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Correlation of Histological Changes Produced in the Gland During Pancreatic Stimulation with Blood Enzyme Levels *

by

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Most of the excretable enzymes produced by pancreatic stimulation are drained through excretory ducts into the duodenum. Only a small amount passes to the interstitial space of the gland from which it is taken to the blood through the lymphatic or venous capillaries of the gland.

When the normal pancreas is stimulated, significant increases in the concentration of these blood enzymes are not detected. A significant elevation (100 % above basal level) occurs only when stimulation is applied to a pathological pancreas (3).

In order to examine this problem more deeply, the diversion of pancreatic enzymes into the blood produced by several stimuli and the histological changes induced in the gland by these stimuli, have been studied simultaneously.

This article corresponds to studies of the normal pancreas.

Materials and Methods**

Forty-eight mongrel dogs weighting between 17-22 kg were anaesthetized with Sodium Pentothal; a blood sample and a biopsy of the pancreas were obtained before and several times after stimulation. The time scheduled for biopsy was 30', 60', 90', 2 h., 3 h., and 6 h. when the stimuli used was Secretin. Blood samples were taken every 15 minutes after stimulation for 1 ½ hour, and every 30 minutes for a total time of 4 hours (amilolytic activity was determined).

Stimulation was induced by Prostigmin (0,03 mg/kg weight), Pancreozymin (1 U./kg weight), Secretin (1 U./kg weight).

For acinar activity evaluation we have adopted the parameters described by BECKER (1, 2), *Stage 1* (storage). Nucleus in basal position and zymogen granules filling the apex of the cell. *Stage 2*. Empty-

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ing of the zymogen granules. *Stage 3.* Complete emptying of granules, and nucleus moving towards the apex. In the basal area a wide basophile zone is formed reflecting a concentration of R.N.A. *Stage 4.* Prozymogen and zymogen granule formation starts again. *Stage 5, 6 and 7.* Belong to this second cycle.

In another group of twenty dogs and as a complement to the previous study, the changes in amylase concentration in the blood were determined after each of the glandular stimuli.

Results are given in tables I, II and III.

Results and Discussion

PROSTIGMIN. Histological changes produced by this stimuli can be summarized

TABLE I

Histological changes induced by stimulation in normal pancreas *

Stimulus	Excretor ducts	Capillaries vessels	Inter-acinar edema	a = time b = stage	Acini (secretory stages)					
				a. basal	30′	60′	90′	2h.	3h.	6h.
Prostigmin	Enlarged (10/12)	Hyperemia (10/12)	Slight (10/12)	b. 1 (12/12)	1-2 (6/6)	1-2 (7/10)	2 (4/4)	2 (7/10)	2 (8/12)	
	Contains thick secretion (10/12)	Enlarged lymph vessels (8/12)		b.		2 (3/10)		2-3 (2/10)	2-3 (3/12)	
				b.				3 (1/10)	3 (1/12)	
Pancreozymin	Enlarged (5/12)	Hyperemia (9/12)	Slight (1/12)	b. 1 (12/12)	1 (6/6)	2 (7/10)		2-3 (8/8)	2-3 (2/12)	
	Contains fluid secretion (4/12)			b.		3 (3/10)			3 (10/12)	
Pancreozymin plus Prostigmin	Enlarged (10/12)	Hyperemia (10/12)	Slight (10/12)	b. 1 (12/12)	1-2 (5/5)	2 (7/10)	2 (1/5)	3 (6/7)	3 (8/12)	
	Contains thick secretion (11/12)	Enlarged lymph vessels (8/10)		b.		3 (3/10)	3 (4/5)	7 (1/7)	4 (3/12)	
				b.					7 (1/12)	
Secretin	Flattened epithelium (9/12)	Hyperemia (4/12)	Slight (6/12)	b. 1 (12/12)	1 (6/7)		1 (11/12)	1-2 (6/6)	1-2 (9/12)	1-2 (6/6)
	Contains thick secretion (6/12)			b.	1-2 (1/7)		1-2 (1/12)		2 (2/12)	
				b.					3-4 (1/12)	

* Techniques of staining: haematoxylin-eosin, tricromic-Masson.

TABLE II

Increase of blood amylolitic activity in normal pancreas stimulation (48 dogs, simultaneously studied for histological changes)

Percentage increase above basal level	Stimulus			
	Prostigmin	Pancreozymin	Pancreozymin plus Prostigmin	Secretin
No significant increase	(11/12)	(11/12)	(12/12)	(10/12)
Increase 50-100 %	(1/12)	(1/12)		
Increase > 100 %				(2/12)

Two techniques were used for the determination of amylolitic activity in each sample, BRANISTEAUX and SOMOGYI.

in: *a*) a mild enlargement of the excretory ducts containing a viscous secretion, *b*) hyperemia and enlargement of lymph vessels, *c*) mild interacinar edema, suggesting that a production of liquid occurs, *d*) a great acinar activity takes place (stage 2, 8/12), (stage 2-3, 3/12), (stage 3, 1/12).

In only one case a moderate diversion of pancreatic enzymes to the blood was detected.

PANCREOZYMIN. Histological changes are characterized by: *a*) excretory ducts being less often dilated and containing a fluid secretion, *b*) hyperemia, c) no interacinar edema being present, *d*) acinar activity being much more marked (stage 2-3, 2/12), (stage 3, 10/12).

Only in one case an increase of less than 100 % in the blood amylase level could be detected.

PANCREOZYMIN PLUS PROSTIGMIN. Changes observed correspond to those produced by both stimuli. The effect on the acinar activity is maximal (stage 3, 8/12), (stage 4, 3/12), (stage 7, 1/12).

In spite of this increased activity and the dilatation of the lymphatic vessels, no important shift of the pancreatic enzymes to the blood has been observed.

TABLE III

Increase of blood amylolitic activity in normal pancreas stimulation (20 dogs)

Percentage increase above basal level	Stimulus			
	Prostigmin	Pancreozymin	Pancreozymin plus Prostigmin	Secretin
No significant increase	(20/20)	(20/20)	(19/20)	(16/20)
Increase 50-100 %			(1/20)	(2/20)
Increase > 100 %				(2/20)

SECRETIN. Histological changes are represented by: *a*) in 75 % of cases a flattening of the epithelium of the excretory ducts being present, *b*) hyperemia in 4/12 cases, *c*) a slight interacinar edema in 6/12), *d*) the stimulus producing minimal activity in the acini.

In spite of this poor acinar effect, shift of the enzymes to the blood was detected in 19 % of cases (6 % with an increase of 50 % above basal level, and 13 % with an increase of 100 %), probably due to the great volume of liquid caused by Secretin, producing temporary obstruction of the excretory ducts, as flattening of the epithelium suggest.

Summary

In a group of 48 dogs, a study was made of the action of Prostigmin, Pancreozymin and Secretin stimuli on the pancreatic gland, histological samples being obtained at different time periods of each stimuli.

The most strong effect on the acinar activity was produced by Pancreozymin, and even more activity is produced if Pancreozymin is administered simultaneously with Prostigmin. The less activity was produced by Secretin.

At te same time amilolytic activity in the blood during the stimulation was checked in a total of 68 dogs. With the stimulation of Prostigmin and Pancreozymin, in only 3 % of the cases there were increases of 50 % above the basal level. On the other hand, Secretin, with less acinar activity, produced increases in 19 % of the cases.

This discrepancy can be explained by the great volume of liquid produced by Secretin. This fast increase of liquid could momentarily obstruct the excretory ducts of the gland diverting the new enzymes towards the interstitial space, from where they pass into the blood by drainage through the lymphatic or venous capillaries of the gland.

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