DNA SYNTHESIS IN VARIOUS CELLS OF THE EXOCRINE PART OF THE INTACT ALBINO RAT PANCREAS

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A differential count was made of the DNA-synthesizing cells in various parts of the exocrine epithelium of the intact pancreas of sexually mature male albino rats sacrificed 1 h after a single injection of thymidine-H^3. The acinar cells showed low proliferative activity (0.18 ± 0.05%). The highest labeling index was found in the epithelium of the ducts. However, the lining membrane of the ducts consisted of a heteromorphic system of cells with a varying level of DNA synthesis. The labeling index of the nuclei of the centroacinar cells was 2.5 times higher than that of the acinar epithelium and amounted to 0.48 ± 0.17%, whereas the epithelium of the intercalary ducts had an extremely low labeling index: 0.09 ± 0.09%, compared with 0.27 ± 0.09% for the intralobular ducts and 0.50 ± 0.08% for the interlobular ducts.

KEY WORDS: DNA synthesis; pancreas; acinar cells; proliferative activity.

The pancreas is regarded as an organ with low proliferative and, consequently, low mitotic activity [4, 5, 7, 10, 12, 15, 16]. The use of thymidine-H^3 showed that the number of acinar cells in the phase of DNA synthesis preceding mitosis is small in the rat and mouse pancreas, namely 0.1-1.0% [2, 6, 8, 11, 13, 14, 16].

The object of this investigation was to study proliferation of the acinar and centroacinar cells as well as the cells of the intercalary, intralobular, and interlobular ducts.

EXPERIMENTAL METHOD

Experiments were carried out on 5 intact male albino rats weighing 150-180 g. To study DNA synthesis thymidine-H^3 was used as the DNA precursor and was injected subcutaneously 1 h before sacrifice in a dose of 0.5 μCi/g body weight. To exclude diurnal fluctuations in cell division the animals were killed at the same time of day (10-11 a.m.), the time of maximal mitotic activity in the epithelium of the gland [4, 5], after starvation for 24 h. Pieces of pancreas were fixed in Bouin's and Carnoy's mixtures and embedded in paraffin wax. Histoautoradiographs were obtained with the use of type R emulsion after an exposure of 25 days. Sections 5 μ in thickness were stained with hematoxylin-eosin and with gallocyanin by Einarson's method. The number of labeled nuclei and the number of mitoses were counted in 7000 acinar cells and the mean number of centroacinar cells and cells of the intercalary, intralobular, and interlobular efferent ducts were calculated per 1000 cells. The labeling index (LI) was expressed in percent and the mitotic coefficient (MC) in promille. The number of labeled fibroblasts in the interacinar connective-tissue septa was determined in 100 fields of vision under a magnification of 630 ×.

The numerical results were subjected to statistical analysis. Differences were regarded as significant for which $P \leq 0.05$.

EXPERIMENTAL RESULTS

The exocrine part of the pancreas has a lobular structure and consists of acini and ducts. The

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TABLE 1. Proliferative Activity of Cells of the Exocrine Epithelium

Rat No.	Epithelium of acini		Epithelium of ducts							
			centroacinar cells		intercalary		intralobular		interlobular	
	LI	MC	LI	MC	LI	MC	LI	MC	LI	MC
1	0,25 ± 0,56	0	0,37 ± 0,38	0	0	0	0,17 ± 0,31	0	0,74 ± 0,25	0
2	0,30 ± 0,42	0,1 ± 0,08	0,78 ± 0,44	0	0,45 ± 0,25	0	0	0	0,29 ± 0,50	0
3	0,22 ± 0,42	0	1,07 ± 0,44	0	0	0	0,65 ± 0,30	9	0,43 ± 0,19	0
4	0,01 ± 0,14	0	0,17 ± 0,01	0	0	0	0,4 ± 0,13	0	0,64 ± 0,31	0
5	0,14 ± 0,28	0	0	0	0	0	0,16 ± 0,25	0	0,42 ± 0,18	0
Mean	0,18 ± 0,05	0,02 ± 0,01	0,48 ± 0,17	0	0,09 ± 0,09	0	0,27 ± 0,09	0	0,50 ± 0,08	0

Note. LI expressed in percent, MC in $^0/_{00}$

interacinar intralobular septa consist of loose connective tissue in which the number of DNA-synthesizing fibroblasts counted was 4.2 ± 0.64 in 100 fields of vision.

The acini are formed by conical cells with a distinct polar differentiation of their cytoplasm and they contain one or, less frequently, two nuclei. An irregular distribution of labeled nuclei is observed in the epithelium of the acini. As a rule the distribution of DNA-synthesizing cells was focal in character. The intensity of thymidine-H^3 incorporation into the epithelium of the acini in albino rats showed considerable variation in the individual animals (Table 1).

The presence of centroacinar cells within the glandular terminal portions is a distinguishing feature of the structure of the pancreas. LI of these cells was 2.5 times higher than in the acinar epithelium, namely 0.48 ± 0.17%.

The secretion of the gland is discharged through a system of ducts lined with simple epithelium. The lining of the intercalary portion consists of simple squamous epithelium which, in most animals studied, had no labeled nuclei (Table 1). The squamous epithelium of the intercalary ducts changed into cubical epithelium as the duct enlarged to become an intralobular duct, and just as in the acinar epithelium, LI showed considerable individual variation, with a mean value of 0.27 ± 0.09% (Table 1, Fig. 1a). The interlobular ducts lined with cylindrical epithelium had an increased number of DNA-synthesizing cells, on the average 0.50 ± 0.08% (Fig. 1b).

Differential counting of the cell populations in the phase of DNA synthesis after injection of thymidine-H^3 thus showed that the acinar cells have low proliferative activity (0.18 ± 0.05%). The epithelium of the ducts had the highest LI. However, the lining of the ducts consists of a heteromorphic system of cells with a varying level of DNA synthesis. LI for the nuclei of the centroacinar cells was 2.5 times higher than for

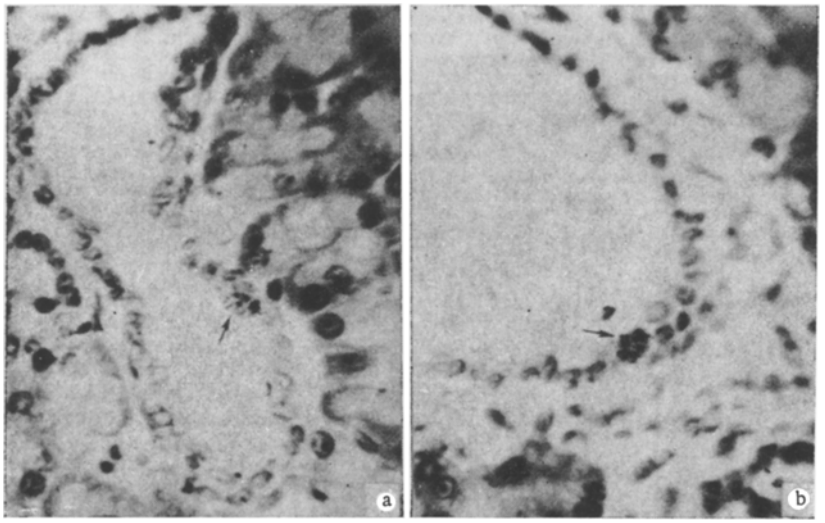

Fig. 1. DNA synthesis in cells of intralobular (a) and interlobular (b) duct.

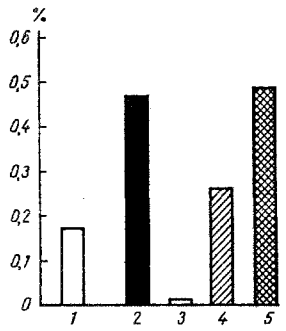

Fig. 2. Diagram of intensity of incorporation of thymidine-H^3 (in percent) in acinar (1) and centroacinar cells (2) and in intercalary (3), intralobular (4), and interlobular (5) ducts.

the epithelium of the acini. A very low LI (0.09 ± 0.09%) was found in the intercalary ducts, compared with 0.27 ± 0.09% in the intralobular and 0.5 ± 0.08% in the interlobular ducts (Fig. 2). Mitoses were found extremely rarely in the structures listed above (Table 1).

It has been shown histoautoradiographically [16] that, starting from the 30th day of the postembryonic period for albino rats, the rate of DNA synthesis in the acinar cells of the pancreas falls sharply by comparison with the early stages of postembryonic development, as a result of a switch during the period of growth to a slow rate of proliferation of the acinar cells, a decrease in the rate of DNA synthesis in them, and lengthening of the S, G_2, and M phases. In labile tissues, such as the epithelium of the small intestine, in which the rapid form of proliferation occurs, this process is absent.

The focal character of the distribution of the DNA-synthesizing cells of the acini is evidently explained by their different functional states. No dependence on blood supply could be established [16].

These results, obtained in experiments on sexually mature intact rats, agree with data in the literature on the low proliferative activity of the acinar epithelium and they make good the absence of information in the literature on the much higher level of DNA synthesis (except in the intercalary ducts) in the cells of the duct system.

The rather lower level of proliferation in the animals investigated than was found by other workers [6, 11] in their experiments was evidently due to the fact that the rats starved for 24 h.

These results shed considerable light on the reactive changes in elements of the exocrine part of the pancreas after various experimental procedures: resection, transplantation, disturbance of the hormonal balance, etc.

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