TRANSPLANTATION OF THE ANTERIOR LOBE OF THE PITUITARY

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UDC 612.433:612.6.02 + 616.433-089.843-092.9

Differentiation and function of homologous pituitary implants are possible in rabbits, rats, and dogs.

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The possibility of regeneration and function of transplants of the adenohypophysis and the conditions essential for it have not yet been established, although it is known that transplantation of the anterior lobe of the pituitary in man produces some clinical effect [1-4].

In this paper we describe the results of 729 homoplastic transplantations of the pituitary.

EXPERIMENTAL METHOD

The pituitary was transplanted by F. M. Lazarenko's method [5]* in rabbits, rats, and dogs. Experiments were carried out on sexually immature and mature thyroidectomized and castrated animals and also on castrated rabbits receiving daily doses of 5, 50, and 500 units folliculin subcutaneously. The donors were rabbit embryos, sexually immature, old, castrated, and pregnant rabbits, and sexually mature rats and dogs.

The adenohypophyses from between 4 and 30 donors were minced and implanted (at different times of year) into the subcutaneous cellular tissue in the abdominal or thyroid region, into the muscles of the tongue, and into the mesentery. In some experiments the material was kept for 2 h in physiological saline with antibiotics at 2°. The implants were extirpated after 1-60 days, fixed in Zenker's fluid with formalin, and embedded in paraffin-celloidin. Sections were cut and stained for glycoproteins (PAS reaction), with azan by Heidenhain's method, for RNA by Brachet's method, and by the Halmi-Dyban method. Appropriate controls were set up. Biological tests of the implants were carried out on mice by Barrnett's method [6].

EXPERIMENTAL RESULTS

After implantation of the pituitary into adult recipients in a state of hormonal balance, practically no activation and proliferation of the epithelial cells took place. They were, however, observed in young rabbits (4-5 weeks) and in pregnant, thyroidectomized, and hypophysectomized recipients. In these cases all three types of cells were activated: principal, oxyphilic, and basophilic cells. Their granules disappeared and they became similar to each other. The basophils reacted first, the oxyphils later. The activated cells increased their rate of RNA synthesis. At the end of the second day amitoses and mitoses appeared in the cells, causing an increase in their number.

With the appearance of new, undifferentiated connective tissue, rich in cells and containing few fibrillary structures, in the implants the epithelium began to invade it either as single cells or as multicellular layers arranged in one or more rows and layers (Fig. 1, I) or of massive groups of cells. A large number of experiments involving transplantation into different regions showed that successful implantation of the anterior lobe of the pituitary is primarily dependent on the blood supply of the region of implantation.

Proliferative activity is also influenced by the state of the donated material: in the case of transplantation of embryonic material nearly all the cells took part in proliferation because of their low level

* This reference and [6] were not included in original Russian – Publisher.

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 10, pp. 75-77, October, 1968. Original article submitted February 20, 1967.

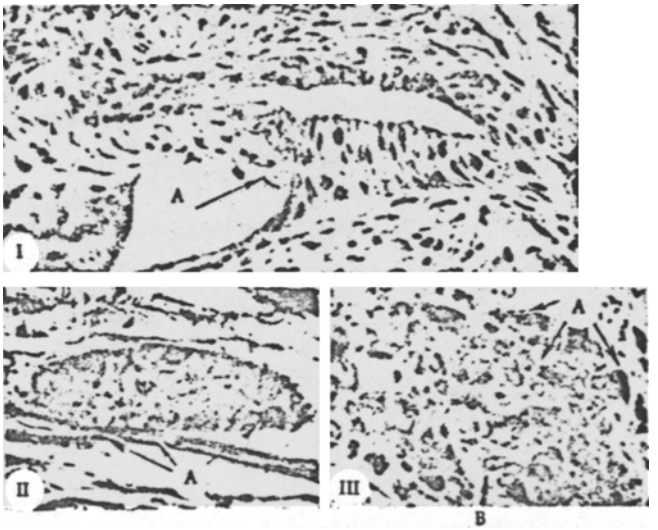

Fig. 1. Tissue culture of the adenohypophysis. I) Stage of 8 days; A) stratified epithelium. Recipient, rabbit aged 2 months, PAS reaction, ocular 7, objective 40; II) stage of 11 days; A) thyrotropic cells. Recipient, hypophysectomized rat. Halmi-Dyban, ocular 7, objective 60, apochromat; III) stage of 20 days; A) basophils, B) mitosis. Recipient, pregnant rabbit. PAS reaction, ocular 7, objective 60, apochromat.

of differentiation, while fewer cells from the pituitaries of pregnant donors remained viable, although they exhibited considerable power of proliferation. The activity and extent of proliferation were increased by storing the material.

As the inflammation subsided, connective tissue differentiated in the grafts, and this process also spread to the newly formed epithelial structures, completing their next stage of development, that of organogenesis, although in accordance with the requirements of the recipient. In the course of organogenesis, structures of lobular type appeared, with blood vessels, and chromophobe and chromophil cells around and within them. Oxyphils appeared first in all recipients; differentiation of basophils was determined by hormonal changes in the recipient. New basophils with a thyrotropic function appeared in the pregnant, thyroidectomized, and hypophysectomized recipients (Fig. 1, II). If the newly formed lobules were surrounded by an adequate number of blood vessels, the number of chromophils in them was as great as in the pituitary in situ, and mitoses were seen among the basophils (Fig. 1, III).

In hypophysectomized rats with subcutaneous implantation of the adenohypophysis, vascularization of the grafts was inadequate and no marked recovery of activity of the thyroid and gonads was observed, although their structure improved. Implants at the stage of 13-14 days, in cases when the recipients were pregnant and thyroidectomized animals, possessed thyrotropic activity as shown by an increase in the mean height of the thyroid epithelium in the experimental mice from 2.44 ± 0.062 to 3.77 ± 0.0065 units ($P < 0.05$).

Death of the newly formed structures occurred at different times determined by the structure of the connective tissue and blood supply of the grafts: where grafts were made into the mesentery, acidophils persisted in the adenohypophyseal parenchyma for more than 2 months, compared with 1 month in the case of successful vascularization of a subcutaneous graft; under usual conditions of transplantation the newly formed structures died within 12-15 days. Subcutaneous grafts of the adenohypophysis are unproductive because of their coarse structure and deficient blood supply.

The implanted adenohypophysis possesses the power of regeneration. Feeding material must be stored and taken from several donors, and the transplantation should be carried out into a tissue with a rich blood supply, and poor in fibrillary structures. The best results are obtained if implantation is carried out in the spring.

Since the new epithelial structures in the implants undergo functional differentiation at a distance from the hypothalamus, it may be supposed that the regulatory influences of the hypothalamus are exerted humorally. That is why the rich blood supply of the implants is so important.

LITERATURE CITED

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