131} without a carrier, one day before they were killed. Transplanted thyroid glands were fixed in Bouin's fluid, and then their radioactivity was measured before washing out the fixative. The gland tissue was subsequently embedded in paraffin wax and serial sections, 7 μ thick, were cut and stained with hematoxylin-eosin and Mallory's stain.

EXPERIMENTAL RESULTS

In mice of the control group (group III), the dimensions of the thyroid gland homotransplants had undergone practically no change 5 days after the transfer. The majority of the transplants were surrounded by hematoma. The connective-tissue capsule enclosing the transplant was thin. Numerous necrotic foci occurred in the center and throughout the lobes. The follicular tissue was preserved in the form of a thin band peripherally and as small masses elsewhere. The transplants were infiltrated by large numbers of leucocytes, the majority of which were lymphocytes. The follicles which remained were of various sizes. Some of them contained a dense homogenous colloid which stained orange with Mallory's stain. Certain follicles exhibited a markedly hypertrophied epithelium of cylindrical form, the cells of which had large nuclei. Colloid was almost completely absent from such follicles.

Uptake of I^{131} by Thyroid Gland Homografts under Various Experimental Conditions 24 h after Injection of Isotope (as % of dose given)

Days after transplantation	Homografts of thyroid gland		
	in mice of control group	in mice deprived of thymus glands	in mice receiving cortisone
5	0,45 0,20 0,034 } $M = 0,033$	0,051 0,236 0,032 0,059 } $M = 0,094$	0,276 0,062 0,085 } $M = 0,144$
10	1,485 0,982 1,133 } $M = 1,2$	1,003 0,893 3,104 1,431 } $M = 1,608$	0,797 0,659 0,913 } $M = 0,787$
20	0,815 0,051 0,433 } $M = 0,433$	1,852 0,154 0,162 0,048 } $M = 0,554$	0,212 0,150 4,414 } $M = 1,592$
40	0,02 0 0 } $M = 0,02$	0 0,499 0,062 0 } $M = 0,14$	

Any residual material within the follicular cavity stained blue with Mallory's stain so that such follicles were evidently functional. Between the follicles which persisted were many isolated thyroid epithelial cells; these represented the remains of follicles which had undergone dissolution. Certain of these isolated cells had suffered dystrophic changes and exhibited pycnotic nuclei and other signs of approaching death. Nevertheless among such cells were many undergoing division.

The vessels of the transplants were markedly expanded in certain places and contracted in others. Clumps of erythrocytes were often visible in the lumen of the vessels. Newly formed vessels grew into the transplants from the surrounding tissues as part of the connective tissue penetration. The percentage of I^{131} taken up by the thyroid gland homografts 5 days after transplantation amounted to 0.033 of the isotope injected (cf. table).

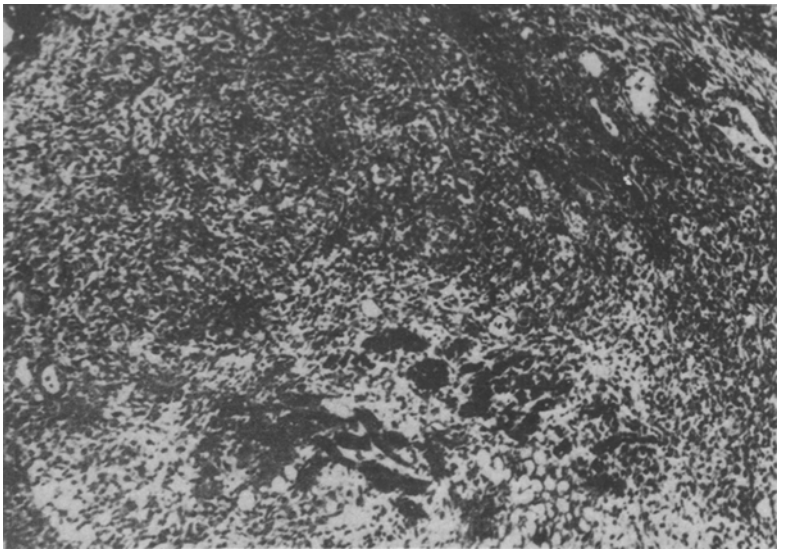

Fig. 1. Homograft of thyroid gland 10 days after transplantation into control recipient. Stained hematoxylin-eosin. Ob. × 10, oc. × 12.5.

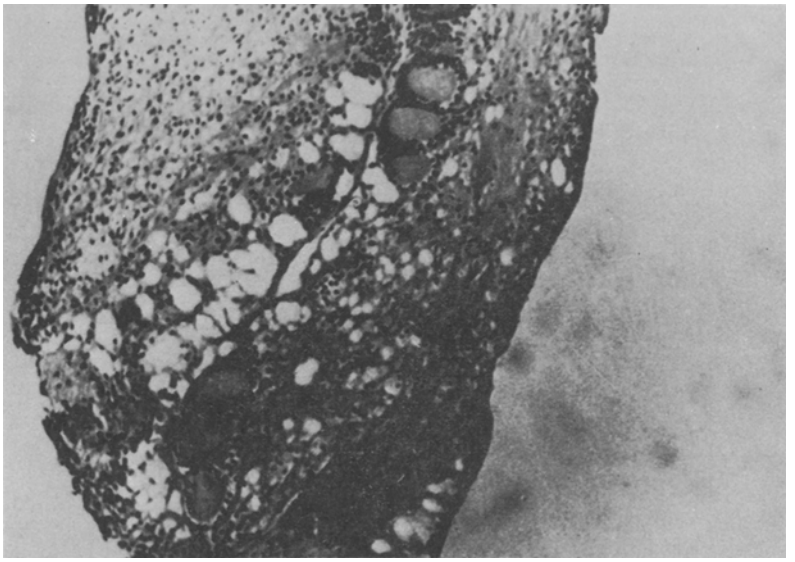

Fig. 2. Homograft of thyroid gland 10 days after transplantation into thymectomized recipient. Stained hematoxylin-eosin. Ob. × 10, oc. × 12.5.

Homografts of the thyroid gland taken from mice of the control group had decreased in size 10 days after transplantation and the majority of them were also surrounded by hematomas. In certain cases, one or two vessels could be seen invading the grafts from the surrounding tissues. The necrotic processes in the homografts were suspended. The connective tissue capsule surrounding the homograft had become rather massive, whereas the amount of follicular tissue had diminished (Fig. 1). Among the cells of the interfollicular epithelium were many that were dying. Very considerable leucocytic infiltration was noticed and this often resulted in leucocytes coming into close proximity with the cells of the thyroid epithelium. The percentage of I^{131} taken up by the homografts 10 days after transplantation amounted to 1.2% of the isotope injected (cf. table).

On the 20th day after transplantation, the thyroid gland homografts in mice of the recipient control group were surrounded with massive connective tissue scars and remained relatively small. Among the follicles which were still intact many contained dying cells and the cells of the interfollicular epithelium were also dying. Leucocytic infiltration did not decrease. The percentage of I^{131} taken up by the thyroid gland homograft on the 20th day after transplantation was 0.433 that of the injected dose of isotope (cf. table).

On the 40th day after transplantation, the thyroid gland homografts in mice of the recipient, control group had suffered almost complete resorption. Examination of serial sections of the connective tissue scars which remained at the site of implantation still revealed the presence of a few follicles and a very few cells of interfollicular epithelium, surrounded by a large number of leucocytes. The percentage of I^{131} taken up by the homograft at this period after transplantation amounted on average to 0.2 of the injected dose of isotope (cf. table).

Among recipients of the experimental group, both thymectomized and cortisone treated mice exhibited a different condition of their homografts to that found in the controls. This difference was manifested at all intervals of time after transplantation but particularly on the 10th day, when the amount of thyroid epithelium still preserved was considerably in excess of that found in the control group (Fig. 2). The thyroid gland homografts among experimental mice did not reveal any leucocyte penetration. No dividing cells were found in the thyroid tissue. The amount of radio-iodine, taken up by the thyroid gland homografts in mice of the experimental groups was greater than that taken up by the controls (cf. table). The homografts of thryoid glands in thymectomized animals did not differ morphologically or functionally from those transplanted into recipients receiving cortisone. On dissection of the latter, it was possible to observe considerable atrophy of lymphoid tissue and the site of the thymus was represented only by the shrivelled capsule of the latter.

The results of the described experiments indicate that thymectomy of adult mice and the injection of large doses of cortisone into them do not improve the chances of survival of thyroid gland homografts, but for a limited time after transplantation their effect on recipients may be to retard the process of destruction of the homograft.

This retardation may explain the emergence of a temporary leucopenia among recipients as a consequence of thymectomy and the injection of cortisone [11]. After the establishment of leucopenia the destruction of the transplanted tissue is accelerated.

The dividing cells in homografts of the thyroid gland among mice of the control group were larger than among mice of the experimental group, hence it can be assumed that suppression of functional activity in the lymphopoietic system of the recipients is accompanied by a decrease in the mitotic activity of cells in the transplanted thyroid tissue.

SUMMARY

The thyroid gland from male mice of the Balb strain weighing 16 g was transplanted homoplastically to male mice hybrids F_1 of the CBA and $C_{57}Bl$ strains. In the first group of recipients the thymus was excised a week before the transplantation, and the second group of mice were given cortisone injection from the day of transplantation. The third group of mice were used for control. Resolution of thyroid homografts in the experimental mice was slower than in the control recipients. This difference was more obvious within ten days of transplantation.

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