

SECRETORY FUNCTION AND MORPHOLOGY
OF THE REGENERATING GASTRIC MUCOSA
AFTER SUBTOTAL AND TOTAL MUCOSECTOMY IN DOGS

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Experiments on eight dogs with a Basow fistula showed that after total or subtotal mucosectomy of the stomach regeneration of the mucosa was observed although, however, the original functional state was not reached. The times taken for restoration of the structure of the mucosa and the degree of restoration of acid, pepsinogen, and mucoprotein secretion varied in the different animals.

There are a few reports in the literature to the effect that morphological and functional regeneration of the gastric mucosa can take place after its removal from the entire surface of the organ; however, the data so far as the degree of restoration of gastric functions is concerned are contradictory. Moreover, no complete account has yet been given of the functional characteristics of the regenerating gastric mucosa, for only its acid-secreting function has been studied [1, 2].

EXPERIMENTAL METHOD

Experiments were carried out on eight noninbred dogs of both sexes weighing from 10 to 22 kg. A Basow fistula was formed in five dogs in the antral portion of the stomach. The initial hourly gastric secretion in response to subcutaneous injection of histamine dihydrochloride in a dose of 0.24 mg/10 kg body weight or in response to intravenous injection of insulin in a dose of two units/10 kg body weight was investigated 6 to 8 times on the 7th-10th day after the operation. A second operation was performed later on the animals: a sparing excision of the tissues of the abdominal wall and the wall of the stomach around the fistula, and through the defect thus formed in the stomach wall the tunica propria of the mucous membrane was removed down to the tunica muscularis mucosae. Completeness of resection of the gastric mucosa was verified macroscopically and morphologically. Small areas of mucous membrane were left in six dogs next to the esophagus and pylorus, while in the other two dogs (Nos. 12 and 111) the whole of the mucosa was removed. The defect in the stomach wall was reused to insert the fistula tube. The wound in the abdominal wall was sutured up to the fistula.

Investigation of the secretion began on the 7th-8th day after the operation. The function tests were accompanied by histological and histochemical investigations. Biopsy for examination of the regenerating mucosa was carried out through the Basow fistula by means of a Wood-Masevich tube (two dogs). Pieces of the stomach wall also were investigated from six animals after death. The tissues were fixed in 12% neutral formalin or by Shabadash's method and stained with hematoxylin-eosin by Van Gieson's method, with mucicarmine, with Best's carmine, by the Dominici-Kedrovskii and McManus methods, and by the PAS reaction.

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TABLE 1. Acid Production by Regenerating Gastric Mucosa of Dogs at Various Times after Subtotal Mucosectomy (in meq/h)

	Dog				
	№ 12 ♂	№ 111 ♀	№ 17 ♀	№ 10 ♀	№ 18 ♀
Original values	21,0—26,0	19,6—24,0	11,2—12,4	8,9—11,0	3,8—4,5
Values after subtotal mucosectomy					
8 days	0,12	—	0,07	0,03	0,34
17 »	—	—	0,88	0,4	0,8
37 »	0,34	—	2,60	—	1,4
45 »	—	—	6,56	1,98	—
58 »	3,20	—	—	—	—
65 »	2,88	—	7,50	—	—
84 »	3,60	5,16	—	3,60	—
106 »	—	6,4	7,80	—	1,8
132 »	—	7,7	—	—	—
199 »	—	—	—	—	2,4
261 »	4,0	—	—	—	2,72
296 »	—	12,6	—	—	—
362 »	—	—	—	—	3,1

TABLE 2. Indices of Gastric Secretion in Dogs 2.5 Years after Subtotal Mucosectomy

Index studied	Normal		Indices found for dogs investigated		
	♀	♂	R, female, 11 kg	L, female, 18 kg	T, male, 22 kg
Hourly volume (in ml/kg body weight)	10,2±0,9	12,5±0,8	55 (112)	100 (184)	150 (275)
Concentration of acid (in meq/liter)	158±3	172±5	128	156	160
Hourly production of acid (in meq/kg body weight)	1,56±0,1	2,09±0,1	7,0 (17,2)	15,6 (28,1)	24 (46)

Note. Indices for dogs investigated are given per animal. Expected values are given in parentheses.

EXPERIMENTAL RESULTS

During the first days in response to injection with histamine a small quantity of gastric juice not containing free HCl was secreted. Free HCl did not appear in the secretion until the 6th-8th week after the operation. As Table 1 shows, the greatest increase in acid production was found between the 6th and 10th weeks after the operation. Later, the increase in acid secretion took place less intensively, and the rate and degree of recovery of this function of the gastric mucosa varied from one animal to another. In all the dogs recovery of acid production was incomplete on account of a decrease in the volume of gastric secretion, whereas the acid concentration was almost back to its original level by the 7th-9th week after the operation, and thereafter it remained a little below the normal level.

Pepsinogen appeared in the insulin-induced gastric juice of the dogs in a low concentration (from 1 to 6 mg%, compared with the initial values of 106-150 mg%) by the 17th-18th day after the operation and possibly even earlier, for before this time a very viscous secretion was produced in response to injection of insulin, which could not be filtered so that it was impossible to determine the pepsinogen. Subnormal (more often) or normal (less often) levels of pepsinogen concentration were reached at different times after the operation (from the 6th to the 30th week), and because of the decrease in volume of the secretion the pepsinogen production remained below or just reached the initial level. The time of appearance of gastromucoprotein could not be reliably determined because the high viscosity of the juice prevented a sufficient quantity of filtrate of gastric secretion for investigation from being obtained for a long time after the operation. The initial values (115-160 mg%) of the gastromucoprotein concentration were reached in two dogs by the 10th-25th week after the operation, while in the rest the values remained below normal throughout the period of observation; the production of this fraction of the gastric juice did not reach its initial level, on account of the decrease in volume of the secretion and in the concentration of mucoproteins, in any dog of this group throughout the period of observation.

A Basow fistula was first formed in three dogs 2.5 years after the operation of subtotal mucosectomy. The initial values of the gastric secretory function were not available for these dogs. The results were

therefore compared with normal values of gastric secretion calculated on the basis of 84 tests of gastric secretion on 15 intact dogs with a Basow fistula. The results of these tests are shown in Table 2. Clearly 2.5 years after the operation of subtotal mucosectomy acid production had not yet reached the expected level mainly because of a decrease in volume of gastric secretion. With regard to the concentration and total output of pepsinogen and gastromucoprotein in the insulin-induced gastric juice, the results obtained were similar to those given for the first five dogs.

Morphological investigations showed that regeneration of the gastric mucosa after mucosectomy begins in the region at the boundary of the resected tissue, subsequently spreading throughout the remainder of the defect in the mucous membrane. On the 10th-12th day after the operation, epithelization of the mucosa was observed, and on the 30th-35th day the regenerated mucosa was almost as thick as normal over a wide area, and it consisted of numerous branching tubular glands arranged irregularly. The secretory function of the epithelium of the glands at this stage of regeneration showed certain special features. The subsequent stage of regeneration (40th-50th days) was characterized by the formation of tubular glands and the appearance of chief cells. At later periods after mucosectomy (4.5 months-1.5 years) no significant difference could be found from the previous data.

LITERATURE CITED

1. J. Chiricuta et al., *Chirurgia* (Bucharest), 18, 929 (1969).
2. G. N. Milton, *Brit. J. Surg.*, 47, 562 (1960).