ULTRASTRUCTURAL CHARACTERISTICS OF GASTRIC ENDOCRINE AND GLANDULAR CELLS

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In the last two decades the endocrine apparatus of the gastrointestinal tract has been intensively studied. By electron-microscopic and immunocytochemical methods more than 10 varieties of endocrine cells (EC) have been identified and international classifications have been worked out [11]. Many investigations have been devoted to the study of EC of the digestive system in many vertebrates and man under normal and in various pathological states.

This paper describes the ultrastructural characteristics of intercellular relations of EC and the glandular cells of the human stomach.

EXPERIMENTAL METHOD

Material from the mucosa of the fundal and pyloric parts of the stomach was taken with a fiberoptic gastroscope, or during gastrectomy on patients with gastric or duodenal ulcer. Pieces of mucosa for light microscopy were fixed in a 10% solution of neutral formalin by Lillie's method. The morphologic picture of the gastric mucosa was assessed in sections stained with hematoxylin and eosin. EC were demonstrated by the Grimelius and Masson–Hamperl methods. Pieces of mucosa for electron-microscopic study were fixed in 2.5% glutaraldehyde solution and then postfixed in 1% buffered OsO_4 solution. After dehydration in alcohols of increasing strength the tissue was embedded in Araldite. Sections 30-40 nm thick were cut on an LKB-4800 Ultrotome, stained with uranyl acetate and lead citrate, and examined in JEM-100B and JEM-100S electron microscopes.

EXPERIMENTAL RESULTS

The study of biopsy material of unchanged gastric mucosa from a patient with peptic ulcer showed that EC are located in the epithelial layer. They are easily distinguishable electron-microscopically because of the presence of specific secretory granules, distributed basally, and of a paler hyaloplasm than that of other glandular cells. The ultrastructural characteristics of different types of EC were described by the writers previously [1-3], and for that reason only facts relating to connections between EC and neighboring glandular cells and to the character of functioning of EC will be described in this paper, without any particular attention to their varieties.

EC are of uncovered and covered types (Fig. 1). Cells of the uncovered type, located on the basement membrane between neighboring cells, have a narrow apical part which reaches up to the lumen of the stomach. These cells have well-marked apical-basal differentation. The view is held that cells of the uncovered type are sensory receptor cells [4, 5, 7]. EC of the covered type, their arrangement, and their relations to neighboring cells and the basement membrane have received less study.

The special staining methods of Grimelius and Masson–Hamperl showed that EC possess processes which leave the cell body and run for a considerable distance (Fig. 2a), but it was virtually impossible to trace the course and topography of the processes of EC and their relations with neighboring cells and the basement membrane. An electron-microscopic study

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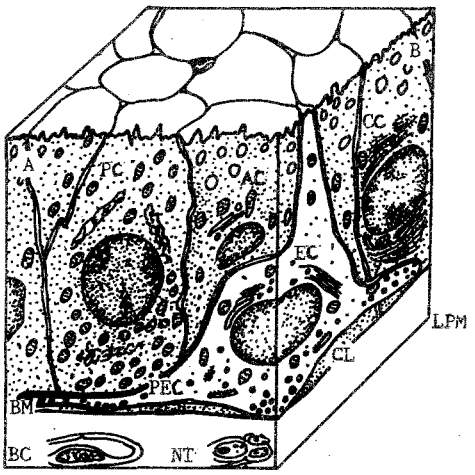

Fig. 1. Diagram showing arragnement of uncovered (plane A) and covered (plane B) types of EC in human gastric mucosa. PC) Parietal cell; CC) chief cell; AC) accessory cell; PEC) process of endocrine cell; CL) cytoplasmic lamina; BM) basement membrane; SG) secretory granule; LPM) lamina propria of mucosa; BC) blood capillary; NT) nerve terminal.

of EC of the covered type showed that quite often they are not found between epithelial cells, but they are discovered (in 33% of cases) beneath one glandular cell [10], located on the general basement membrane. EC may be covered by parietal, chief, or accessory cells (Fig. 2, b-d). It must be pointed out that the body of EC is not always entirely on the basement membrane and does not always have a function with it. Often in the space between the cell body and the basement membrane there is a thin lamina of cytoplasm of a neighboring glandular cell. The edges of the cytoplasmic lamina, which penetrates beneath EC from both sides, may not meet, or they may meet, or even overlap each other (Fig. 2b, c; Fig. 3a, b). This relationship of EC to the basement membrane and the presence of cytoplasmic laminae between them evidently subserve a definite function. The presence or absence of cytoplasmic laminae reduces or increases the area of contact between cells and the basement membrane. We know, moreover, that it is the basal surface of EC that is secretory. Consequently, it must be assumed that these cytoplasmic laminae are regulators of EC secretion of a unique kind. This view is supported also by the fact that it is in the region of direct contact of the plasma membrane with the basement membrane that is a major location of secretory granules (Fig. 2d), and the site of their outflow through the plasma membrane by exocytosis (Fig. 3c). This mechanism of secretion is characteristic of EC [7, 9]. The processes of EC have a quite complicated arrangement, for they penetrate between cells, in the intercellular space at the base of the cell, and lie on the basement membrane or touch it (Fig. 3d), but frequently on moving away from the basement membrane, they penetrate into the intercellular space for a considerable distance from it. Often the processes of EC run along the basement membrane and are covered by the body of one glandular cell (Fig. 3e), but sometimes the cytoplasm of the glandular cell envelope the process of an endocrine cell. We also found cases of invagination of a process of EC into the body of a parietal cell (Fig. 2e). Such close contact of the processes of EC with several glandular cells is evidently essential for paracrine and endocrine regulation of the activity of a group of neighboring glandular cells. Despite their considerable length, the processes of EC nearly always contain many secretory granules (Fig. 3d, e). The mechanism of secretion of the processes of EC remains unclear. A study of more than 200 electron micrographs of EC did not reveal a single case of extrusion of secretion from the processes of EC by a mechanism of exocytosis. Of course, the stage of outflow of the secretory product accounts for only a short time in the secretory cycle, and for that reason it cannot always be detected, or it has to be assumed that a diffuse mechanism of secretion, with preliminary dissolving of the granules in the cytoplasm, is observed

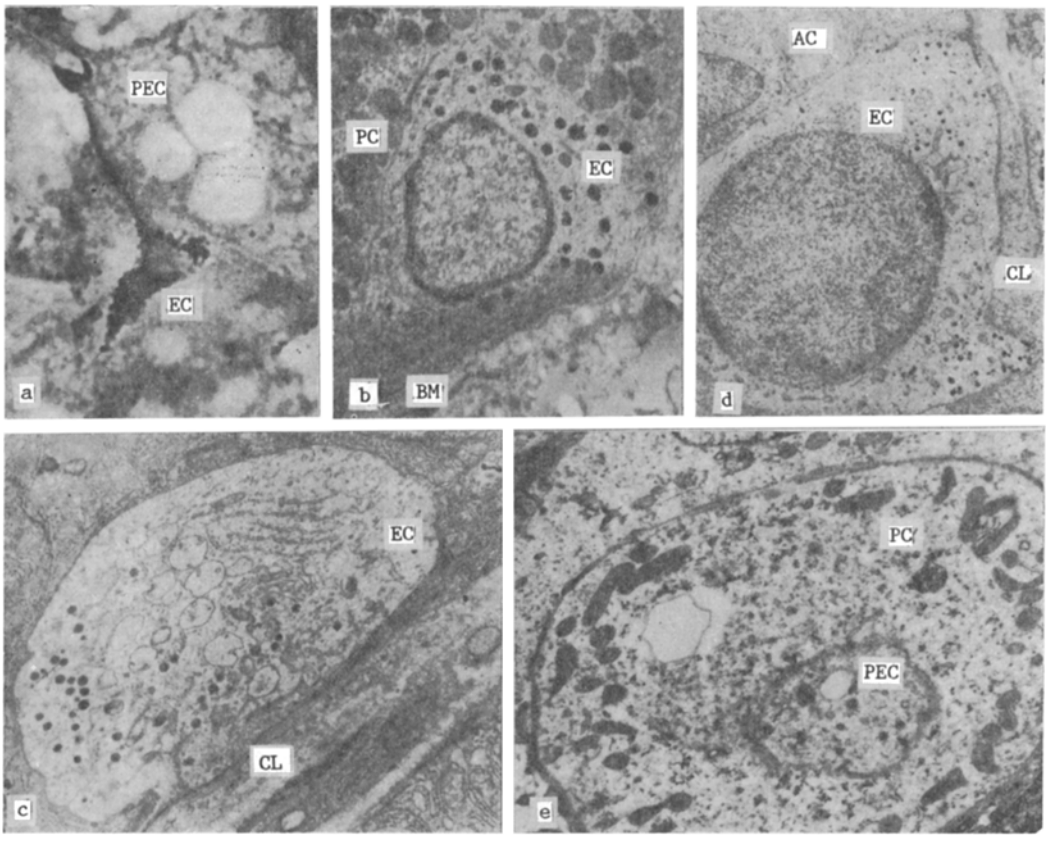

Fig. 2. Structure of gastric EC. a) Branched EC. Fundal part of stomach of a patient with ulcer, from unchanged mucosa. Grimelius' stain. 600 ×; b) endocrine EC cell located on basement membrane beneath a parietal cell. Gastric fundus of a patient with ulcer 1 year after circular astrotomy. 10,000 ×; c) Endocrine D_1 cell covered by a chief cell and separated from basement membrane by cytoplasmic lamina. Gastric fundus of a patient with duodenal ulcer. 12,500 ×; d) higher concentration of secretory granules in region of contact of endocrine EC cell with basement membrane. Pyloric part of stomach of a patient with gastric ulcer. 6800 ×; e) invaginated process of EC in cytoplasm of parietal cell. Fundal gland in stump of stomach 6 years after resection. 8000 ×.

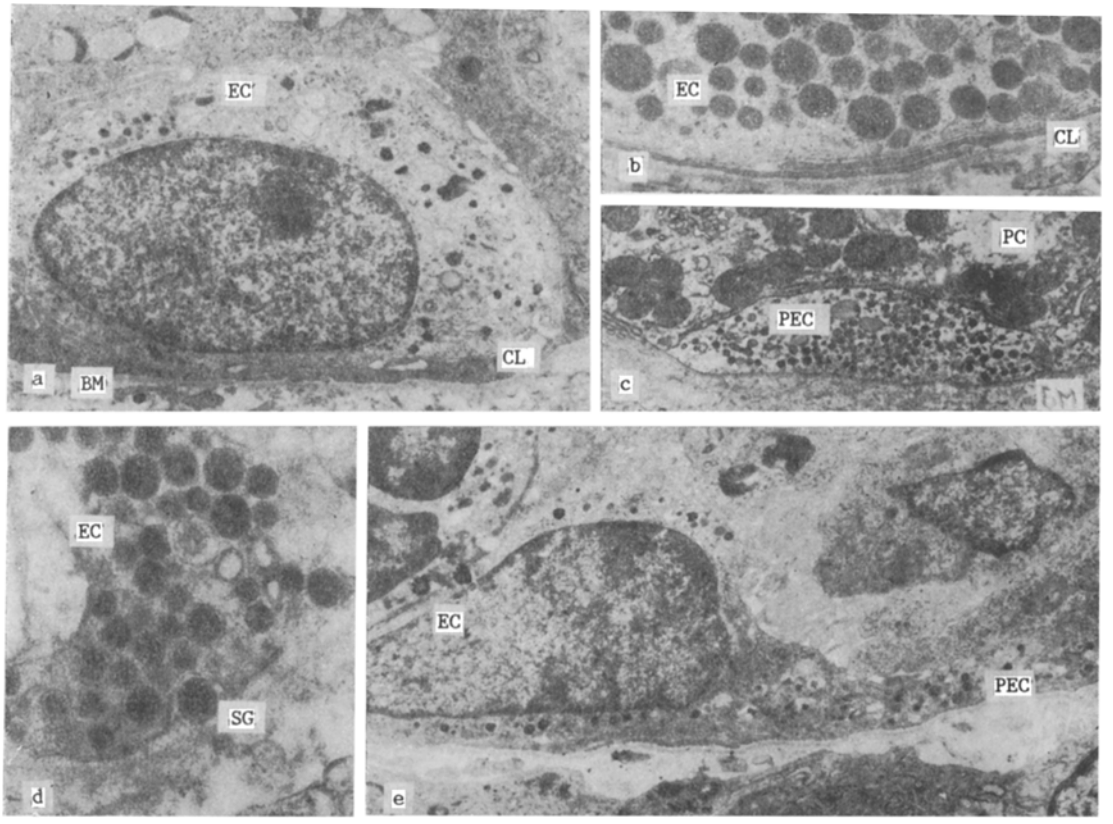

Fig. 3. Changes in ultrastructure of gastric EC. a) Cytoplasmic laminae between endocrine ECL cell and basement membrane. Fundal part of stomach 1.5 years after selective proximal vagotomy. 12,000 ×; b) basal part of endocrine D cell, cytoplasmic laminae of neighboring cells overlap each other. Fundal part of stomach 1.5 years after selective proximal vagotomy. 26,000 ×; c) basal part of endocrine A_1 cell, release of secretory granule by a mechanism of exocytosis. Fundal part of stomach of a patient with duodenal ulcer. 46,000 ×; d) secretory granules in body and process of endocrine ECL cell. Fundal part of stomach 1.5 years after selective proximal vagotomy. 8000 ×; e) process of EC located on basement membrane and covered by parietal cell. Fundal part of stomach of a patient with duodenal ulcer. 8800 ×.

in processes that are not in contact with the basement membrane [6]. Immunohistochemical investigations [8] have revealed long cytoplasmic processes in EC, running in all directions and maintaining connections between EC as well as between glandular cells. On the basis of these facts the authors cited consider that EC can be responsible for the functional synchronization of neighboring fundal glands.

The EC of the stomach and their processes thus form intimate and unique connections with the surrounding glandular cells and basement membrane, and this is the structural basis of the complex endocrine and paracrine regulartory functions of cells of the endocrine apparatus of the gastrointestinal tract.

LITERATURE CITED

1. K. A. Zufarov, K. I. Rasulev, and Sh. R. Zhuraev, Fiziol. Zh. SSSR, No. 9, 1229 (1978).
2. K. A. Zufarov, and K. I. Rasulev, Folia Morphol. (Prague), 31, 230 (1983).
3. K. A. Zufarov, K. I. Rasulev, and Sh. R. Zhuraev, Klin. Med., No. 10, 92 (1983).
4. E. Solcia, C. Capella, R. Buffa, et al., in: Gastrointestinal Hormones, ed. by G. B. J. Glass, Raven Press, New York (1980).
5. V. V. Yaglov and G. A. Lomonosova, Usp. Sovrem. Biol., 99, No. 2, 264 (1985).
6. W. Forssmann and L. Orsi, Z. Zellforsch., 101, 419 (1969).
7. T. Fujita and S. Kobayashi, Gut Hormones, Edinburgh (1978), p. 414.

8. H. Inokuchi, W. Kawai, Y. Takeuchi, and J. Sano, Cell Tissue Res., 235, 703 (1984).
9. S. Kobayashi and T. Fujita, Gastro-Entero-Pancreatic Endocrine System, Tokyo (1974), p. 49.
10. W. Rubin, J. Cell Biol., 52, 219 (1972).
11. E. Solcia, J. M. Polak, A. G. Pearse, et al., Gut Hormones, Edinburgh (1978), p. 40.