ULTRASTRUCTURE OF THE PARIETAL CELLS OF THE STOMACH AND THEIR FUNCTIONAL ACTIVITY

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Submicroscopic changes in the parietal cells of the fundal portion of the stomach were compared with the results of measurement of the intragastric pH by direct vision in the same areas of the mucous membrane in 18 patients admitted to hospital for treatment in the remedial dietetic department. After brief (36 h) starvation, when the pH of the mucous membrane was indistinguishable from normal, no changes were found in the ultrastructure of the parietal cells. With an increase in the duration of starvation the gastric secretion gradually became alkaline and the pH of the stomach wall changed from 2.02 after 3 days of starvation to 4.8-5.0 after 20-30 days of starvation. Corresponding changes took place in the ultrastructure of the parietal cells: the tubulovesicles became flattened and subsequently disappeared, the lumen of the intracellular tubules diminished, and the microvilli were shortened. The results of comparison of the submicroscopic changes with the pH measurements indicate that submicroscopic changes of this type correspond to depression of functional activity of the parietal cells.

Key words: parietal cells of the stomach; intragastric pH measurement; remedial starvation.

Numerous investigations of morphological changes in the parietal cells of the gastric epithelium during stimulation by various substances have recently been published [2, 3, 7, 8]. Comparison of the ultrastructure of the parietal cells before and after stimulation has enabled submicroscopic criteria of their functional activity to be defined. However, the ultrastructure of the parietal cells has not yet been studied during a period of depression of gastric secretory activity. There are only isolated reports [5] of investigations of the action of atropine sulfate on the ultrastructure of the parietal cells.

In all the investigations cited above the acid-forming function of the parietal cells was judged on the basis of tests of the secretion liberated into the lumen of the stomach. No attention was paid to so important a factor as the heterogeneity of the secretory activity of the mucous membrane. The submicroscopic structure of the cells and the functional state of this part of the gastric mucosa have not been studied, although knowledge of the activity of the metabolic and secretory processes in pieces of tissue taken for investigation would lead to more reliable morpho-functional correlations.

The object of this investigation was to compare ultrastructural changes in the parietal cells of the gastric mucosa with changes in pH of the same parts of the stomach wall during inhibition of secretory activity observed in the course of prolonged remedial starvation.

EXPERIMENTAL METHOD

This paper gives the results of a combined study of the mucous membrane of the gastric fundus in 18 patients admitted to hospital for treatment in the department of remedial dietetics of the Research Institute of Psychiatry at various stages during starvation (from 36 h to 30 days).

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Gastroscopic investigations and gastric biopsy were carried out on these patients to determine the risk of the method of treatment by prolonged starvation, for according to experimental data [1, 4, 6], food deprivation is accompanied by considerable damage to the gastric mucosa amounting in some cases to the formation of erosions and ulcers.

During endoscopic investigation with the Olympus GFK gastrofibroscope the pH of the stomach wall over an area of under 5 mm^2 was measured under visual control with a miniature antimony pH-detector introduced through the biopsy channel of the gastroscope. This area of the mucous membrane was then removed by the biopsy probe for morphological examination. The biopsy tissue specimens thus obtained were treated by the standard method adopted in the writers' laboratory. Ultrathin sections were examined in the UÉMV-100V and IEM-100V electron microscopes.

The results of the electron-microscopic investigation were subjected to morphometric analysis with the object of measuring the area occupied by the secretory structures of the parietal cells (the tubulovesicles and intracellular tubules). The measurements were made by means of a control system (grid) with 100 control dots. The area of the secretory structures was expressed as a percentage of the total area of the parietal cell.

EXPERIMENTAL RESULTS

Brief starvation for 36 h produced no appreciable changes either in the ultrastructure of the parietal cells or in the pH of the stomach wall. However, by the third day of starvation evidence of reduced functional activity appeared in the submicroscopic picture of the parietal cells. The lumen of the intracellular tubules was reduced, their microvilli were short, and many tubulovesicles could be seen both in the body of the cell and in its apical part (Fig. 1a). This state of the cells, in Sedar's opinion [8], is the resting state. However, during this period the total area occupied by secretory membranes was reduced almost by half (Fig. 2), from 22.8% under normal conditions to 12.3% on the third day of starvation. The pH of the stomach wall altered from the normal level of 0.85-1.5 (mean 1.0) to 2.02. At the same time the number of cristae in the mitochondria of the parietal cells fell by 20-25%.

On the 5th-8th day of starvation changes were found in the ultrastructure of the tubulovesicles – the organelles containing precursors of hydrochloric acid. They became shrunken as if they had lost their contents. The volume of the tubulovesicles themselves was only 27% of their usual volume, and the area occupied by secretory structures in the cell fell to 5.8%. Very few microvilli were seen on the surface of the cells facing the lumen of the glands (Fig. 1b). Against the background of these few signs of depression of parietal cell function a considerable shift in the pH of the mucous membrane to the alkaline side (pH 3.17) was observed.

On the 10th day the area occupied by secretory membranes fell to 4%. At this time cells were seen with no microvilli on the apical surface and with even fewer tubulovesicles, which had now collapsed.

At the later stages of remedial starvation (20-30 days) the ultrastructure of nearly all the parietal cells was characterized by intracellular tubules with very short microvilli (Fig. 1c) and by the almost total absence of tubulovesicles around them. Meanwhile the area of the cell occupied by secretory membranes was only 3.5% and the pH was shifted even further toward the alkaline side, to reach values (4.8-5.0) at which pepsinogen was no longer activated or converted into pepsin. In this period the number of cristae in the mitochondria of the parietal cells was reduced almost by half.

The state of the cell structures connected with secretory processes and also the pH of the stomach wall linked with them probably depend on the quantity of energy produced in the cell. A decrease in the number of cristae observed during starvation leads to a decrease in the quantity of high-energy phosphates formed in the mitochondria. The decrease in the energy reserves of the cell leads to depression of the functional activity of the parietal cells. The processes of transport and concentration of chlorides from the blood plasma (against the steep electrochemical gradient) into the parietal cell and from it into the lumen of the stomach are inhibited. The area occupied by the secretory membranes was considerably reduced by the 3rd-5th day. There is some disagreement here with the observations of Sedar [8] and Helander and Hirschowitz [3], according to whom the decrease in the number of tubulovesicles is evidence of high functional activity of the parietal cells and the discharge of secretion products into the lumen of the glands.

It was discovered in the course of the investigation that in the early stages of remedial starvation a process of fatty degeneration began to develop in the cytoplasm of the parietal cells. This was reflected in the appearance of large foci of local breakdown of the cytoplasm (cytosegresomes) in the cells. These

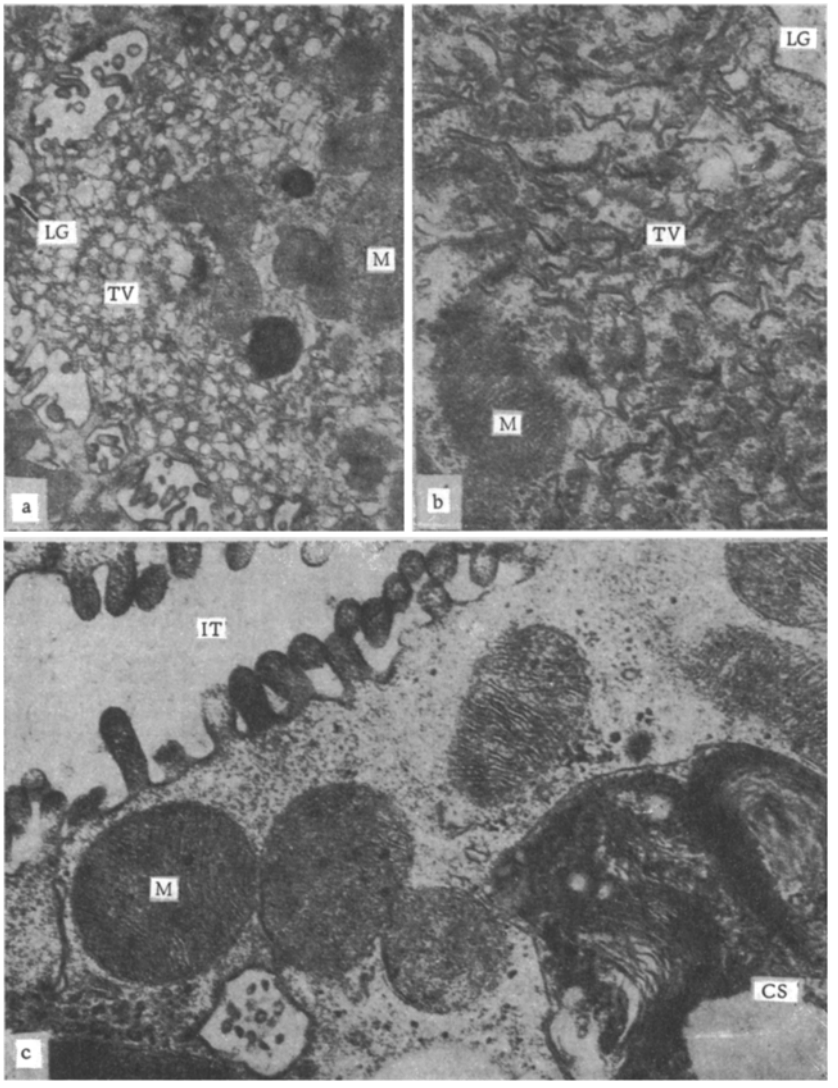

Fig. 1. Parietal cells of gastric mucosa at various stages of remedial starvation: a) 3rd day of starvation: numerous tubulovesicles in apical part (8000×); b) 5th day of starvation: changes in ultrastructure of tubulovesicles (10,000×); c) 28th day of starvation: absence of tubulovesicles near intracellular tubule, shortening of microvilli (17,000×). N) nucleus; M) mitochondria; IT) intracellular tubule; LG) lumen of gland; LD) lipid droplets; MF) myelin figures; TV) tubulovesicles; CS) cytosegresomes.

structures, evidently autophagic vacuoles, contained not only drops of neutral lipids but also myelin lamellae and lipofuscin deposits. In Pfeiffer's opinion [6], during starvation autophagic vacuoles digest products of cell metabolism into simpler chemical compounds for reutilization by the cell. However, the components observed in the cytosegresomes in the present experiments (myelin lamellae, lipofuscin) were resistant to the action of the lysosomal enzymes and formed "residual bodies." In the late stages of remedial starvation the degenerative process affected most of the parietal cells of the gastric mucosa (as well as other cells). Meanwhile solitary cells with no evidence of fatty degeneration were seen in a wide range of functional states.

It can be concluded from these observations that the decrease in secretion of hydrochloric acid in the early stages of remedial starvation is the result of the absence of food stimulation. During the development of adaptation and the appearance of spontaneous secretion, the gradual alkalification of the stomach wall can evidently be explained by the development of fatty degeneration in the parietal cells and a consequent depression of their functional activity.

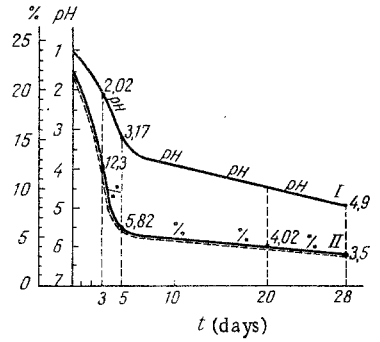

Fig. 2. Change in pH of stomach wall (I) and in area of secretory membranes of parietal cells (II) depending on duration of remedial starvation. Abscissa, time (in days); ordinate, area of tubulovesicles and of intracellular tubules (as % of total area of cell) and pH of stomach wall.

By a combination of electron-microscopic investigation of the parietal cells of the stomach with morphometric analysis with the results of intragastric measurement of pH in the same part of the stomach tissue under direct vision it is thus possible to describe the dynamics of submicroscopic changes in these cells during the gradual depression of their secretory activity.

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