DEVELOPMENT AND FUNCTION OF EMBRYONIC PANCREATIC ISLET CELLS IN THE ANTERIOR CHAMBER OF THE RAT EYE

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KEY WORDS: implantation; endocrine tissue; anterior chamber of the eye.

Immunological rejection remains one of the chief causes limiting the successful iso-, allo-, and xenografting of organs and tissues in experimental and clinical medicine. The presence of immunologically priveleged regions in the body such as the brain, testes, anterior chamber of the eye, etc., offers the prospect of long-term viability and function of transplatned tissues [1, 4, 6]. The large size of some organs, intended for orthotopic transplantation, prevents the use of the regions mentioned above. This is not a drawback which applies to the endocrine organs and, in particular, the endocrine tissue of the pancreas. To achieve complete or partial compensation of experimetnal diabetes mellitus it is necessary only to transplant a few cubic micrometers of endocrine tissue of the gland [1-3, 5-8]. The present writers showed previously [2] that the conditions are available in the anterior chamber of the eye (ACE) for survival and function of allografted pancreatic endocrine tissue.

The aim of this investigation was to study processes of differentiation and organogenesis taking place in cells of endocrine tissue of the embryonic pancreas, implanted into ACE of rats – both intact and with alloxan diabetes.

EXPERIMENTAL METHOD

Fragments of embryonic pancreas were transplanted into ACE of 49 mature, healthy Wistar rats and rats with experimental diabetes mellitus by the method described previously [2]. During the operation the animals were anesthetized lightly with ether. The use of a small volume of implanted embryonic endocrine tissue, the high percentage of endocrine cells contained in it, and their antigenic immaturity created favorable conditions for the solution to the problems posed. For analysis of the grafts, histological sections were stained with hematoxylin and eosin and with aldehyde-fuchsin by Gomori's method in our own modification [2], whereby specific granules could be selectively revealed in the β-cells of the pancreatic islets.

EXPERIMENTAL RESULTS

The experiments showed that the exocrine component of the graft in the early stages of culture consisted of tubular and alveolo-tubular structures structures, some of them showing cystic changes. The exocrine epithelium was characterized by cells of flattened or cubical shape, diffuse basophilia of the cytoplasm, hyperchromia of the nuclear structures, and absence of signs of secretion. Destructive and atrophic changes in the acini continued to progress in the later stages.

Endocrine β-cells of the implants were discovered in two different tissue modifications: solitary scattered cells and islet complexes (Fig 1). Single insulocytes were located in different parts of the implant among its fibrous structures. They were also found very frequently in the composition of the epithelial-tubular structures of the acini. Insulocytes are polygonal cells with well defined nuclei, and some of them are binuclear. In the cytoplasm, on the side facing the capillary, aldehyde-fuchsinophilic granules are present. Later, in the β-cells, morphological specialization continues in the direction of differentiated pancreatic endocrinocytes.

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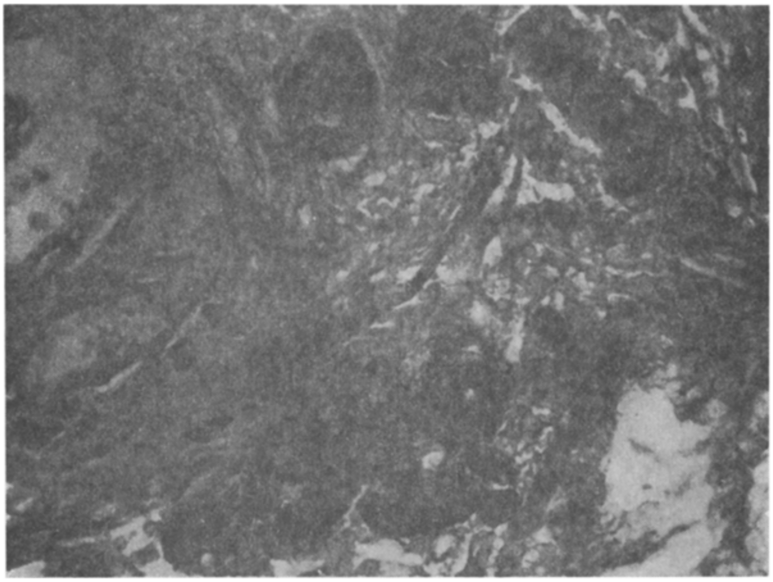

Fig. 1. Islets of Langerhans and single β-cells in ACE of a rat with alloxan diabetes 45 days after implantation. Islet cells packed with specific granules. Here and in Fig. 2: stained with aldehyde-fuchsin: 280 ×.

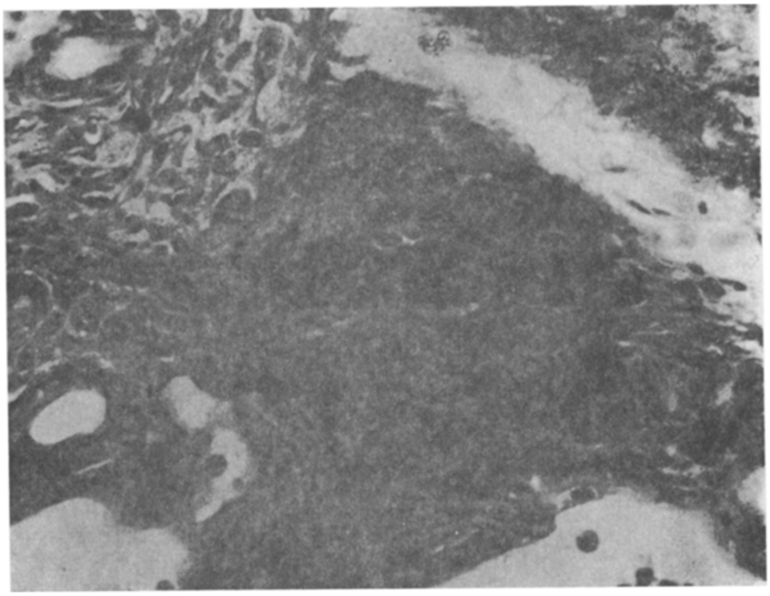

Fig. 2. Implant in ACE of rat with experimental diabetes 45 days after transplantation. β-cells with varied content of specific granules among epithelial structures.

Islet complexes contain from 3-5 to 80-100 endocrine cells and closely resemble in their morphology the islets of Langerhans of the rat pancreas. The dynamics of development of epithelial structures in the implants in the early and later times of observation show that the liquid of ACE is a favorable medium for endocrine cell culture. This applies not only to the preservation of their morphology, growth, and development, but also to the appearance of signs of high functional activity. For instance, β-cells of the islets, which give a strong aldehyde-positive reaction, also are found in those stages of the experiments when the exocrine tissue is completely replaced by connective tissue or has undergone marked atrophy.

The intensity of the aldehyde-fuchsinophilic reaction, correlating with synthesis of the hormone insulin, was quite distinct both individual β-cells and in the islet complexes.

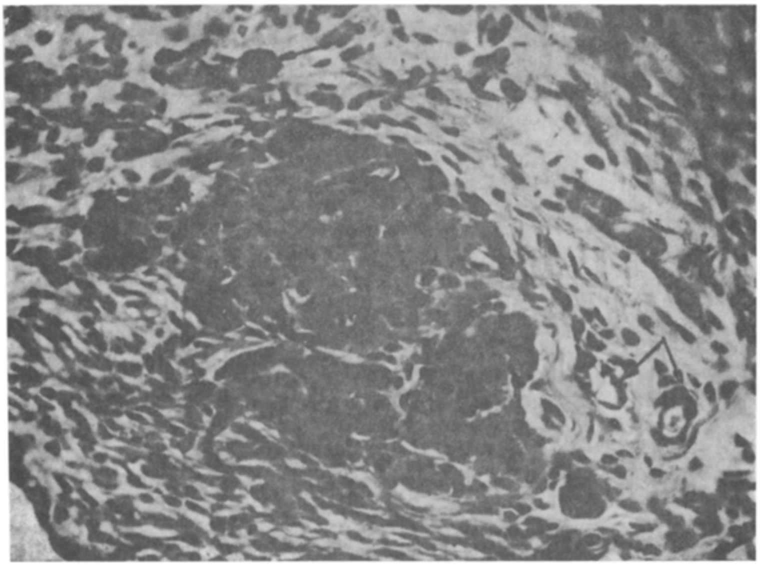

Fig. 3. Islet of Langerhans in ACE of rat with experimental diabetes 45 days after grafting. Vessels of the microcirculatory bed and mitosis of an endocrine cell are visible in the stroma of the islet. Here and in Fig. 4: hematoxylin and eosin; 280 ×.

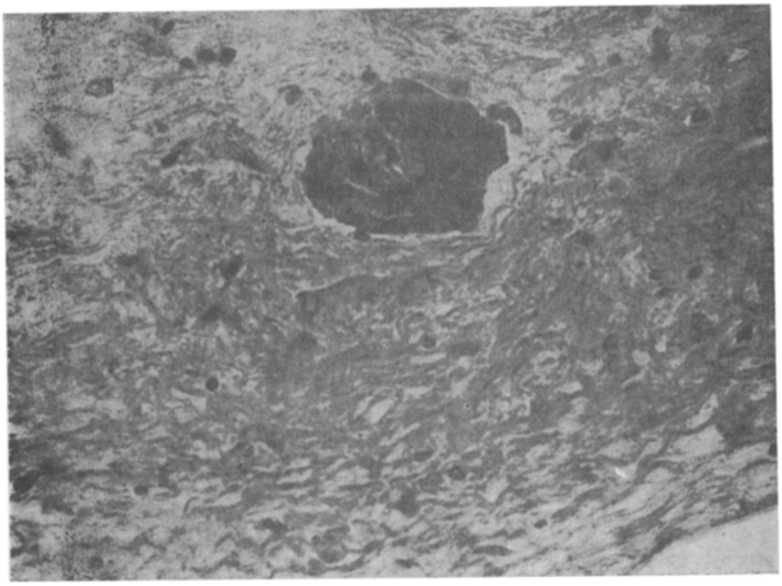

Fig. 4. Implant into ACE of intact rat 30 days after grafting. Single islet of Langerhans in a connective-tissue stroma.

It must be emphasized, however, that later some degree of heterochromia was found; unequal intensity of the histochemical reaction, which also is observed in the islets of the normal pancreas. The endocrine cells of the implants are evidently at different stages of functional activity, a characteristic feature of function of the islets of Langerhans under physiological conditions (Fig. 2).

An essential aspect of the morphology and physiology of the islet cells of the implant is their relations with the microcirculatory system. We know that endocrine organs characteristically have not only a rich network of blood vessels, but also intimate connections of the secretory cells with them. A similar picture also was observed in the endocrine tissue of the implant, in which blood vessels growing from the iris and ciliary body break up into capillaries of sinusoidal type, and interweave closely among the islet cells (Fig. 3). By virtue of these and other conditions of existence of the graft, its endocrine part preserves the organ type of structure to a greater degree and for a longer time. With respect to viability, the endocrine cells of the implanted part of the gland, despite the connective-tissue and cellular environment, have an undoubted advantage over the exocrine component.

A series of experiments with transplantation of the embryonic pancreas into the ACE of healthy rats is of great importance for determination of the character and nature of the processes taking place in the implanted gland. In these cases a rather different picture was observed: the developing endocrine tissue of the implant less frequently formed organ structures characteristic of adult animals, in the form of typical islets of Langerhans which, in turn, consisted of a few small endocrinocytes, and were poorly vascularized (Fig. 4). Mitoses were hardly ever found in such implants and acinar-endocrine differentiation did not take place.

This analysis shows that fragments of embryonic pancreas, implanted into ACE of rats, progressively "rid themselves" of the acinar parenchyma of the organ, whereas its endocrine part develops, differentiates, is revascularized, and restores its physiological activity. The fact that the normal blood glucose level is maintained in diabetic rats for a long time [2] can be explained on the grounds that the endocrine tissue in ACE is under immunologic protection. The formation of organ structures by the endocrine cells of the implant, their morphological maturity, and their functional capacity are all evidence that the conditions are created in ACE for morphological and functional reconstruction of the endocrine part of the pancreas.

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EFFECT OF HELIUM-NEON LASER ON POSTRADIATION REPAIR IN SKELETAL MUSCLES OF OLD RATS

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Ionizing radiation has a damaging action on the regenerating capacity of skeletal muscles, which may continue for quite a long time [6, 8, 12]. Intensification of energy and protein metabolism in the postradiation period may reduce the radiation effect. It has been shown that if the time of appearance of radiation damage in a muscle (i.e, the process of regeneration) is delayed, only in young rats, which have a more active metabolism than old rats, is significant recovery of the regenerative capacity of the muscle tissue observed [9]. Recently published data indicate increased activity of metabolic processes in the tissues under the influence of helium-neon laser radiation [4, 7, 11]. It has been shown that red laser radiation increases the intensity of metabolic processes in normal muscle of old rats [1].

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