

EFFECT OF SMALL DOSES OF ALLOXAN ON REGENERATION OF THE ISLET TISSUE OF THE PANCREAS

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Alloxan is known to act selectively on the islet tissue of the pancreas. After administration of large doses of the compound it is mainly the β -cells of the islets which die, as a result of which a typical pancreatic diabetes develops [2, 5-8]. Recent experiments have shown that small, subdiabetic doses of alloxan have an action opposite to that of large doses, causing regeneration and hyperplasia of islet tissue [1, 3]. We have studied the reaction and reparative regeneration of the islet tissue of the pancreas during administration of small doses of alloxan.

EXPERIMENTAL METHODS

Experiments were carried out on male albino rats weighing 100-150 g, receiving an ordinary mixed diet and kept in identical conditions. In some animals (controls) $\frac{2}{3}$ of the pancreas was removed under general ether anesthesia, while in others the identical operation was preceded by injection of alloxan (5 subcutaneous injections of a 5% aqueous solution in a dose of 5 mg/100 g body weight). Material for histological investigation was taken 2, 5, 10, and 15 days after partial pancreatectomy. The number of rats for each period varied from 4 to 6. The portion of the pancreas removed at operation, and also the regenerating fragment of the organ taken after different intervals, were weighed, fixed in Bouin's fluid, and embedded in paraffin wax. Sections were stained with Mayer's hematoxylin and eosin, with aldehyde-fuchsin, and with methyl green and pyronine.

The portion of the pancreas left after operation was conventionally subdivided into the zone next to the region of injury and the distant zone. Measurements of two diameters of the islet cells and their nuclei were made with an ocular micrometer. Thirty cells and nuclei were measured in each zone of all the animals.

EXPERIMENTAL RESULTS

In the partially pancreatectomized animals not receiving alloxan regeneration of the islet tissue took place both in the zone next to the region of injury and in the parts of the organ at a distance from the site of the defect. In the early periods (2nd and 5th days) after partial pancreatectomy, new islet cells were formed in the region of injury from epithelial tubules and bands appearing as a result of reconstruction and proliferation of the glandular elements of the organ. These small islets thus formed consisted mainly of large β -cells (see table), associated with the remodeled epithelial structures (Fig. 1a). In the zone remote from the region of injury, the acinar cells were transformed into islet cells. Among the acinar tissue solitary β -cells were found; at the periphery of the islets transitional cells were observed with signs of both external-secretory and islet cells (Fig. 1b).

Ten and fifteen days after operation the number of islets in the pancreas of the control animals increased; some increase in the size of the islets and of their component cells by comparison with the initial state also was observed (see table). The largest islets were found in the parts of the organ further from the site of injury. It is noteworthy that these findings, demonstrating an increase in the amount of islet tissue in the pancreas of albino rats after partial resection of the organ, are in agreement with the results obtained by G. V. Segida [4], who studied the reparative regeneration of the pancreas in guinea pigs.

In the albino rats receiving 5 injections of alloxan each, no destructive changes were observed in the islet tissue. In the area of the pancreas removed during pancreatectomy the number of small islets was slightly larger

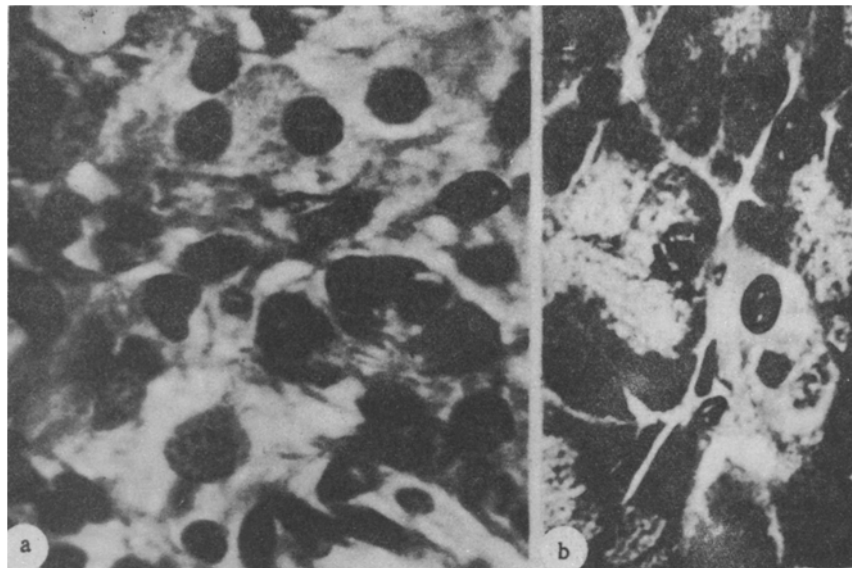


Fig. 1. Formation of new islet cells from epithelial tubules in the zone next to the region of injury (a), and from acinar tissue in the zone remote from the defect (b). Pancreas of an albino rat 5 days after operation. Magnification $\times 960$.

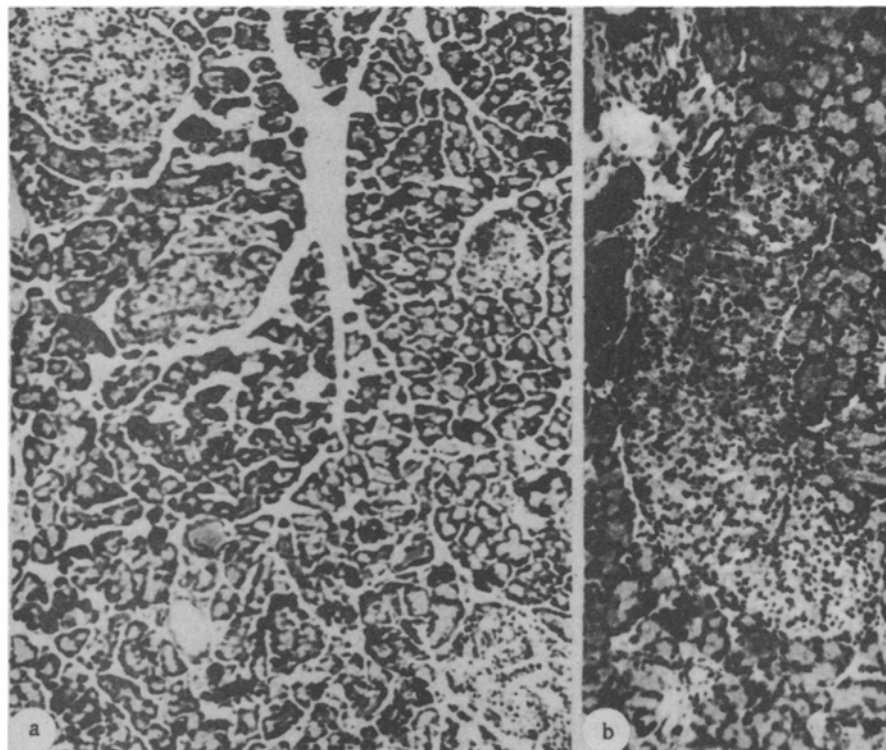


Fig. 2. Changes in the residual part of the pancreas of a rat after pancreatectomy and administration of alloxan. a) After 5 days; 4 islets in a row; b) after 10 days: hypertrophied islet. Magnification $\times 108$.

Dimensions of Islet Cell (in μ) in Albino Rats at Various Periods after Partial Pancreatectomy (mean of two diameters)*

Time after resection (in days)	Zone of pancreas	Control		Receiving alloxan	
		cells	nuclei	cells	nuclei
—	Resected part (initial state)	11.04	5.10	12.17	6.14
5	Next to region of injury	14.61	6.54	15.30	6.91
	Distant from region of injury	11.42	5.99	12.75	6.23
15	Next to region of injury	12.40	6.25	12.69	6.46
	Distant from region of injury	12.32	6.20	12.56	6.50

* The difference between the dimensions of the islet cells and nuclei in the animals of the various experimental groups given in the table is statistically significant, except in the case of the dimensions of the cells of the control animals in the zone further from the region of injury 5 days after operation.

than that in the controls. The islets consisted mainly of enlarged and slightly swollen β -cells containing large nuclei (see table). These results demonstrate that the brief administration of a small dose of alloxan modified the functional state of the islet cells of the pancreas at the moment of operation, causing a slight increase in their secretory activity.

During histological investigation of the parts of the pancreas left behind after partial pancreatectomy and taken from animals receiving alloxan, considerable hypertrophy and hyperplasia of the islet cells were observed. Two and 5 days after the operation, in the animals of this group, numerous small and medium-sized islets and solitary large β -cells could be seen among the acinar parenchyma. In some areas of the remnant of the pancreas 4-6 islets of medium caliber could be seen in a row (Fig. 2a). The islets consisted mainly of hypertrophied β -cells (see table) with clearly defined borders; few α -cells were found in the islets and their structure was substantially unchanged. The cytoplasm of the β -cells appeared finely vacuolated and their nuclei were enlarged and contained little chromatin. By comparison with the controls the processes of regeneration of β -cells were intensified. In the remodeled acinar cells lying next to the islets, the concentration of ribonucleoproteins fell, the specific zymogen granules disappeared, the nuclei increased in size, and the cytoplasm stained in a manner similar to the β -cells of the islets.

At the later periods (10th and 15th days) after injury a considerable increase in the size of the islets was observed in the experimental rats, mainly as a result of the transformation of acinar into islet tissue. In the part of the head of the pancreas remaining after partial pancreatectomy, normally containing small islets, some very large islets were seen (Fig. 2b).

SUMMARY

A study was made of the reaction and reconstructive regeneration of the insular tissue of albino rat pancreas with administration of low alloxan doses (five subcutaneous injections of 5% aqueous solution of alloxan — 5 mg per 100 g body weight). Preliminary short-term administration of a low alloxan dose caused no destructive changes in the insular tissue of partially pancreatectomized animals; it activated the secretory function of the beta-cells, leading to the formation of new islets by transforming the acinar tissue into isletins.

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