

REGENERATION OF THE GASTRIC MUCOSA AND REDUCED SECRETION AFTER PARTIAL REMOVAL OF THE MUCOSA

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The recent investigations of Marx, confirmed by Spyrkes and Stoikitse have shown that in patients suffering from duodenal ulcer the gastric mucosa contains a much higher number of oxyphilic cells, which cells produce hydrochloric acid, than the mucosa of healthy persons. Van Geertruyden [2] observed that in patients suffering from peptic ulcer in the vicinity of a gastroenteroanastomosis the degree of increased acidity is directly proportional to the number of oxyphilic cells found in the mucosa of the stomach stump.

In view of these facts we began to search for an experimental model, enabling us to observe the regeneration of the dystrophic gastric mucosa affected by "gastritic" and "ulcerative" changes. It was our basic aim to achieve a "controlled" decrease of the gastric secretion by diminishing the functional potential of those cells which produce hydrochloric acid within the gastric mucosa.

EXPERIMENTAL METHODS

An operation — subtotal removal of the gastric mucosa — was carried out on 60 dogs.

By means of a broad gastrotomy almost the whole gastric mucosa from the cardia to the prepyloric region can be removed (by scraping it off with a knife); only a narrow zone of mucosa in the pylorus-antrum region of about 3-5 cm width is preserved, which zone does not contain acid-producing cells; in this antral part the mucosa is firmly attached to the submucosa, consequently the separation of the mucosa is extremely difficult and causes considerable damage to the submucosa which later may lead to drawn-in stenotizing scars.

In the remaining part of the stomach the mucosa can easily be separated. In this manner about $\frac{9}{10}$ of the gastric mucosa can be removed. Histological investigation showed that we had removed the epithelial layer of the mucosa including the underlying loose connective tissue as far as the muscularis mucosae.

The operation is technically simple, does not lead to hemorrhage and does not cause shock.

For 4-7 days the animals are kept on a liquid diet; after that they are given the full standard ration. The behavior of the operated animals, their gain in weight and the function of the hemopoietic system are all normal.

The operated animals were observed for 1 year and 9 months; part of the animals were sacrificed at different times. During the period mentioned above we carried out the following investigations:

Morbid anatomical investigations. The stomach of the sacrificed animals was inspected with the naked eye; subsequently paraffin sections were prepared from various parts of the stomach and were stained with hematoxylin-eosin and with Van Gieson's stain.

Functional investigations. The secretory function of the stomach was followed up after the regeneration of the mucosa. The gastric juice was collected through a Pavlov fistule after injection of 5 mg histamine per 10 kg weight and 0.6 International Units of insulin per kg weight. The free, bound and the total acidity of the gastric juice was estimated by titration with N/10 NaOH.

Pathophysiological investigations. The condition of the regenerated mucosa was investigated by injection of 0.2 g atophan (cinchophen) per kg weight, given daily until the animals' death.

EXPERIMENTAL RESULTS

At autopsy macroscopic investigation of the animals, sacrificed at different times, showed that the gastric mucosa underwent an extremely rapid regeneration: between the 20th and the 30th day the whole internal surface of the stomach, from which the mucosa had been removed, was covered by a new, splendid and moist mucosa. The stomach wall remained elastic and showed no visible inflammatory changes.

Within a few days after the operation the wound surface is covered by a thin fibrous layer in which small islets of gastric epithelium can frequently be found (Fig. 1, a). After two weeks proliferation of the epithelium can be observed which creeps upon the wound surface, beginning from the edge of the remaining mucosa. In some places the proliferation originates from the very rare persisting islets of epithelium; in consequence there are two sources of epithelization.

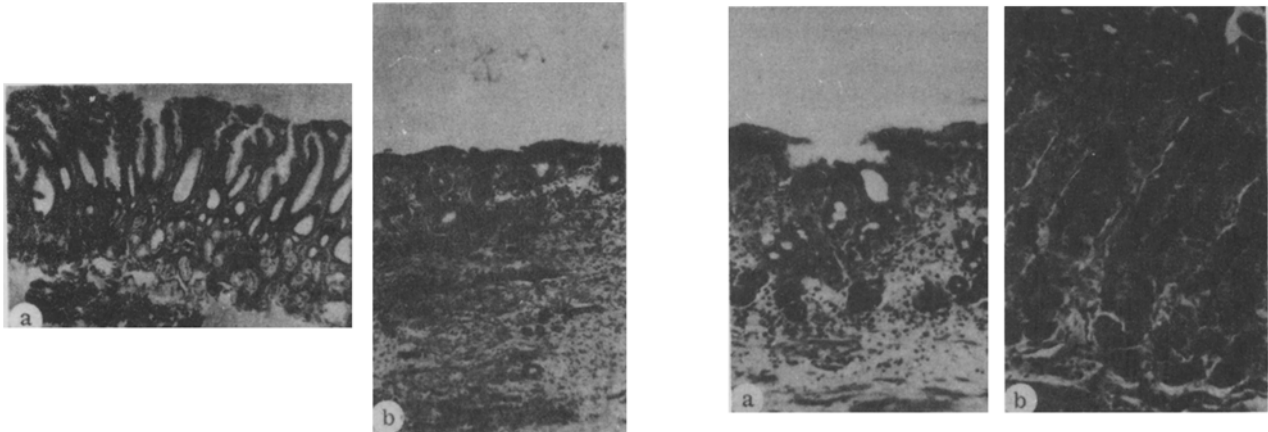


Fig. 1. Regeneration of the gastric mucosa in the first days after the partial removal of the mucosa.

Fig. 2. Regeneration of the gastric mucosa 4-6 weeks after the partial removal of the mucosa.

After 4-6 weeks the whole internal surface of the stomach is covered by a new mucosa (Fig. 2, a); the thickness of the latter reaches $\frac{1}{3}$ to $\frac{1}{2}$ of the normal mucosa (Fig. 2, b). The mucosa is formed by columnar epithelium similar to the normal epithelium of the gastric mucosa. In some places ramified tubular processes can be seen which do not possess fundus glands and parietal cells. In some places the glands consist of contorted canals, which are in some cases dilated.

In various parts of the regenerated mucosa circumscribed zones of differentiation with fundus glands can be seen; in these cases the number of oxyphilic cells is small, they are reduced in size and have a lowered affinity to stains.

No erosions can be seen on the regenerated mucosa surface, not even 6 months after the operation. In some places foci of chronic inflammation appear in the submucosa which in time become less marked.

After 6, 12 or 18 months there are still no fundus glands in the restored mucosa or they are very weakly developed. The mucosa is much thinner than the normal mucosa. In some parts of the stomach wall zones of slight chronic inflammation can be seen.

The results of the functional investigations coincide with the morbid anatomical findings.

The more extensive the resection of the gastric mucosa, the smaller the quantity of gastric juice and of hydrochloric acid obtained after injection of histamine or insulin. In case of extensive resection reaching to the pylorus a marked decrease in the gastric secretion accompanied by an decrease in the acidity can be observed.

E. G. Dog No. 9 ("Nero") responded before the resection of the mucosa to the injection of histamine with a gastric secretion of about 200 ml and a concentration of hydrochloric acid corresponding to 135 clinical units; 2 months after subtotal resection (9/10th) of the mucosa, however, at a time when the regeneration of the mucosa had been completed long ago the same dose of histamine elicited the secretion of approximately 47 ml with a concentration of hydrochloric acid corresponding to 10 clinical units; 6 months after the operation the quantity of gastric juice was still diminished: 50 ml and the total acidity corresponded to 104 clinical units.

It thus appears that after the operation the quantity of gastric juice decreases approximately 4 times; the total acidity does not decrease to the same extent but practically remains decreased compared to the total quantity of gastric juice produced by the regenerated mucosa.

If insulin was used to stimulate gastric secretion similar results were obtained. In view of the possible dystrophic changes in the regenerated mucosa, changes which might lead to a greater proneness to exulceration, we studied the reaction of the mucosa to atophan (cinchophen) as daily injections of this substance lead to the development of acute ulcers; these ulcers usually lead to perforation within 12-15 days after the beginning of the treatment.

4 dogs were given injections of atophan after a more or less extensive resection of the mucosa ($1/2$, $2/3$, $9/10$, and total resection of the mucosa). In the first dog, in which the operation had been performed several months earlier and covered one half of the stomach surface the atophan ulcer led to perforation on the 12th day and caused the animal's death. The ulcer was situated in the prepyloric part of the stomach where the mucosa had not been damaged.

The second dog (resection of the upper $2/3$ of the mucosa) perished on the 26th day under symptoms of atophan-induced cachexia. Autopsy revealed the presence of a non-perforated ulcer in the prepyloric part of the mucosa which part had not been damaged; the regenerated mucosa remained intact. The third dog (resection of $9/10$ of the mucosa) perished on the 31st day under symptoms of atophan-induced cachexia. Autopsy revealed the presence of a superficial ulcer in the immediate vicinity of the pylorus on the part of the mucosa which had not been affected by the operation. The 4th dog in which the whole mucosa from the cardia to the pylorus had been resected was in a satisfactory condition without any symptoms of cachexia 40 days after the beginning of the atophan treatment.

From the above results it follows that the regenerated mucosa is apparently resistant and shows no signs of dystrophy.

Our findings show that the gastric mucosa has a considerable capacity for regeneration. By varying the extent of mucosa resection a more or less marked decrease in the acidity of the gastric juice can be achieved.

In those cases in which 90% of the mucosa are resected and in which the operation was carried out very thoroughly the quantity and quality of the gastric juice undergo changes and the juice shows a marked tendency to a lower acidity.

Development of the above method would enable us to use the described surgical technique in dystrophic conditions of the gastric mucosa (drug-resistant gastritis accompanied by increased acidity, beginning stages of polyposis, ulcers, etc.). All methods used in the past to achieve a decrease in the quantity and acidity of gastric juice have led to serious disorders (antral gastrectomy of the Polya-Reichel or Finsterer type, upper pole gastrectomy of the Deloy type and bilateral vagotomy of the Dragstedt type.). The method of mucosa resection described by us, on the other hand, offers great advantages as it preserves the innervation and the blood supply and does not traumatize the stomach muscles. Only the gastric mucosa i.e., the part of the stomach above all affected by the dystrophic changes, is removed.

At present the method of mucosa resection may serve for experimental morphological and functional studies on the gastric mucosa as it enables us to investigate more precisely the role played by the mucosa in different stomach regions (fundus, antrum, etc.) in digestion, circulation, etc.

The value of this "mucosa surgery" will obviously have to be confirmed by numerous and prolonged studies on a large number of animals.

SUMMARY

Restoration of the gastric mucosa after the removal of its various lengths was studied in 60 dogs. As shown, gastric mucosa possessed a great restorative ability; in a month after its excision complete reepithelization of the internal surface of the stomach took place. The newly formed mucosa possessed a reduced number of oxyphilic cells.

Functional investigations demonstrate that gastric secretion is considerably reduced after the operation. The new gastric mucosa is in good trophic condition.

LITERATURE CITED

1. V. Bacov, *Scoarta Cerebrala Si Organele Interne*. Bucuresti (1949).
2. J. Van Geertruyden, *Acta. Gastroent. Belg.* Vol. 20 (1957), p. 569.