MORPHOLOGICAL CHANGES IN THE JEJUNAL MUCOSA AFTER BILATERAL SUBDIAPHRAGMATIC VAGOTOMY

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Bilateral subdiaphragmatic vagotomy in rats leads to development of a combination of structural and ultrastructural changes in the jejunal mucosa and in its epithelial cells – enterocytes and goblet cells. In the early stages after the operation (1 and 7 days) morphological changes of destructive character predominate in the organ, whereas in the late stages (60 and 120 days) structural changes of a compensatory nature become increasingly predominant.

KEY WORDS: vagotomy; jejunum; mucosa; enterocyte; goblet cell.

Recent investigations have shown that division of the vagus nerves leads to the development of a combination of structural and ultrastructural disturbances in some digestive organs (stomach [17], pancreas [4, 11]). The small intestine has not been adequately studied from this standpoint. The few investigations so far described (with one exception [15]) used the light microscope and they were not dynamic in character [7, 9, 13-15], so that no clear idea can be obtained of the principles of the morphological changes in the organ and its structural components under these conditions on the basis of the results obtained. Meanwhile the solution of this problem is not only of theoretical but also of considerable practical importance, for in modern clinical surgery operations associated with total or selective vagotomy are widely used in the operative treatment of gastric and duodenal ulcer. It must also be remembered that complications affecting the small intestine are among the commonest complications after such operations.

The object of this investigation was to make a combined dynamic study of morphological changes in the jejunal mucosa after bilateral subdiaphragmatic vagotomy in rats.

EXPERIMENTAL METHOD

Altogether 73 albino rats (males) weighing 140-160 g were used; 35 animals underwent bilateral subdiaphragmatic vagotomy and the rest were controls. The animals were killed in pairs (experiment–control) 1, 7, 14, 19, 30, 60, and 120 days after the operation. The rats were starved for 24 h before sacrifice. For light-optical microscopy fragments of the proximal part of the jejunum were fixed in Carnoy's fluid and embedded in paraffin wax; sections were cut to a thickness of 5-7 μ. A semiquantitative analysis of pathohistological changes in the mucous membrane and a morphometric determination of the thickness of the epithelium covering the villi were carried out on sections stained with hematoxylin–eosin and the number of intraepithelial lymphocytes was counted. Goblet cells were counted in sections stained by Culling's method, by means of which all their different types can be revealed simultaneously (cells containing acid, neutral, or both acid and neutral mucopolysaccharides). For electron-microscopic investigation pieces of jejunum were prefixed in glutaraldehyde, fixed in Millonig's mixture, and embedded in Durcupan. Sections cut on the LKB ultratome were examined in the IEM 7A electron microscope.

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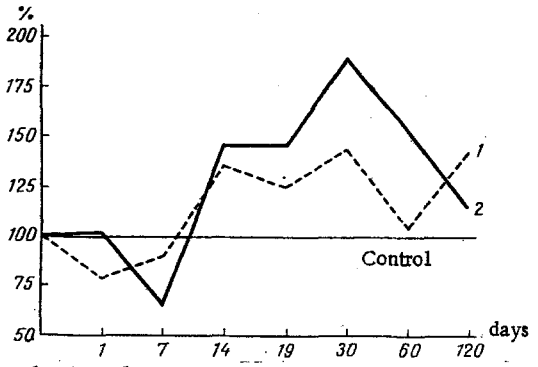

Fig. 1. Number of goblet cells on villi (1) and in crypts (2) of jejunal mucosa of vagotomized rats. Abscissa, time after operation (in days); ordinate, number of goblet cells (in %).

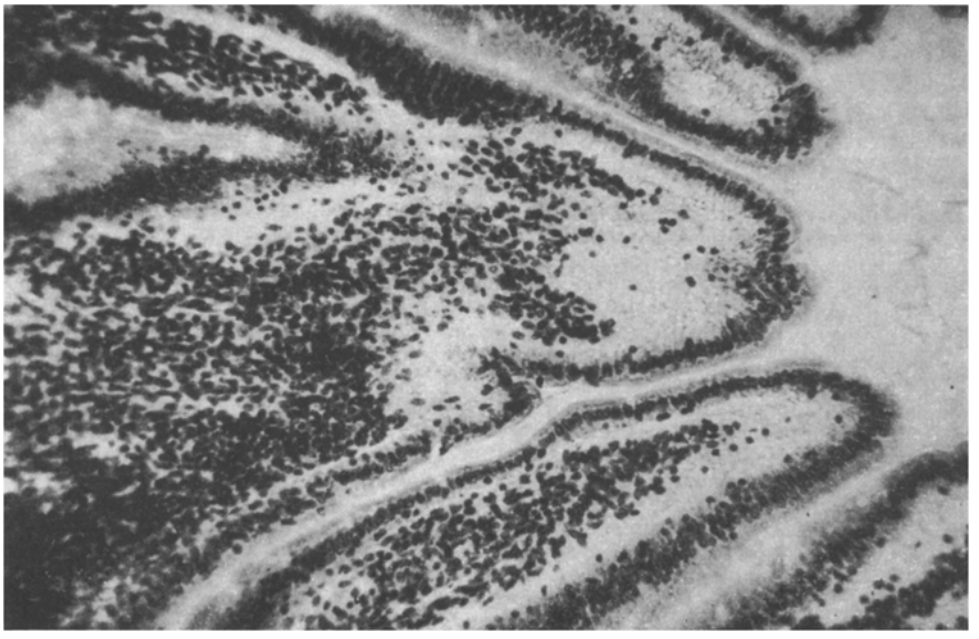

Fig. 2. Lymphoid infiltration of stroma of villi (7 days after operation). Hematoxylin–eosin, 300 ×.

EXPERIMENTAL RESULTS

Examination under the light microscope revealed inflammatory changes and circulatory disturbances in the jejunal mucosa. The "alternative" component of inflammation was manifested as disturbance of the integrity of the epithelium and simplification of its structure, with a disturbance of the regularity of orientation of its cells. The degenerative component was manifested as pycnosis of the nuclei of some enterocytes and swelling of the collagen fibers of the submucous layer. The exudative component of inflammation consisted of edema of all structural components of the mucosa and infiltration of its tunica propria with leukocytes. Disturbances of the circulation in the mucosa were very moderate and consisted of vasodilatation in the tunica propria and the submucous layer, with stasis of blood. The changes described were most marked 1, 7, and 30 days after vagotomy. The number of goblet cells on the villi was very slightly increased in the early period after vagotomy (1 and 7 days), it increased substantially after 14, 19, and 30 days, then fell until 60 days, and rose again 120 days after the operation (Fig. 1). The number of intraepithelial lymphocytes on the villi was increased 1, 7, and 30 days after the operation (Fig. 2), was indistinguishable from the control after 14, 19, and 120 days, and was slightly reduced 60 days after the operation.

Electron-microscopic investigation of the epithelial cells of the jejunal mucosa after vagotomy revealed some regular changes of a destructive and compensatory character. Disturbances of structural organization common to both enterocytes and goblet cells consisted of dilatation of the tubules and cisterns of the cytoplasmic

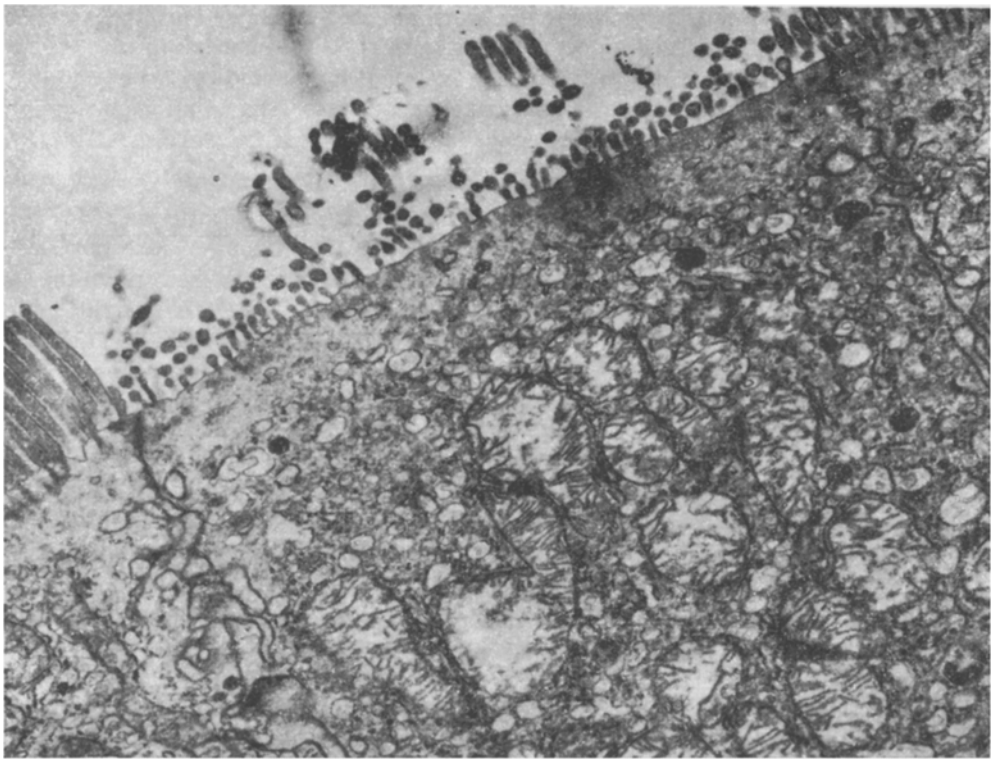

Fig. 3. Enterocyte. Shortening and fragmentation of microvilli of brush border. Disturbance of internal structure of mitochondria: translucency of their matrix and fragmentation of cristae (1 day after operation). Electron micrograph, 4200×.

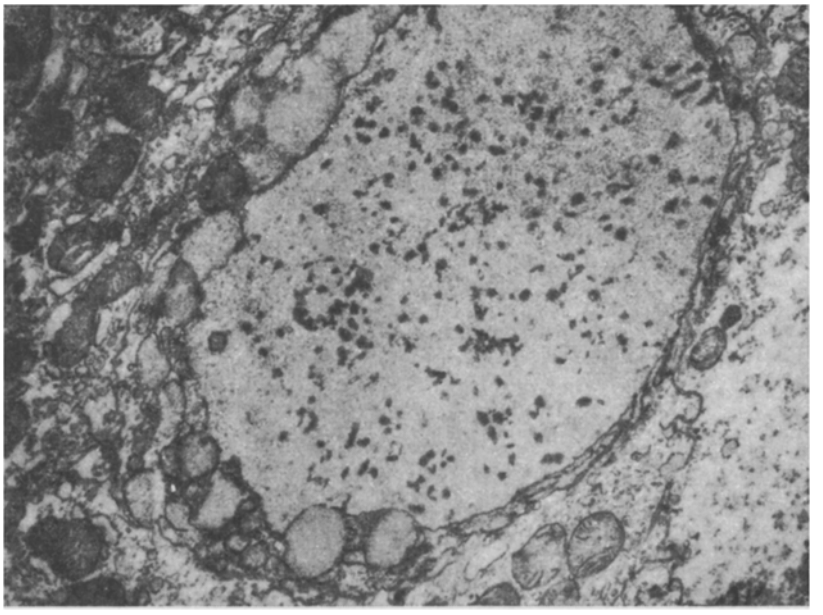

Fig. 4. Goblet cell. Marked homogenization of accumulation of secretion (1 day after operation). Electron micrograph, 5500 ×.

reticulum, disturbance of the architecture of the lamellar complex and dilatation of its cisterns and vesicles, and the appearance of lysosome-like and multivesicular bodies and autophagous vacuoles in the cytoplasm and complete autolysis of individual cells. In some mitochondria focal (or diffuse) translucency, fragmentation, or complete destruction of the cristae was observed, whereas in others the matrix was condensed and the number of cristae increased. Specific ultrastructural changes in the enterocytes consisted of focal disturbances of regular orientation of the microvilli in the brush border and loosening (or condensation) and

vesiculation of the terminal network; the goblet cells were characterized by aprogressively more homogeneous accumulation of the secretory product. Compensatory ultrastructural changes in the enterocytes and goblet cells were manifested as an increase in the number of free ribosomes and polysomes in the cytoplasm and the appearance of large mitochondria with many densely packed cristae. The submicroscopic changes described did not affect all cells of the epithelium but were focal in character. They were most marked on the first, seventh, and 30th days after vagotomy (Figs. 3 and 4).

The results of this investigation can be summed up by saying that definite positive correlation was observed between the results obtained by light-optical and electron microscopy. For instance, the times after vagotomy when marked inflammatory changes were found with the light microscope in the jejunal mucosa (1, 7, and 30 days) coincided with the times when the electron microscope revealed considerable disturbances of ultrastructural organization of the principal cell forms of the intestinal epithelium. Parallel with subsidence of the inflammatory changes in the mucosa, the intensity of the destructive processes in its epithelial cells decreased and the relative contribution of compensatory changes in their ultrastructure increased. These observations were supported by measurement of the thickness of the epithelial layer on the villi (an important index of its morphological and functional state): The greatest decrease in thickness of the intestinal epithelium was found 1 and 30 days after vagotomy. It is interesting to compare the dynamics of the structural and ultrastructural changes in the jejunal mucosa and in the epithelial cells with changes in the number of intraepithelial lymphocytes. Their number was greatest 7 and 30 days after the operation when, as was stated above, the inflammatory changes in the mucosa and destructive changes in its epithelial cells were clearly defined. This fact can be taken as evidence of the important contribution of autoimmune reactions (especially of the system of cellular immunity) to the development of the neurodegenerative changes in the small intestine. The increase in number of goblet cells observed 14, 19, 30, and 120 days after vagotomy was perhaps a manifestation of the compensatory reaction of the intestinal epithelium, aimed at intensifying mucous production and so protecting the inner surface of the jejunum when in a "weakened" (because of its disturbed innervation) state against the action of aggressive factors in the chyme.

Comparison of the results of this morphological analysis of the jejunal mucosa after vagotomy and the results of investigations of the morphology of this organ after other types of denervation (central denervation [8]) reveals their evident similarity. It can accordingly be concluded that the combination of structural changes in the jejunum described above is not specific for vagotomy. In addition, morphological changes very similar in character have been found in the small intestine in many other pathological states: in cholera [16], acute dysentery [20], enterocolitis and salmonelliasis [1], virus hepatitis [19], nontropical sprue [18], and after partial resection of the small intestine [12]; it can therefore be concluded that this combination of structural changes is not in general specific for denervation. Finally, its similarity to morphological changes arising in certain organs after exposure to factors of widely different nature (the liver to toxic agents [2, 3], the pancreas to extremal influences [6], the heart [10] and the kidney [5] to increased functional loads) indicates that this particular combination of structural changes in the small intestine is likewise not organ-specific.

LITERATURE CITED

1. A. F. Blyuger, Kh. M. Veksler, I. N. Novitskii, et al., Biopsy of the Small Intestine in Acute Intestinal Infections [in Russian], Riga (1973).
2. V. M. Blesler, N. A. Chernogryadskaya, E. M. Pil'shchik, et al., Normal and Pathological Cytology of the Liver Parenchyma [in Russian], Leningrad (1969).
3. Yu. K. Eletskii, "Morphological and metabolic changes developing in the liver in acute alcoholic poisoning," Doctoral Dissertation, Moscow (1970).
4. O. M. Zorina, in: Regulation of Morphogenesis and Regeneration of the Digestive Glands [in Russian], Leningrad (1974), pp. 54-55.
5. K. A. Zufarov, V. M. Gontmakher, S. D. Yuldashev, et al., in: Proceedings of the Sixth Conference on Results of Recent Research into Regeneration and Cell Division [in Russian], Moscow (1971), pp. 58-60.
6. Yu. N. Kopaev, "The effect of some extremal factors on the functional histology of the digestive system (experimental investigation)," Doctoral Dissertation, Moscow (1969).
7. V. A. Kotel'nikov, in: The Surgical Treatment of Diseases of the Abdominal Organs [in Russian], Sverdlovsk (1966), pp. 17-24.
8. V. P. Kulik and A. N. Maksimenkova, Function and Morphology of the Transplanted Intestine [in Russian], Moscow (1974).
9. L. I. Omel'yanenko, Abstracts of Proceedings of the Second Conference on Regeneration and Cell Multiplication [in Russian], Moscow (1960), pp. 9-15.

10. D. S. Sarkisov and B. V. Vtyurin, Electron Microscopy of Destructive and Regenerative Intracellular Processes [in Russian], Moscow (1967).
11. A. B. Stroganova, "Regeneration of the exocrine part of the pancreas under normal conditions and after subdiaphragmatic vagotomy," Candidate's Dissertation, Moscow (1972).
12. É. A. Tursunov, "Morphological and functional changes in the small intestine after resection of its proximal part," Candidate's Dissertation, Tashkent (1972).
13. W. Ballinger, J. Jida, J. Aponte, et al., Surg. Gynec. Obstet., 118, 1305 (1964).
14. J. Bejar, S. Broitman, and N. Zamchek, Gut, 9, 164 (1968).
15. R. Elliott, W. Barnett, et al., Surg. Gynec. Obstet., 124, 1037 (1967).
16. H. C. Chen, V. Reyes, and J. Fresh, Virchows Arch. Abt. B, Zellpath., 7, 236 (1971).
17. A. Halaris, Europ. Surg. Res., 3, 13 (1971).
18. Z. Lojda, in: Intestinal Absorption, Vol. 4a, London (1974), pp. 43-122.
19. C. Meitens and A. Vogel, Dtsch. med. Wschr., 95, 950 (1970).
20. A. Takeushi, Am. J. Path., 47, 1011 (1965).