THE EFFICACY OF TRANSPLANTATION OF THE THYROID GLAND INTO THE ANTERIOR CHAMBER OF THE EYE

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Notwithstanding many years' experience of the clinical application [1, 13, 14] and experimental study [5, 7, 14] of homoplastic transplantation of the thyroid gland, we still lack sufficient evidence on which to draw conclusions regarding the possibility of true survival of these homografts [9, 17]. Reports of the survival of the thyroid gland [1, 4, 6, 11] either are premature [8] or are based on the purely one-sided study of histological [2, 12] or functional [1, 4] data. Research in which the physiological activity of thyroid gland transplants is estimated by the development or absence of thyroprival cachexia in experimental animals in the postoperative period is unconvincing. The observations of Enderlen [14] and others show that cachexia may develop in those animals in which the glandular structure of the transplants is preserved. An essential condition of experimental work on the transplantation of the thyroid gland is a control autopsy of the animals after the end of the experiment to determine the presence or otherwise of aberrant thyroid gland tissue [9 , 15].

The object of our investigation was to ascertain the efficacy of auto- and homotransplantation of the thyroid gland into the anterior chamber of the eye in rabbits.

EXPERIMENTAL METHOD

In the performance of the experiments we tried to use animals of the same color, sex, and age as donor and recipient. Transplantation was carried out, as a rule, after a preliminary thyroidectomy, i.e., in conditions of "normal starvation" [8, 16]. The excised glands were usually transplanted immediately, either into the same rabbit (autotransplantation, 7 experiments), or into another (homotransplantation, 14 experiments). In 36 experiments auto- and homotransplantation were performed simultaneously. The gland was transplanted whole, apart from a very small portion taken for control histological examination. All transplantations were made into the anterior chamber of the eye, so that a constant visual observation could be kept on the grafts. The technique of intraocular transplantation has been described by M. G. Rudnitskii [8] and others. Operations were carried out on 32 rabbits altogether, and 62 transplantations were performed (in 2 cases into one eye).

At the end of each experiment control autopsies of the animals were made and the grafted thyroid glands were extracted and prepared histologically (fixation in 10% neutral formalin solution, embedding in celloidin, staining with hematoxylin and eosin or by Van Gieson's method.

EXPERIMENTAL RESULTS

Morphological examination during the first 2 or 3 days after transplantation showed no significant differences in the auto- and homografts. In each case two zones were clearly differentiated: a central (necrotic) and a peripheral (with only slight changes). The grafted gland had lost its normal structure, and disintegration of the principal structural elements was observed. Many follicles were deformed and collapsed, and their colloid was dispersed. The follicular epithelium showed a chaotic arrangement. The borders of the epithelial cells were obliterated, their nuclei had disintegrated, their chromatin had escaped, and among the granules of chromatin were seen macrophages, infiltrating the central part of the graft. In the peripheral zone, especially at the point of contact between the graft and the iris, the follicular structure was preserved. Some follicules were filled with eosinophilic colloid. The epithelium of the follicles was cubical, with well stained nuclei, and here and there it was desquamated. Leukocytic infiltration with lymphocytes was also observed here, and was more marked in the homografts.

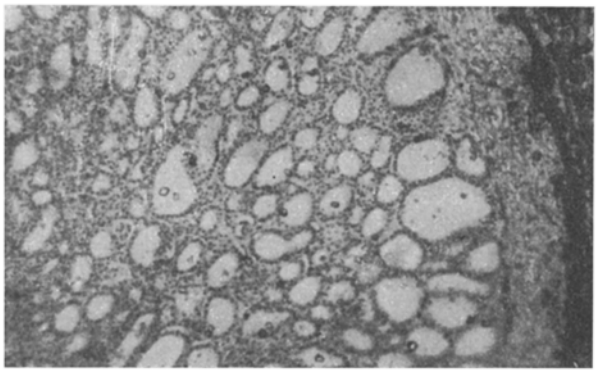

Fig. 1. Microstructure of an autografted thyroid gland 115 days after transplantation. Magnification 144 ×.

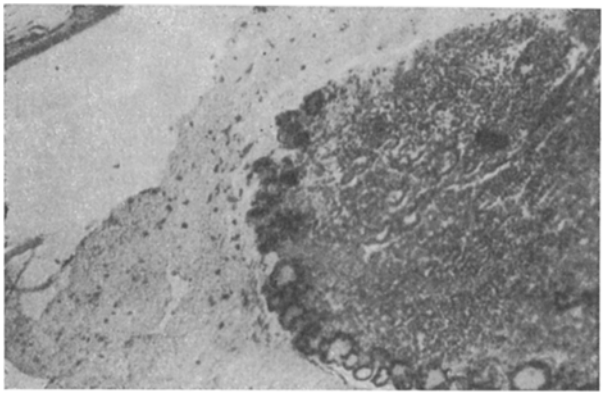

Fig. 2. Microstructure of a homografted thyroid gland 65 days after transplantation. Magnification 144 ×.

In addition to the destruction, disintegration of the cellular elements was observed, characterizing one of the most important and distinctive features of the thyroid gland – the plasticity of its structure [3]. Proof of this statement was given by the restoration of the glandular elements in the central (necrotic) zone of the transplant at an early stage (after 10-14 days).

Five days after transplantation the grafts were in closer contact with the surrounding iris and cornea. The zonal structure of the grafts remained, but the zone of necrosis was less extensive than at the earlier periods; the peripheral zone with signs of restoration of the typical glandular structure had become wider. Here newly formed small follicles could be seen side by side with surviving follicles. Larger follicles subsequently appeared, filled with colloid. In the homografts mainly small follicles appeared, irregularly shaped and not containing colloid.

Two weeks after transplantation the processes of regeneration in the autografts were more intensive and spread to the deeper layers, and the originally necrotic central zone was "revived." Follicle formation was observed in both the peripheral and central zones of the grafts. In the peripheral zone, side by side with newly formed follicles, could be seen surviving large follicles, but these were not present in the center. In the homografts these repair processes were present only in the peripheral zone, immediately adjacent to the iris, whereas the central zone of the graft was undergoing connective-tissue replacement.

In the course of the third week a more marked difference appeared in the histological structure of the auto- and homografts. Whereas in the autografts at this time the structural reorganization was basically complete, and restoration of the microscopic structure of the thyroid gland was taking place, the homografts were again undergoing severe dystrophic changes. Few follicles were present in such grafts. The greater part of the gland appeared to be replaced with young connective tissue in which, here and there, epithelial cells were seen to be disintegrating.

At later periods – 2, 3, 4 and 5 months after transplantation – the autografts possessed a well marked histological structure, revealing its dependence on the trophic influences from the iris. In several cases not only had the iris fused with the graft over a considerable distance in the region of direct contact, but it enveloped the graft and showed marked proliferation from the side of the cornea. The graft possessed a rich network of blood vessels and the typical follicular structure of the thyroid gland (Fig. 1). The homografts at these times were, as a rule, replaced by fibrous connective tissue. Only in a few areas of the homograft was the glandular structure preserved. For instance, in one rabbit sacrificed 65 days after the operation, around the periphery of the homograft small surviving follicles were seen, some of which contained colloid. In the center of the graft were many chaotically arranged follicular cells, some of which had undergone destruction. The graft was in close contact with the iris but did not touch the cornea (Fig. 2). The autograft of this same rabbit preserved its typical glandular structure.

By histological examination of the homografts at the later stages in 3 experiments we were able to detect well defined thyroid gland tissue.

The homograft examined 78 days after operation had a richly vascularized, glandular structure. Many follicles of different sizes, with high cylindrical epithelium, were seen in the graft, and small, newly formed follicles were also present. This morphological picture indicates increased function of the homograft. The autograft of this rabbit had

almost the same histological structure. The only difference was that the epithelium of the autograft was slightly higher then that of the homograft. We did not, however, observe this similarity in the microstructure in all experiments.

The autograft examined 120 days after transplantation had a typical glandular structure with a well developed vascular plexus. It possessed many large and small follicles with high epithelium and containing colloid. The autograft was in a state of hyperfunction. In the homograft of the same rabbit the epithelium was flattened and the follicles distended to such a degree that the very thin walls were apparently torn in places. These changes characterized diminished function of the gland.

In the experiment lasting 129 days a considerable resemblance was observed between the histological structure of the auto- and homografts. Each consisted of round follicles, lined with cubical or slightly flattened epithelium and filled with palely stained colloid. Each graft was in a state of hypofunction.

In the experiments in which the thyroid gland was simultaneously autografted and homografted, the glands preserved their structure after long periods in only 3 of the 18 experiments, whereas the autografts were preserved in 16 of 18 experiments.

The trend of the animals' body weight, development, and behavior revealed the high efficacy of simultaneous auto- and homotransplantation of the thyroid gland. Of the 18 rabbits of this group, only 2 died in the period soon after the operation, whereas the remaining 16 gained in weight, were well developed and active, and showed no signs of hypofunction of the thyroid gland. Two rabbits in which the grafts appeared to the naked eye to have been absorbed at the end of the 4th week after grafting were sacrificed after 3 months. Autopsy of these animals revealed traces of gland tissue in situ. This accounted for their good development, despite the fact that no grafts were found on histological examination.

The same picture was observed in 2 rabbits on which only homografting was performed. Eight rabbits of this group died soon (during the first 18 days) after operation, showing signs of thyroprival cachexia.

As a rule a definite correlation was observed between the histological structure and the indices of functional activity of the grafts in our experiments. The exception was one rabbit which died with signs of thyroprival cachexia developing at the end of the fourth month after transplantation, notwithstanding the histological preservation of the graft. This case demonstrates the dangers of relying only on the morphological control (in the usual method of investigation) when the results of transplantation are being evaluated.

Our experiments showed that the most successful survival of the grafts takes place when they are in close contact with the iris, as a rule of which the blood supply and nutrition of the transplanted gland are assured. The formation of new follicles could be studied, and took place in all cases more intensively in the zone adjacent to the iris.

Long preserved grafts underwent total reorganization, similar to that occurring during reparative regeneration, or gland tissue was formed in them de novo (for example, in the ground substance of the cornea) as a result of the invasion of epithelial bands from the graft. The longest preservation of the histological structure of the graft in animals in the best condition was observed after the simultaneous auto- and homoplastic transplantation of the thyroid gland.

LITERATURE CITED

1. N. A. Bogoraz, Kazansk. Med. Zh., (1927), No. 1, p. 58.
2. M. L. Borovskii, Arkh. Pat., (1946), 8, Nos. 5-6, p. 119.
3. A. A. Voitkevich, Dokl. AN SSSR, (1959), 128, No. 5, p. 1092.
4. T. E. Gnilorybov, Vestn. AMN SSSR, (1956), No. 2, p. 35.
5. A. G. Lapchinskii, In: Problems of Transplantation and Conservation of Organs and Tissues [in Russian], Moscow (1959), p. 85.
6. M. S. Mitskevich, Izv. AN SSSR, Seriya biol., (1958), No. 2, p. 149.
7. I. V. Radzimovskii, Excision and Transplantation of the Thyroid Gland [in Russian], Kiev (1891).
8. M. G. Ruditskii, Homoplastic Transplantation of the Adrenal and Ovary [in Russian], Khar'kov (1940).
9. M. G. Ruditskii, Problemy Endokrinol., (1960), No. 4, p. 8.
10. I. M. Shapiro, Arkh. Biol. Nauk, (1941), 63, No. 1, p. 47.
11. D. Bennett and A. Gorbman, Endocrinology, (1951), v. 49, p. 310.
12. H. Christiani, Arch. de physiol. norm., (1895), 5 ser., v. 7, p. 65.
13. H. Conway, et al., Plast. reconstr. Surg., (1959), v. 23, p. 469.
14. Enderlen and E. Lexer.

15. H. Kühne, Brun's Beitr. klin. Chir., (1952), Bd. 184, S. 190.
16. E. Lexer, Die freien Transplantationen. Stuttgart (1919).
17. V. Staudacher, Bull. Soc. int. Chir., (1959), v. 18, p. 615.
18. M. F. A. Woodruff and M. Sparrow, Quart. J. exp. physiol., (1958), v. 43, p. 91.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
