

STRUCTURAL CHANGES OF THE MUCOUS MEMBRANE OF THE STOMACH AFTER EXPERIMENTAL RESECTION

N. A. Nilova

Laboratory of Pathomorphology (Head, Corresponding Member AMN SSSR
A. A. Solov'ev), Institute of Normal and Pathological Physiology (Director,
Active Member AMN SSSR Prof. V. V. Parin), AMN SSSR, Moscow

Presented by Active Member AMN SSSR N. A. Kraevskii

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Gastric resection is a common operative procedure in cases of gastric or duodenal ulcer. It has been found that usually in such cases removal of $\frac{2}{3}$ to $\frac{3}{4}$ of the stomach frequently leads to functional disturbances and serious consequences.

Experimentally it is not easy to determine the cause of these complications [2,3,6,7,9], and not nearly enough attention has been paid to the significance of structural changes affecting the functional condition of the gastric mucosa. Nevertheless changes of this kind would appear to be of the greatest importance clinically in relation to the postoperative disturbances, particularly in connection with impairment of gastric juice secretion after resection.

Our aim has been to study structural changes in the gastric mucosa of the remaining part of the stomach and alterations in the glandular apparatus after extensive gastric resection. These studies are related to those of Yu. M. Lazovskii et al. [4,5] on the functional morphology of the stomach.

EXPERIMENTAL METHOD

Gastric resection was carried out in 11 dogs by the widely-used clinical method of Bil'rot II modified by Hofmeister and Finsterer*. The portion of the stomach removed amounted to $\frac{2}{3}$ or $\frac{3}{4}$ of the distal portion which included the pyloric region, the intermediate zone, and the glandular field of the body of the stomach. In the remaining portion there was a glandular area of the cardia and fundus, and sometimes a small portion of the body of the stomach. A microscopic study of the mucosa was made 6, 7, 8, 11, 14, 15, and 23 months, 2 years, and 3 years 8 months after resection. The material was fixed in 12% neutral formalin. Sections were cut of portions of rolled up gastric mucosa, and included both the anterior and posterior walls of the remaining stomach, of the lesser curvature, and of the region of the anastomosis; they were stained by the usual methods and by the method of Dominicha-Kedrovskii, by Best's carmine, and by Meyer's musicarmine. Selective staining of the different secretory granules by these methods indicated not only the structure of the gland but also its functional condition.

EXPERIMENTAL RESULTS

At various times after the resection in almost all the experimental animals the gastric mucosa of the remaining portion of the stomach appeared smooth and there was no erosion and no gastric ulcers. As histological studies showed the regenerative changes consisted for the main part of a recovery of those portions of the glandular areas which had remained after the operation. In three cases there was some hypertrophy of the mucosa of the glandular areas. In most experiments the regeneration was not completed normally, or was held back, and various changes could be seen in the mucosa. Because these changes could be interpreted as stages of a single process occurring after the operation we have arranged the results of our histological investigation not in terms of the dates of the experiment, but to correspond with the stages of development of the observed changes which did not always correspond on a time scale. The animals formed a continuous series with respect to the degree and extent to which these changes were manifest.

*The operation was carried out by N. Sh. Amirov.

Weight of Experimental Dogs before the Operation and at Various Times after It

Dog	Time after operation	Weight (in kg)		Difference in weight (in kg)	Loss in weight	General condition
		before the operation	before post mortem			
Veta	1 year, 3 months, and 3 days	14.0	16.0	+2	Weight increased	Good
Naf	1 year, 3 months, and 1 day	14.0	13.20	-0.8	$\frac{1}{17}$ of original wt.	Good
Jack	6 months and 1 day	22.0	17.2	-4.8	$\frac{1}{4}$ " "	Satisfactory
Dunai	8 months and 17 days	20.0	12.8	-7.2	$\frac{1}{3}$ " "	Not satisfactory
Valet	2 years and 12 days	15.7	10.5	-5.2	$\frac{1}{3}$ " "	Satisfactory
Naidenysh	1 year, 11 months, and 7 days	21.7	12.3	-9.4	about $\frac{1}{2}$ orig. wt.	Variable (satisfactory or poor)
Belyanka	11 months and 4 days	15.7	10.5	-5.2	$\frac{1}{3}$ of original wt.	Poor
Anitra	1 year	8.9	5.6	-3.3	$\frac{1}{3}$ " "	Grave
Inga	7 months and 4 days	18.0	12.8	-5.2	$\frac{1}{3}$ " "	Grave
Laima	3 years, 8 months, and 1 day	15.5	10.40	-5.1	$\frac{1}{3}$ " "	Very grave
Zhuchka	1 year, 2 months, and 23 days	15.0	10.0	-5.0	$\frac{1}{3}$ " "	Very grave

The Table shows certain indices of the general condition of the animals; the extent of the changes in the remaining portion of the stomach to a large extent agree with the relative loss of body weight.

The least well shown changes occurred in the dogs Veta and Naf. In the first the only change was an initial proliferation of the epithelium of the gastric pits, and in the second, proliferation of the epithelium led to lengthening of the glands and to an uneven thickening of the mucous membrane.

When the proliferation was more vigorous (in Jack) the gastric pits became deeper and branched so as to be directed not only towards the depth of the mucosa, but they sometimes emerged onto the surface in the form of papillary structures.

Further development of the process (In Dunai) led even to a reorganization of the principal glands: the parietal cells from the neck of the glands penetrated into the body and base of the gland replacing the chief cells. New forms of cell arose which from the outline and position of the nucleus and from the structure of the cytoplasm appeared to be intermediate between the chief and parietal cells. In the subsequent development (of Valet) the reorganization of the principal glands, and the hyperplasia of the gastric pits were even more strongly shown. The cells of the proliferating epithelium contained numerous mitotic figures, and differed from the other cells by having an enlarged and paler nucleus.

In Naidenysh and Belyanka, on the anterior walls of the remaining portion of the stomach besides changes which we have already described there was also a marked displacement of the glands, and between them there was a large amount of stroma (particularly in Naidenysh); there was considerable infiltration by lymphoid elements with groups of plasma cells. However, in the posterior walls the structure of the mucous membrane was typical of the fundus. The principal glands were elongated.

In Anitra and Inga the proliferation of the epithelium of the gastric pits, the outgrowth of the gastric pits which showed a large number of mitoses, the shortening of the glands and their replacement by pits showing hyperplasia, and reorganization of the glands was more widespread. On this account in glands showing the characteristics of intermediate glands developed, and in parts glands of Shterk appeared. In the lumen of the enlarged gastric pits clusters of dilatations could be seen. Among the glandular cells cubical or more flattened cells with a large pale nucleus took the place of the usual prismatic cells; forms intermediate between parietal and chief cells, between cells of a covering epithelium and cells of the pyloric glands or parietal cells developed. There was a great reduction in the number of lining cells.

In Laima and Zhuchka there were absolutely no typical chief cells in the glandular area of the fundal region or in the proximal part of the glandular of the body of the stomach. Not only were there no chief glands, but chief cells, neck cells, and parietal cells were absent also. The mucous membrane consisted of deeply branched gastric pits or glands which it was difficult to attribute to a particular type of structure (tubular, alveolar, or compound). In Zhuchka the mucous membrane often consisted of an outgrowth of gastric pits which were deep and branched, and in whose

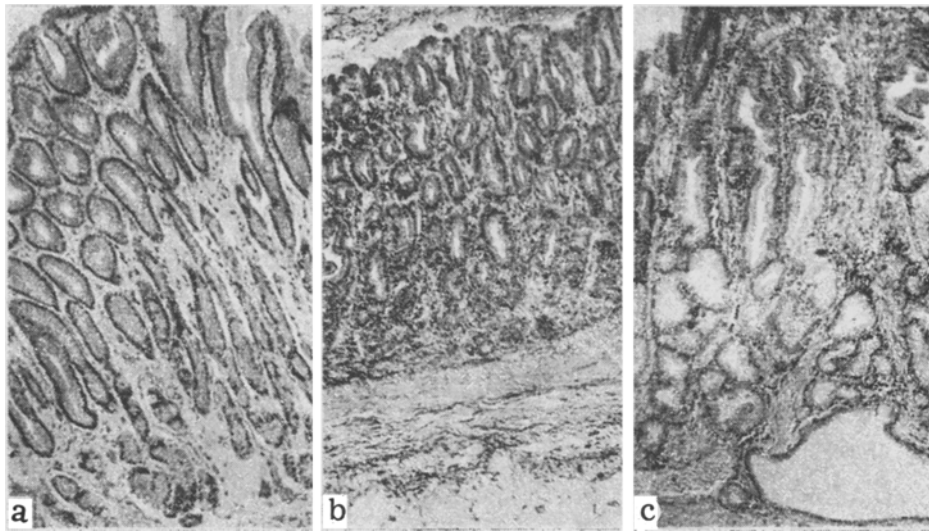


Fig. 1. a) Proliferating epithelium of a gastric pit; occasional shortened chief glands. Magnification 70 \times ; b and c) complete disappearance of the chief glands and their replacement by large numbers of gastric pits lined by undifferentiated cells; appearance of bunches of cavities. Magnification 48 \times .

lumens there were clusters of dilations. From the nature of the secretion and from its nuclear and cytoplasmic structure the epithelium lining the gastric pits, and the new glands resembled those found in the atypical epithelium of Anitra and Inga, but in addition goblet cells were present. In all the glandular elements mucoid substances were stained red by Best's carmine. In Laima the stroma of the mucous membrane contained a large number of lymphoid follicles and was intensely infiltrated by lymphoid elements (Figs. 1 and 2).

If therefore we compare the changes recorded in the different dogs and arrange them as an ascending series we get the impression of a single process developing in the gastric mucosa of the remaining portion of the stomach. Any one particular case represents a certain stage of development. Initially, as a result of mitoses in the gastric pits there is a proliferation of the epithelium lining the gastric pit, and this must be interpreted as regeneration occurring after removal of a large amount of mucous membrane and some damage to the remaining glandular zones. Deeper and branched gastric pits developed. Clusters of cavities may develop in cases where there is a considerable outgrowth from the gastric pits and proliferation of the lining epithelium. The outgrowth of the gastric pits may occur not only

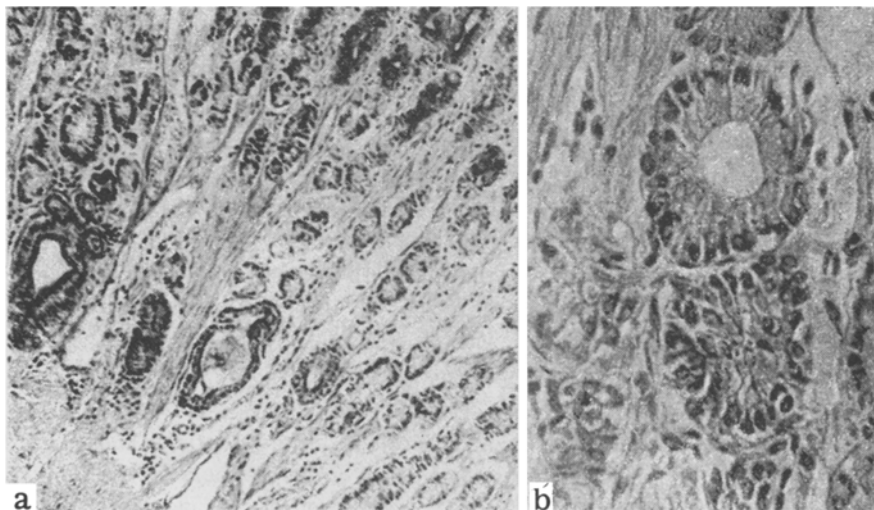


Fig. 2. Death of the chief glands and change in their cellular composition. a) Magnification 90 \times ; b) magnification 300 \times .

in the thickness of the gastric mucosa but also at its surface, so as to form papillary structures. Growth into the depth of the stomach wall occurred only in the region of the anastomosis. However, regeneration under these conditions is incomplete: there is no differentiation of the cells, and there is an involution of the cell forms, and new forms of epithelium appear. All the remaining and the newly formed cells give the specific colouring for mucopolysaccharide and mucoproteins, i.e., they produce gastric mucus [1]. As this process develops the chief glands at first shorten being replaced by outgrowing gastric pits, and finally disappear completely. At the same time in the chief glands highly differentiated chief cells are replaced by less differentiated intermediate forms of cells or by parietal cells. The lining cells disappear. The reorganization of the gland takes place gradually and leads to a development of new atypical glands resembling in some ways the intermediate glands, glands of Shterk, and pyloric glands.

The gradual involution and death of the chief cells in the remaining portion of the stomach leads at first to a reduction in the formation of pepsinogen and of chlorides, and to an increase in the secretion of mucous substances; with the death of the chief glands the secretion of pepsinogen and chlorides ceases, and only mucous substances continue to be secreted.

The involution and death of the chief glands, dedifferentiation of the glandular cells, and the appearance of atypical structures of the mucosa occurred at different rates in the different dogs, and was restrained or enhanced at various stages. Nevertheless the profound changes develop chiefly after a long time (15 months or 3 years 8 months). The rate of development of the process appears to depend upon the original condition of the dog. The condition of the animal depends in turn upon the stage of development of the process of the remaining portion of the stomach. In cases when there is no death of chief glands in the stomach the animals remained in good general condition, they were active and lively, their appetite was good and they responded well to the surrounding medium (Veta, Naf, Jack). However Anitra, Inga, Laima, and Zhuchka, in whom profound changes were observed in the mucous membrane of the residual portion of the stomach coupled with a complete involution of the glands, were in a poor or even serious condition; they were weak, emaciated, and towards the end of the experiment they lost weight catastrophically and ceased to react to environmental stimuli (see the table). They suffered from anemia and hypoproteinemia.

Our results together with clinical observation on patients with total gastric resection [8] indicate that in these cases there is a profound nutritional disturbance which may be fatal. The mechanisms are not well understood. However on the basis of our own functional and morphological studies we may conclude that necrosis of the chief cells plays an important part in bringing about the severe disturbances in the general condition.

SUMMARY

Gastric resection was performed on 11 dogs by means of Hofmeister-Finsterer's modification of the Billroth II operation. The structure of the gastric mucosa of the remaining portion of the stomach was studied at various periods (from 6 months to 3 years and 8 months) after the operation.

The changes that occurred were a gradual involution of the chief glands, dedifferentiation of the chief cells, disappearance of the parietal cells, and the appearance of new cells in the mucosa of an atypical structure. Various stages of this process were reflected in the animal's general condition. When the changes were profound and widespread the animal became exhausted, and the general condition was grave. The greatest disturbances were found chiefly in cases when the postoperative period was most prolonged.

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