As already stated, by the end of the experiment the number of nerve terminals containing only synapse-like vesicles in the median eminence was increased. If these vesicles are carriers of acetylcholine, this suggests that cholinergic control over pituitary functions by the hypothalamus is intensified in this period. Acetylcholine, which does not act directly on hormonopoiesis in the pituitary cells, is known to facilitate the forced liberation of hypothalamic hormones into capillaries of the median eminence [3]. This fact explains to some degree activation of the liberation of the contents of the secretory granules from the nerve terminals of the median eminence observed 12 and 18 months after injection of ^{75}Se-selenomethionine.

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ULTRACYTOCHEMICAL STUDY OF OXIDOREDUCTASES IN PARIETAL CELLS OF THE GASTRIC MUCOSA IN GASTRIC CARCINOMA

A. G. Perevoshchikov, I. B. Bukhvalov, É. A. Mikhailov, and N. T. Raikhlin

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The parietal cells of the stomach produce hydrochloric acid. The acid-forming function is often disturbed in some pathological processes in the stomach (chronic gastritis, carcinoma). However, the mechanism of this phenomenon is not yet fully explained.

Biochemical investigations [1, 2, 4-7] have shown that a large quantity of energy is required in order to secrete hydrochloric acid. The main source of this energy is the numerous mitochondria present in the parietal cells. Pokrovskii et al. [4] state that the most powerful substrate for the mitochondrial respiratory chain in the parietal cells is succinate, whereas Gapparov [1] also found a sharp increase in cytochrome oxidase activity in the mitochondria of these cells.

To discover the possible causes of the disturbance of hydrochloric acid secretion in gastric carcinoma an ultracytochemical study was undertaken of succinate hydrogenase (SDH), cytochrome oxidase (CCO), and NADH-dehydrogenase (NADH-DH) activity in the parietal cells of the mucosa of the normal stomach and of the stomach of patients with gastric carcinoma, whose gastric juice was found to have persistently reduced secretion of hydrochloric acid or even achlorhydria.

EXPERIMENTAL METHOD

Biopsy material taken for diagnostic purposes from the gastric mucosa of two groups of subjects was investigated. Group 1 consisted of seven persons with normal acidity of their gastric juice, and with no evident tumor in their stomach; group 2 consisted of five patients with gastric carcinoma accompanied by re-

Laboratory of Histochemistry and Electron Microscopy, Department of Pathological Anatomy of Human Tumors, and Department of Endoscopy, All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Kraevskii.)

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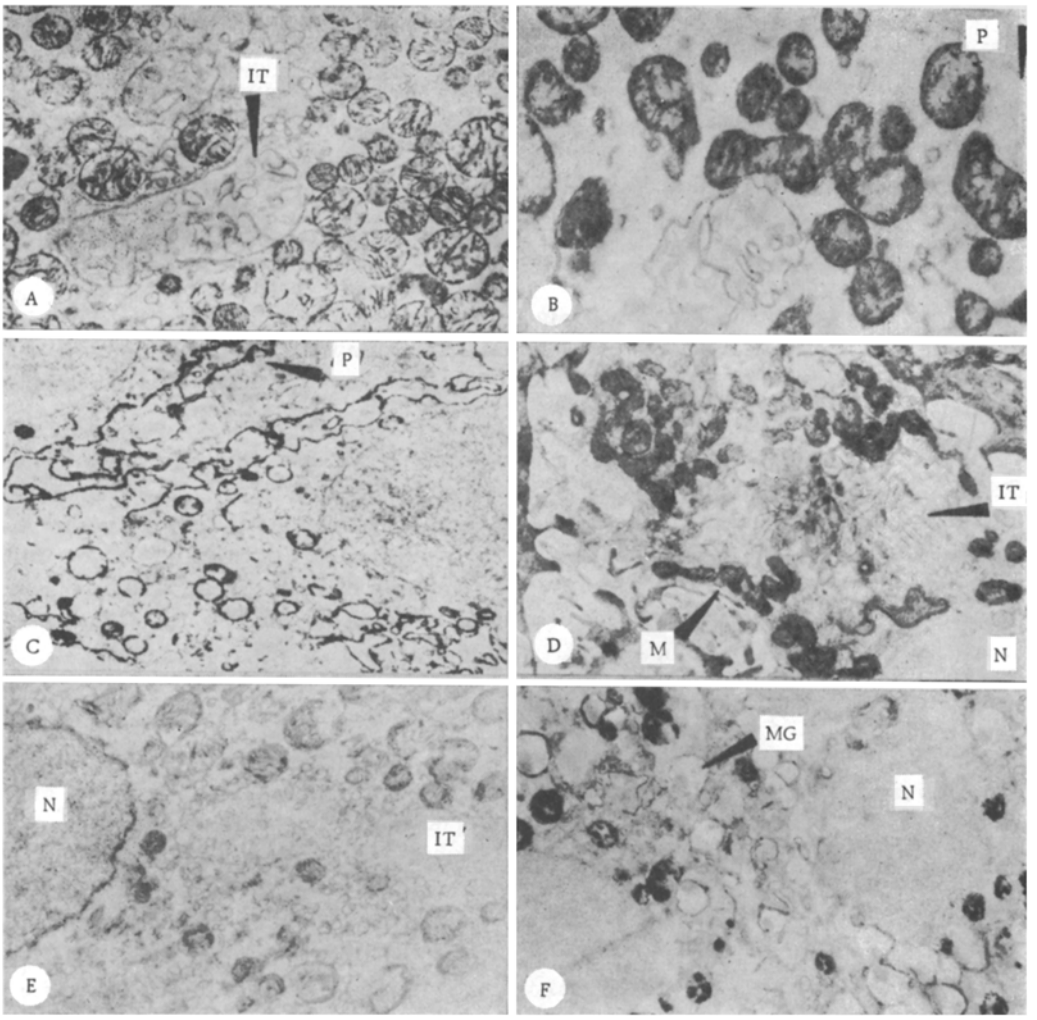

Fig. 1. Oxidoreductases in parietal cells of normal gastric mucosa (a-c), and also in parietal (d, e) and accessory (f) cells of mucosa in gastric carcinoma. a) CCO: reaction product located both in outer membrane and in cristae of mitochondria, 5000×; b) SDH: reaction product associated with mitochondrial membrane formations and crystalline in form, 10,000×; c) NADH-DH: reaction product localized both in mitochondria and in plasmalemma of cells, 5000×; d) CCO: absence of enzyme activity in mitochondria of parietal cell from region of mucosa remote from tumor, 6600×; e) SDH: cristae of many mitochondria appear electron-dense, reduced in places, no reaction product in them or on outer mitochondrial membrane, 5000×; f) high SDH activity in mitochondria of accessory cell located some distance away from tumor: cell contains characteristic mucoid granules, diffuse distribution of reaction product in chromatin of nuclei, 5000×. Sections in a-f not stained. N) Nucleus, IT) intracellular tubule, M) mitochondrion, P) plasmalemma, MG) mucoid granules.

duced acidity of the gastric juice or achlorhydria. Material from patients of group 2 was taken from the mucosa at a distance from the tumor. The enzymes SDH, NADH-DH, and CCO were demonstrated ultracytochemically.

Pieces of gastric mucosa, immediately after removal and without prefixation, were washed in 0.25 M sucrose with 3 mM magnesium acetate for 15 min, and cut into cubes measuring less than 1 mm^3 in the cold in a drop of the same solution. They were then quickly transferred for the histochemical reaction to incubation medium made up when required. The composition of the incubation media and subsequent processing of the pieces of tissue were as described previously: for SDH in [9], for NADH-DH in [8], and for CCO in [10]. After the histochemical reactions the pieces were dehydrated and embedded in Epon-812. Semithin sections 3-5 μm thick were cut from all the blocks, and, by means of a special M-90 microscope and TM-60 trimmer (from

Reichert, Austria), the blocks were trimmed away around the parietal cells. Ultrathin sections were cut on the LKB-III Ultrotome (Sweden) and examined in the JEM-100C (Japan) electron microscope. Specificity of the histochemical reactions for oxidoreductases was verified by incubating the pieces of tissue in medium without substrate, and also with inhibitors: for CCO with the addition of 0.01M sodium cyanide to the incubation medium, for SDH with 36 mM sodium malonate, and for NADH-DH, by inactivation by fixation in 4% formaldehyde for 30 min at 22°C. All controls were negative, indicating the specificity of these methods of determination of oxidoreductases.

EXPERIMENTAL RESULTS

When the parietal cells of the mucosa of the normal stomach from persons with normal acidity of their gastric juice were studied, the product of the ultracytochemical reaction for SDH and CCO was localized entirely in the mitochondria of these cells. NADH-DH activity was found both in the mitochondria and in the plasmalemma of the parietal cells.

The distribution of the reaction product in the mitochondria for the above-mentioned oxidoreductases differed in certain respects. For instance, CCO activity was associated with mitochondrial membranes and was uniformly distributed both in the outer membrane and in the cristae (Fig. 1a); no reaction product could be detected in the matrix. The product of the reaction for SDH had a similar distribution to that for CCO but it was crystalline in form (Fig. 1b). NADH-DH activity in swollen mitochondria was found on the outer membrane of these organelles. However, in individual mitochondria in which the cristae were intact the reaction product was found as well. The plasmalemma of the parietal cells also possessed NADH-DH activity (Fig. 1c). A diffuse distribution of the reaction product for this enzyme was found in the karyoplasm of some cells.

The study of SDH activity showed that in individual parietal cells of the normal mucosa the reaction product was associated with membranes of intracellular tubules, tubulovesicles, plasmalemma, and nucleolemma. In some cases it was diffusely distributed in the cytoplasm or in the nuclear chromatin. In such cases it was not present, or was present only in traces, in the mitochondria of these cells. The possibility cannot be ruled out that this distribution of the product of the reaction for SDH in the parietal cells was caused by diffusion of the enzyme from the mitochondria.

The ultracytochemical study of the above-mentioned oxidoreductases in the parietal cells of the mucosa at a distance from the tumor in patients with gastric carcinoma with reduced activity of the gastric juice, or even with achlorhydria, thus revealed a marked decrease in their activity.

CCO activity in the mitochondria of some parietal cells was completely absent (Fig. 1d), and in others it was present only in traces. The product of the reaction for CCO in the mitochondria of these cells, by contrast with normally functioning cells, was associated mainly with the outer membrane and was irregularly distributed. Clearing of the matrix and reduction of the cristae also were observed in the mitochondria. In some parietal cells the mitochondria were of the usual structure, but trace activity of cytochrome oxidase also was observed in them, both in the outer membrane and in the cristae. In rare cases single parietal cells with well-marked activity of this enzyme in their mitochondria were found.

SDH activity was absent in some parietal cells (Fig. 1e), and in others it was considerably weakened or was redistributed inside the mitochondria. The product of the reaction for SDH in this case was associated entirely with the outer membrane of the mitochondria and none was present in the cristae. Occasionally parietal cells preserving their SDH activity in the mitochondria were found. As regards NADH-DH activity in the mitochondria and plasmalemma of these cells, located at a distance from the tumor, it was practically completely absent.

In other epithelial cells located near the tumor and, in particular, in accessory cells (Fig. 1f) high activity of these enzymes was found. This fact is a unique control for the disturbance of mitochondrial function in the parietal cells in patients with gastric carcinoma and with reduced acidity of their gastric juice.

It can thus be concluded from these investigations that the decrease in hydrochloric acid secretion by the gastric mucosa observed in patients with carcinoma depends mainly on a permanent deficiency of oxidoreductases in the mitochondria of the parietal cells. Evidently the energy substrate (ATP molecules) required to supply the energy for hydrochloric acid secretion is not produced in sufficient quantity in these organelles. However, as the writers showed previously [3], ATPase activity bound with the villi of the intracellular tubules and with folds of the basal and lateral plasmalemma of the parietal cells, is preserved in gastric carcinoma.

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MORPHOFUNCTIONAL CHANGES DUE TO LITHIUM CHLORIDE IN THE RAT THYROID GLAND

V. V. Semenov, V. A. Glumova, N. M. Petrov, and V. M. Kuznetsova

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Lithium preparations are nowadays being used on an ever-increasing scale in the treatment of various diseases. Lithium was originally used in psychiatry in the treatment of manic states [4, 8], but its range of application is by no means confined to this. A number of recent investigations have demonstrated the new fact that lithium acts on the tissue complexes of the thyroid gland [3, 6], but the mechanism of this action is variously explained. Some workers [11, 12] consider that lithium prevents the accumulation of iodine and secretion of thyroid hormones, whereas others consider that lithium has a direct inhibitory action on liberation of hormones from the tissue of the gland and the elimination of thyroxine from the body [5, 10]. There is also evidence that lithium inhibits the breakdown of thyroglobulin and the stimulating effect of thyrotrophic hormone [9].

Because of the ambiguous and, in some cases, the contradictory data on the effect of lithium salts on the thyroid gland it was decided to study the dynamics of morphological and functional changes in the thyroid gland under the influence of various doses of lithium chloride. No such investigations could be found in the accessible literature.

EXPERIMENTAL METHOD

Experiments were carried out on 96 male albino rats divided into four groups: one control and three experimental groups, with 24 animals in each. Lithium chloride was given per os to the experimental rats daily for 6 weeks in the following doses: 0.5 meq/kg to group 1, 1.0 meq/kg to group 2, 2.0 meq/kg to group 3. Intravital function testing of the thyroid gland was then carried out by the radioindication method. For this purpose a subcutaneous injection of ^{131}I was given to 12 animals of each group in a dose of 740 Bq/kg body weight, and the iodine-accumulating function of the gland was tested by means of the DSU-61 apparatus 2, 4, 6, 12, 24, 48, and 72 h after injection of the isotope. After radiometry of the thyroid glands the animals were decapitated and the protein-bound ^{131}I (PBI-131), thyroid hormones (T_3 and T_4), the coefficient of effective

Department of Biology, No. 2, Department of Internal Medicine, and Department of Histology, Izhevsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.)

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