EFFECT OF AGE ON ABILITY OF THE RAT PANCREAS TO REGENERATE

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After resection of 16 and 43% of the pancreatic tissues in rats aged 9-11, 20-28, and 75 days, recovery of the lost mass of tissue is not complete during the first 9 weeks. Partial pancreatectomy does not prevent growth and differentiation of the residual part of the organ.

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It has been shown experimentally that the completeness of morphological and functional recovery after extensive resections of mammalian internal organs such as the liver andlungs is largely determined by the age of the animals at operation: the younger they are, the more complete the recovery [1, 3].

Few investivations have been made of the effect of age on the ability of the mammalian pancreas to regenerate, yet because of the great physiological importance of this organ and the relative frequency with which it is effected by disease in old age, this problem merits detailed investigation.

The object of this investigation was to study the ability of the pancreas to regenerate after extensive resection in rats at different stages of postnatal development.

EXPERIMENTAL METHOD

Between 15 and 43% of the pancreatic tissues were resected from albino rats aged 9, 11, 20-28, and 75 days. The parts removed were always taken from the head of the pancreas, related to the spleen and stomach. That part of the organ surrounded by the loop of duodenum was left intact (Fig. 1). The remnant of the pancreas was fixed in Carnoy's fluid by the method described previously [4, 5] 3, 7, 14, 34, and 64 days after resection. After fixation, the organ removed from the experimental and control animals was weighed. The general structure of the gland was studied in sections stained with hematoxylin-eosin, and the number of mitoses in 5000 acinar cells was counted for each animal. At each time of investigation, 6 or 7 (or more) experimental animals and the same number of controls were sacrificed. The numerical data were subjected to statistical analysis by the Fisher-Student method.

EXPERIMENTAL RESULTS

When recovery of the organs was studied in growing animals, allowance had first to be made for the fact that increase in size and weight of that part of the organ left after resection with the passage of time could be due to a combination of normal and regenerative growth.

In fact, as visual observations and determination of the weight of the residual pancreas after partial pancreatectomy carried out on rats at different stages of postnatal development showed, the increase in weight of the residual organ in animals undergoing the operation (during the first 3-4 weeks after operation) was due more to normal growth than to regeneration.

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TABLE 1. Dynamics of Changes in Body Weight and Weight of Pancreas at Different Times after Pancreatectomy in Rats of Different Ages

Series	Group of animals	Age of operation (in days)	Quant. of tissue removed (in %)		Body weight and weight of pancreas after operation •			
					7 days	7 days	14 days	34 days
I	Experimental	9—11	15		17,3(7)	24,6(6)	44(8)	78(3)
					65	86	197	396
	Control				16,4(8)	25,0(6)	50(6)	75(4)
					73	96	318	535
				E/C	86	87	71	70
III	Experimental	20—23	16		29(9)	29(4)	37(8)	130(8)
					161	175	217	454
	Control				29(8)	39(13)	39(8)	128(6)
					204	316	305	684
				E/C	78	63	66	68
IV	Experimental	21—23	43		31(6)	50(7)	81(6)	—
					138	188	286	—
	Control				43(7)	63(7)	100(7)	—
					279	363	616	—
				E/C	65	64	57	—

Note. Top number gives body weight (in g), bottom number weight of pancreas (in mg). Here and in Table 2, number of animals shown in paretheses. $\frac{E}{C}$ denotes ratio between relative weight of pancreas in experimental animals and weight of total pancreas in control (in %).

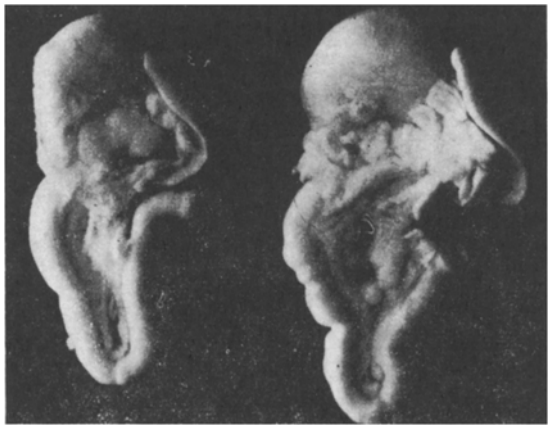

Fig. 1. Total preparations of pancreas and organs related to it (spleen, stomach, duodenum) from rats aged 23 and 28 days. On the left—residual part of gland after resection of head of pancreas, surrounded by loop of duodenum (rat aged 23 days); on the right—total pancreas from intact rat aged 29 days. 10×.

Irrespective of the age of the animal at operation, the weight and size of the residual organ never attained those of the control (Tables 1 and 2; Fig. 2). The size of the resected part did not affect the outcome of the process. For example, after removal of 15% of the total mass of the pancreas from rats aged 9-11 days, at no time of observation (from the 3rd to the 34th day) had the residual organ attained the weight of the control pancreas (Table 1, series I). After resection of 40% of the mass of the pancreas from rats of this same age (Table 2, series II), the result was the same. Similar results were also obtained after resection of 16 and 43% of the pancreas from rats aged 20-28 days (Tables 1 and 2, series III-V).

Furthermore, during growth of the animals, the ratio between weight of the residual pancreas in the experimental animals and the weight of the total organ in the controls fell. This indicates that the growth of the injured pancreas gradually lagged behind growth of the intact organ. This is a characteristic response of the pancreas to resection at any age. The older the animal, the more clearly this pattern is revealed. During the first month after resection at any age, the pancreas exhibited virtually no regenerative power (Table 1). Ability to regenerate first appeared 2 months after the operation. The younger the animal, the more completely the resected mass of pancreatic tissue was made good. For example, two months after

TABLE 2. Body Weight and Weight of Pancreas after Resection of 40-43% of Its Mass in Animals of Different Age Groups Two Months after Operation

Series	Group of animals	At beginning of expt.		At end of expt.			E/C
		age in days	body weight (in g)	body weight (in g)	wt. of pancreas abs. (in mg)	wt. of pancreas rel. (in %)	
II	Experimental	11	17	254 (19)	836	0,32	80
	Control			258 (11)	1072	0,4	
V	Experimental	23—28	54	289 (24)	748	0,27	70
	Control			298 (11)	1160	0,39	
VI	Experimental	75	167	300 (13)	642	0,21	48
	Control			315 (5)	1505	0,44	

See Note to Table 1.

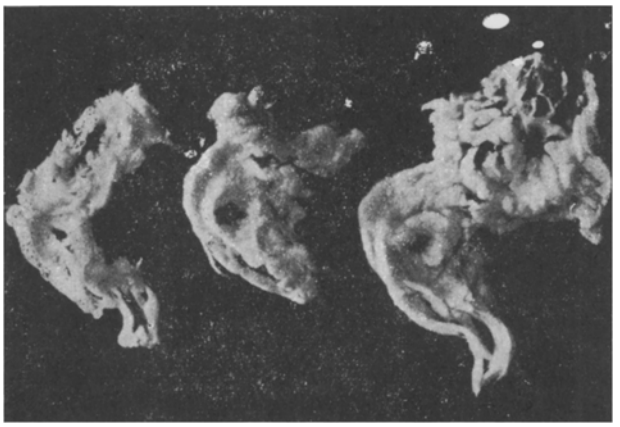

Fig. 2. Total preparations of pancreas from rats two months after beginning of experiment. On the left (1st and 2nd), pancreas from experimental animals, resected part of organ not regenerated; on the right, pancreas of intact animal.

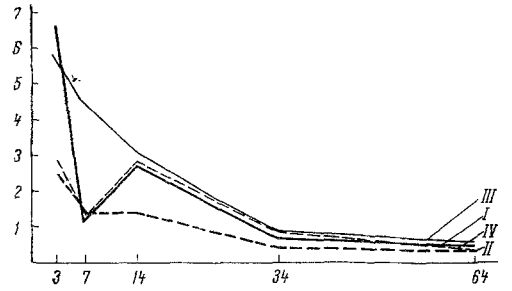

Fig. 3. Mitotic activity of acinar cells of pancreas at various times after resection of organ from rats aged 20-28 days. I and III) Mitotic activity after resection of 16 and 43% of mass of organ; II and IV) mitotic activity in corresponding control groups. Abscissa, days after operation; ordinate, number of mitoses (in %).

resection of the mass of the pancreas from rats aged 11, 28, and 75 days (series II), the ratio between the weight of the residual pancreas in the experimental animals and the weight of the total organ in the controls ($\frac{E}{C}$) for these are groups was 80, 70, and 48%, respectively (Table 2).

The results given also show that in adult rats (aged 75 days) no regeneration of the pancreas was observed under these experimental conditions. It is difficult at present to state what is responsible for this fact. It is worth mentioning, however, that in previous investigations using the same experimental technique regenerative hypertrophy of the pancreas was observed [4]. On the other hand, restoration of the resected mass of the organ was by no means complete, however, in agreement with results obtained by other workers [2, 7, 8].

Determination of the level of proliferative activity of the acinar cells in rats aged 21-28 days following resection of 16 and 43% of the mass of their pancreas shows that resection causes an increase in the number of mitotically dividing cells .

The mitotic activity of the acinar cells remained appreciably elevated during the first week after pancreatectomy (Fig. 3). The differences between the number of mitoses in the experimental and control series are statistically significant on the 3rd and 7th days after removal of 43% of the mass of the organ ($P = 0.017$ and 0.018). In all other cases they are not significant.

Despite the slow and incomplete regeneration of the resected mass of the pancreas at all investigated age groups, the injured organ remained capable of growth and differentiation. Its histological structure remained similar to that in the control. In both the experimental and control series, the ratio between the quantity of insular and of acinar tissue (expressed in percentages) fell with age: in rats aged 75 days, two weeks after resection of 43% of the mass of the pancreas it was 1.79, falling to 0.85 after 2 months; the index in the control series fell during this period from 0.64 to 0.47. The decrease in the relative content of insular tissues in the rat pancreas with age was observed by the writer previously, in a special investigation of the structure of this organ at different stages of its postnatal ontogenesis [6]. The relative content of insular tissue remained higher in the injured organ than in the control.

As a whole, the results of this study of the response of the rat pancreas to partial pancreatectomy at different ages demonstrate the relatively weak regenerative power of this organ.

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