HISTOLOGICAL CHANGES PRODUCED BY ADRENALECTOMY IN THE PANCREATIC EPITHELIUM OF RABBITS WITH EXPERIMENTAL DITHIZONE DIABETES

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Experiments on 30 rabbits showed that adrenalectomy intensifies the morphological and functional changes in the exocrine (especially the ducts) and endocrine systems induced by dithizone. The increase in the number of small islets to twice the control level, and the increase in the number of A-cells as a result both of their hyperplasia in existing islets and of the transformation of the exocrine epithelium into A-cells are evidently compensatory and adaptive reactions of the pancreas and they confirm the results of biochemical investigations indicating alleviation of the course of diabetes in adrenalectomized animals.

Morphological changes in the pancreas in experimental dithizone diabetes coincide with the disturbance of carbohydrate metabolism [2, 3, 5, 7]. The metabolic disturbances are considered to be connected not only with a lesion of the islet apparatus but also with reactive changes in the efferent ducts [4, 6]. However, the morphological changes in the pancreas after adrenalectomy have not hitherto been studied in animals with experimental diabetes, and the problem of the influence of the adrenals on the course of dithizone diabetes remains unsolved [1, 9-11].

In the investigation described below the histological structure of the pancreas was studied in rabbits after bilateral adrenalectomy and the effect of adrenalectomy on the morphology of the pancreas in animals with diabetes was examined. Dithizone was used to produce experimental diabetes.

EXPERIMENTAL METHOD

Thirty rabbits weighing 2-2.5 kg were divided into three groups: 1) healthy animals (control), 2) adrenalectomized rabbits (killed 12-60 days after operation), 3) rabbits with diabetes induced by dithizone which were adrenalectomized and killed 12-63 days later. Paraffin sections were stained with paraldehyde-fuchsin by Gabe's method and with gallocyanin by Feulgen's method. The number of A- and B-cells (2500-3000 in each animal) was counted, the volumes of the nuclei of the A- and B-cells were calculated in cubic microns, and the ratio B/A and percentage of B-cells were determined. The islets of Langerhans, in which the cells were counted, were divided into five classes: I) 6-16 cells, II) 16-30 cells, III) 31-60, IV) 61-100, and V) more than 100 cells [8].

The blood sugar was determined by the Hagedorn–Jensen method. The numerical results were subjected to statistical analysis and differences were taken as significant for which $P \leq 0.05$.

EXPERIMENTAL RESULTS

The blood sugar of the healthy rabbits varied between 106 and 129 mg%.

The islets were round or oval in shape. After staining with paraldehyde-fuchsin specific granules were revealed in the B-cells (Fig. 1). The small number of A-cells in the large islets were displaced as

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a rule to the periphery. The small islets consisted mainly of B-cells. The efferent ducts consisting of three to eight cells had no goblet cells. The larger intra- and interlobular ducts, whose walls were lined with high prismatic epithelium, contained goblet cells which were visible after staining with paraldehyde-fochsin.

TABLE 1. Volume of A- and B-Cells (in μ^3) in Different Classes of Islets of Langerhans in Three Groups of Rabbits

Group of animals	Less than 16 cells		16—30 cells		31—60 cells		61—100 cells		More than 100 cells	
	A	B	A	B	A	B	A	B	A	B
1	58,2±25,9	80,8±30,1	66,0±22,3	83,0±20,6	78,0±41,3	75,0±7,54	76,0±33,8	83,0±25,0	93,2±52,5	96,0±43,1
2	77,8±12,4	93,3±12,7	78,9±3,13	98,1±23,7	82,0±4,64	108,0±1,88	81,0±7,34	105,0±3,76	68,3±6,3	98,7±13,5
3	61,4±6,85	127,0±9,95	61,2±4,83	103,0±1,37	68,2±5,37	146,0±44,8	—	—	—	—

Adrenalectomy led to significant morphological changes in the insular apparatus and in the exocrine part of the pancreas, while the blood sugar fell from 90 to 76 mg%. Two weeks after adrenalectomy the granules had partly or completely disappeared, vacuolation of the cytoplasm was slight, pycnosis of solitary nuclei of the B-cells was present and the A-cells were hypertrophied (Fig. 2). Later (after 1-2 months) there was an increase in the degenerative changes in the islets of Langerhans: the polymorphism, pycnosis of the nuclei, and vacuolation of the B-cells were all increased; often B-cells completely deprived of their B-granules were seen. The volume of the nuclei of A- and B-cells was greater than in the control (Table 1). Just as in the early stages hypertrophy and, less frequently, hyperplasia of the A-cells were present. The number of small islets (classes I and II) was 47% of the total number counted. By contrast with the control the cytoplasm of the cells of the acinar epithelium of the exocrine portion of the pancreas was often vacuolated. The duct system of the gland showed considerable morphological changes. In the adrenalectomized animals, by contrast with the control, the epithelium of the intra- and interlobular ducts was greatly flattened. Polymorphism and degeneration of the cell nuclei were found. Solitary goblet-cells were seen only in the interlobular efferent ducts. The tunica propria of the mucus membrane of the ducts was sclerosed by comparison with the control. New A- and B-cells were formed in the rabbits of this group by transformation of the acinar cells.

In the rabbits of group 3 (adrenalectomy plus diabetes) the blood sugar was 350 mg%. Adrenalectomy reduced the percentage of B-cells in the diabetic animals and also the ratio B/A in all classes of islets (Table 2).

Specific granules were absent from most of the B-cells (Fig. 3). The large islets had degenerated. Compared with the animals of group 2 the volume of the nuclei of the B-cells was increased in the rabbits of group 3 (Table 1), the hypertrophy of the A-cells was less marked, whereas the hyperplasia of the A-cells was seen more clearly. Mitotic division among the A-cells was more frequent than in the animals of groups 1 and 2. In the small islets, the number of which had increased to 80% (from 42% in the control; $P \leq 0.05$), A-cells were numerically highly predominant. Transformation of the epithelium of the terminal portions into endocrine A-cells was seen much more often than after adrenalectomy alone. The active participation of the epithelium of the pereinsular acini in the exo-endocrine transformation was noteworthy. Besides this feature, the transformation of central acinar cells into A-cells was observed. The predominance of A-cells in the small islets and the numerous pictures of transformation of the epithelium of the exocrine portion of the pancreas into A-cells were evidence of inhibition of the regenerative capacity of the B-cells.

By contrast with the animals of groups 1 and 2, in the rabbits of group 3 goblet-cells appeared in the small efferent ducts and their number in the intralobular and interlobular efferent ducts was considerably increased. These changes were evidently connected with the action of dithizone. Adrenalectomy on the diabetic animals led to late (after 40-60 days) degenerative changes in the efferent ducts characteristic of the adrenalectomized animals.

The study of the histological changes in the pancreatic epithelium of rabbits after adrenalectomy performed on animals with experimental dithizone diabetes showed that the operation intensified the morphological and functional changes in the exocrine (especially the ducts) and endocrine systems induced

TABLE 2. Ratio B/A and Percentage of B-cells in Three Groups of Rabbits

Group of animals	Less than 16 cells		16–30 cells		31–60 cells		61–100 cells		Ratio B/A as a whole
	B/A	B	B/A	B	B/A	B	B/A	B	
1-	3,34±0,73	76	2,2±0,48	65	2,29±0,10	73	2,66±0,45	66	2,59±0,45
2-	1,84±0,38	66	2,09±0,19	64	2,34±0,21	67	2,76±0,22	70	2,26±0,09
3-	1,96±0,39	64	1,64±0,20	60	1,47±0,66	60	—	—	1,68±0,15

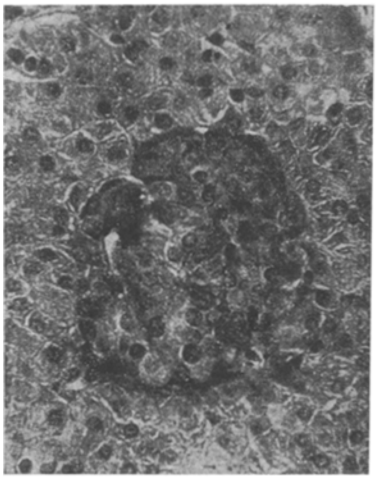

Fig. 1

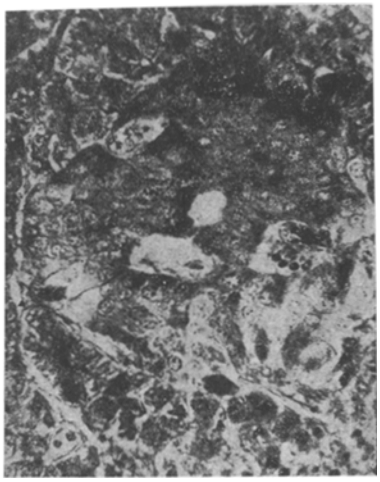

Fig. 2

Fig. 1. Intensive granule formation in B-cells of islets of Langerhans in a control rabbit. Here and in Figs. 2 and 3, paraldehyde-fuchsin, 280 ×.

Fig. 2. Islet of Langerhans 2 weeks after adrenalectomy: hypertrophy of A-cells (on the right).

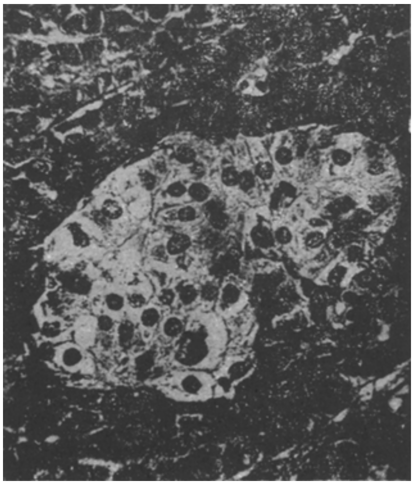

Fig. 3. Islet of Langerhans (adrenalectomy plus diabetes): degranulation of cytoplasm, polymorphism of nuclei.

by dithizone. The increase in the number of small islets to 80% compared with 42% in the control and the increase in the number of A-cells both on account of hyperplasia of the cells in existing islets and of the transformation of exocrine epithelium into A-cells, are evidently compensatory and adaptive reactions of the pancreas and they confirm the results of biochemical investigations [10] which demonstrated alleviation of the course of diabetes in adrenalectomized animals.

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