STATE OF THE ENDOCRINE PART OF THE PANCREAS AFTER ITS RESECTION DURING PARABIOSIS

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The reaction of the endocrine part of the pancreas to parabiosis and its regeneration after resection of the gland during parabiosis were investigated. Nonsyngeneic parabiosis was found to have a marked effect on this part of the gland, manifested by a considerable increase in mitotic activity and in the quantity of islet tissue of the gland compared with acinar tissue. Syngeneic parabiosis had a less marked action on the endocrine part of the gland. After a certain time evidence of destruction began to appear in this part of the gland also, but it was weaker than in the exocrine part.

Previous papers contained data on reparative processes in the exocrine part of the pancreas during parabiosis. Regeneration was shown to exhibit certain special features which depended on the conditions of parabiosis.

The present paper gives the results of a study of regeneration of the endocrine part of the pancreas after resection during parabiosis.

If it is remembered that during nonsyngeneic parabiosis an immunologic reaction develops in the partners, the study of the state of the endocrine part must be particularly interesting because most endocrine glands are known to participate in the immunologic reaction [3, 5]. However, no data on the state of the endocrine part of the pancreas during immunogenesis could be found in the literature. No reference to the study of regeneration of the islets of Langerhans during parabiosis likewise could be found in the literature.

EXPERIMENTAL METHOD

Three series of experiments involving celomic parabiosis were carried out on male mice. At the time of union, the splenic part of the pancreas (about 40% of the total tissue) was resected from one partner. At each time of observation five to eight pairs of mice were used in the experimental and control series. Series A was concerned with parabiosis of syngeneic CBA mice and resection of the gland in one partner. Series B was concerned with parabiosis in CBA mice with $(CBA \times C57B1/6y)F_1$ hybrids and resection of the gland in the CBA partner. Series C was concerned with the same type of parabiosis but resection of the gland from the hybrid partner. The following controls were set up: 1) single mice with resection of the gland; 2) parabiotic partners without resection of the gland; 3) single mice of the same age without resection of the gland. Sections 7 μ in thickness were stained with hematoxylin–eosin, with aldehyde–fushcin and counterstained by Halmi's method, and impregnated with silver by Gomori's method. Brachet's and Feulgen's reactions were carried out. The degree of regeneration of the islets was determined from their morphology, their size, and the ratio between their area and that of the exocrine part of the gland (the Richardson-Young index), mitotic activity, and the dimensions of the cells and nuclei.

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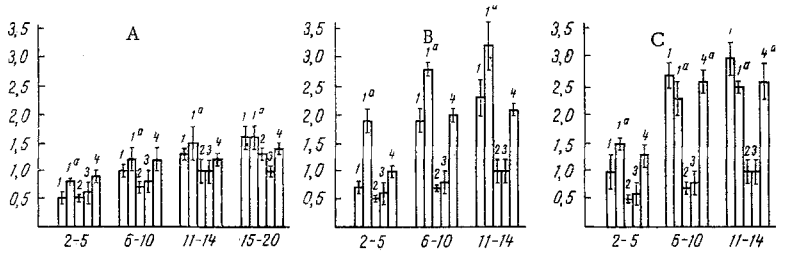

Fig. 1. Ratio between endocrine and exocrine parts of the pancreas in parabiotic mice after its resection: A) syngeneic parabiosis; B) nonsyngeneic parabiosis, resection of gland in CBA partner; C) nonsyngeneic parabiosis, resection of the gland in F_1 hybrid partner. 1) Resected gland of partner; 1^a) intact gland of partner after resection; 2) resected gland of single mouse; 3) intact gland of single mouse; 4) intact gland of CBA partner; 4^a) intact gland of F_1 hybrid partner. Abscissa, days after operation; ordinate, ratio between endocine and exocrine parts of gland.

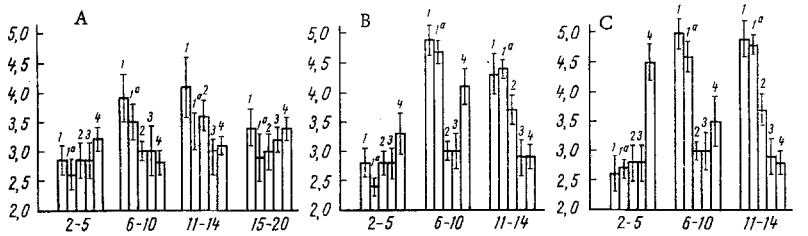

Fig. 2. Area of islets of Langerhans of pancreas in parabiotic mice after its resection (in conventional units). Ordinate, area of islets. Remainder of legend as in Fig. 1.

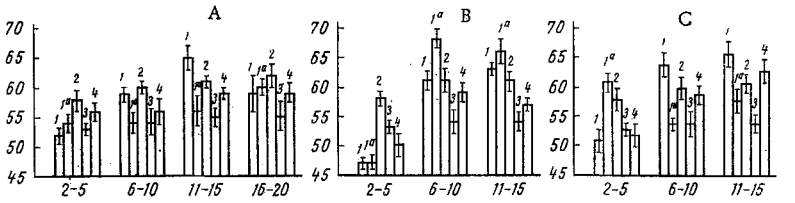

Fig. 3. Area of islet cells of pancreas of mouse partners after its resection during parabiosis. Ordinate, area of cells (in μ^2). Remainder of legend as in Fig. 1.

EXPERIMENTAL RESULTS

Regeneration of the endocrine part of the pancreas after its resection during parabiosis differed appreciably from its regeneration in single mice. In the resected gland of single animals regeneration of the islet tissue took place by the end of the 2nd week (Fig. 1), while subsequently the ratio between the endocrine and exocrine parts was a little higher than in the control intact animals of the same age. In the case of syngeneic parabiosis (series A) restoration of the quantity of islet tissue was observed on the 10th day, i.e., sooner than in the resected gland of single mice.

Under the conditions of nonsyngeneic parabiosis (series B and C) regeneration of the endocrine part took place much more actively, especially in the resected gland of the hybrid (series C). The Richardson-Young index returned to normal much earlier in nonsyngeneic parabiosis than in syngeneic and in the resected organ of the single mice. Later there was a gradual increase in the amount of endocrine tissue of the gland, most marked in the gland of the hybrid (Fig. 1, series C). Intensive growth of the endocrine elements led to a disturbance of their quantitative ratio with the exocrine part toward the end of the period of observation. The ratio between the islet-cell and acinar portions of the gland in nonsyngeneic parabiosis was significantly higher than in the resected organ of syngeneic partners and of the single animals ($P < 0.01$).

In the intact partner during nonsyngeneic parabiosis the Richardson-Young index was significantly higher than in the control, as was seen most clearly in series B, where the intact mouse was the hybrid ($P < 0.01$). In syngeneic parabiosis the quantity of islet tissue was not increased in the intact partner compared with the control ($P = 0.2$).

The results are in agreement with a change in mitotic activity in the islet cells of these animals [6]. The mitotic index was higher in nonsyngeneic parabiosis both in the resected gland and in the intact organ of the partner. The proliferation of the endocrine cells and the marked increase in the quantity of islet tissue were more conspicuous not only after resection of the gland during parabiosis, but also in the control, in intact nonsyngeneic partners without injury to the gland, when the parameters studied were higher than in the resected gland of the single animal.

The dimensions of the islets in the resected gland during parabiosis were increased much more than in the control after resection of the gland in the single animal. However, in syngeneic parabiosis the mean area of the islet was smaller than in the nonsyngeneic partners (Fig. 2; $P < 0.05$ and < 0.01). In series A and the control the islets reached their largest size by the 14th day, while during nonsyngeneic parabiosis the highest value of the mean area of the islets occurred sooner (before the 10th day; see Fig. 2, series B and C). In later periods, a slight decrease in the mean area of the islets took place in the resected gland of the parent (series B), whereas in series C, in which the gland of the hybrid was resected, there was no visible decrease. In all series of experiments an increase in the mean size of the islets was observed in the intact partner compared with the intact single animal, but in syngeneic parabiosis the differences were not significant.

During parabiosis the islets in the resected gland and in the intact organ of the partner appeared heterogeneous. Some of them contained degranulated pale cells and a hardly distinguishable capillary network, while others were intensely stained; they contained large DNA-rich nuclei, and their capillary network was dilated.

Changes in the size of the cells and nuclei differed under the different experimental and control conditions. In single mice the highest value of the mean area of the cells and their nuclei was found by the 16th-20th days. During parabiosis the largest cells were observed in series B (Fig. 3) in the intact F_1 hybrid partner on the 6th day of the experiment.

These experiments demonstrated the marked activating effect of parabiosis on regeneration of the endocrine part of the pancreas. Evidence in support of this conclusion is given by the marked proliferation of the endocrine cells and an increase in the quantity of islet tissue.

Considering that in both series (B and C) with nonsyngeneic parabiosis the most marked increase in the endocrine tissue was observed in the gland of the hybrid, this suggests that the immunologic reaction to the endocrine part of the hybrid's gland has a definite effect. Indirect confirmation of these results is given by the observations of Lambert and Frank [13] who described higher proliferative activity in allografts than in autografts.

Investigations have shown [1, 9-11, 14, 15] that antibodies and antigens, in a certain concentration, can induce cell division. The stimulant action of immunization has been shown by Isfan [12]. Meanwhile the present experiments indirectly confirm data in the literature that only low concentrations of antibodies have a growth-stimulating effect, for during the period of intensive immunogenesis the indices of regeneration were stabilized or lowered.

The marked pathomorphological reaction of the endocrine part of the pancreas of parent mice on their parabiosis with hybrids is interesting. By contrast with the acinar part, no marked changes of a destructive character were observed, but frequently by the 10th-13th day degranulated and vacuolated cells were observed in some islets. Data on changes in the organs of parents during their parabiosis with hybrids have been published [5, 7, 8]. Lymphocytes of the hybrids, received by the parents in the early stages of parabiosis, probably acted as inducers of proliferation of the gland cells, in agreement with the growth-stimulating action of lymphocytes sensitized by operation by Babaeva et al. [2]. At a later period of parabiosis their effect was harmful to the parent organism.

LITERATURE CITED

1. A. G. Babaeva, Regulation of Processes of Compensatory and Regeneration Hypertrophy. Author's Abstract of Doctoral Dissertation, Moscow (1970).
2. A. G. Babaeva, N. E. Kraskina, and L. D. Liozner, Tsitologiya, No. 12, 1511 (1969).

3. V. Ya. Batunina and A. A. Yarilin, in: Problems in Neuro-Endocrine Pathology [in Russian], Gor'kii (1965), p. 127.
4. L. N. Gulyanskii, Some Problems in the Pathogenesis of Parabiotic Intoxication. Author's Abstract of Candidate's Dissertation, Smolensk (1970).
5. Ya. L. Rapoport and I. I. Finkel' Dokl. Akad. Nauk SSSR, 148, No. 5, 1224 (1963).
6. V. M. Starshinova, Byull. Éksperim. Biol. i Med., No. 10, 93 (1971).
7. E. Cornelius, E. Yunis, C. Martines, et al., Lab. Invest., 19, 324 (1968).
8. E. Eichwald, E. Lustgraaf, and M. Strainer, J. Nat. Cancer Inst., 23, 1193 (1959).
9. J. Forber and G. Makaness, Lancet, 2, 1203 (1963).
10. P. Gorer and N. Kaliss, Cancer Res., 19, 824 (1959).
11. R. Grasbeck, C. Nordman, and A. Chapelle, Lancet, 2, 385 (1963).
12. T. Isfan, Microbiologia (Bucharest), 15, 225 (1970).
13. P. Lambert and H. Frank, Bull. Soc. Int. Chir., 25, 639 (1966).
14. E. Letterer, Dtsch. med. Wschr., 88, 2527 (1963).
15. G. Moller, J. Nat. Cancer Inst., 30, 1153 (1963).