Ultrastructural Analysis and Autoradiography of the Gastric Mucosa in Chronic Gastroduodenal Ulcer

G. A. Lapii and G. I. Nepomnyashchikh

UDC 616.33/.342-018.7-02:615.83]-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 8, pp. 198-202, August, 1994
Original article submitted April 25, 1994

The mucosa of the fundal and pyloric portions of the stomach in chronic gastroduodenal ulcer is shown to exhibit structural and functional heterogeneity. Regularities of the regenerative-plastic reactions in the epithelium are revealed from the indexes of ^{3}H-uridine and ^{3}H-thymidine incorporation. Inflammatory-sclerotic changes of the gastric mucosa showed different proliferative and metabolic activity of epitheliocytes.

Key Words: *gastroduodenal ulcer; gastric mucosa; epithelial cells; ultrastructure; autoradiography*

The gastric mucosa (GM) is one of the boundary tissues of the organism, the state of which has acquired special importance under modern ecological conditions. Morphofunctional changes in the stomach in chronic pathological processes of the digestive system, notably gastroduodenal ulcer, are attracting increasing attention [1,6,9,11]. Yet despite the wealth of publications on this problem, the morphogenesis of the pathological reactions in ulcer disease has been little studied [2,4,10,12,13].

The aim of the present study was to explore, using complex morphological analysis, the structural-functional reorganizations occurring in the GM in chronic ulceration.

MATERIALS AND METHODS

We studied biopsy specimens from the fundal and pyloric portions of the stomach of 110 patients with ulcer disease (men aged 19-55). In 65 examinees the ulcers were in the stomach and in 45 patients in the duodenal bulb. For light-optic investigation paraffin sections were stained with hematoxylin and eosin in combination with Perls reaction and Van-Gieson staining, and the Schiff-iodine reaction was performed. Semithin sections of specimens embedded in Epon-Araldite were stained with azure II; ultrathin sections were contrasted with uranyl acetate and lead citrate and examined in a JEM 100B electron microscope.

Tissue fragments to be used in autoradiography were incubated in medium 199 containing one of the radioactive precursors (the concentrations of ^{3}H-uridine and ^{3}H-thymidine being 200 and 100 μCi/ml, respectively), and then routinely treated for electron microscopy. Semithin sections 1 μ were coated with photoemulsion M for nuclear investigations and exposed for 5-7 days at 4°C. The index of labeled nuclei was counted under a light microscope (×900); the results were statistically processed using Student's *t* test.

RESULTS

Light-optic examination of biopsy specimens in chronic gastroduodenal ulcer demonstrated that in all cases the GM (of the fundal and pyloric portions) was altered outside the ulcerated focus. The pattern of structural reorganizations made it possible to identify three types of lesions, which fit into the morphological picture of catarrhal, catarrhal-sclerotic, and

Laboratory of the Ultrastructural Basis of Pathology, Research Institute of Regional Pathology and Pathomorphology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk. (Presented by L. D. Sidorova, Member of the Russian Academy of Medical Sciences)

0007-4888/94/0008-0895$12.50

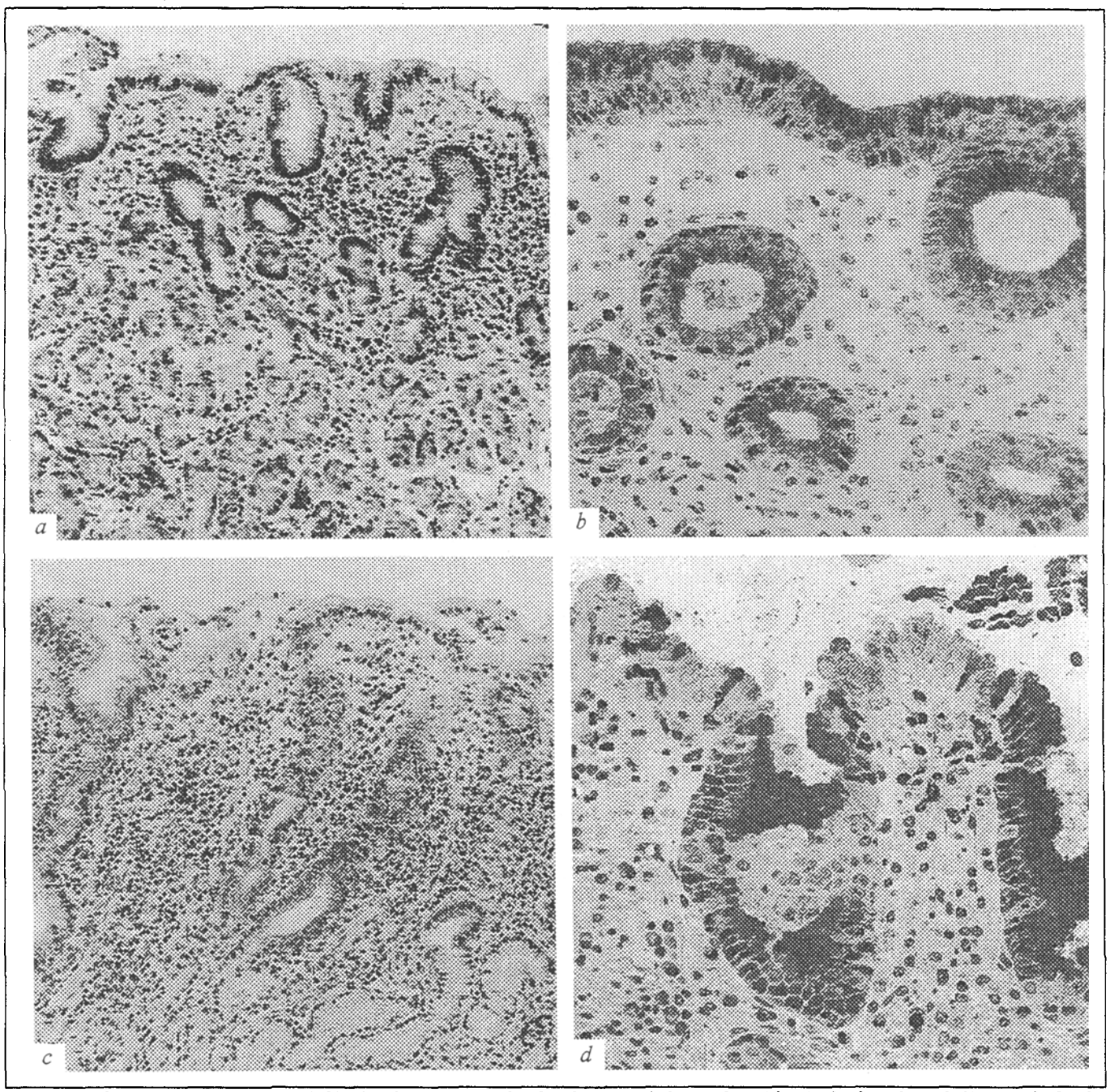

Fig. 1. Light-optic examination of GM in chronic gastroduodenal ulcer. *a*) dystrophy of luminal-foveal epithelium and glands, diffuse infiltration of lamina propria; fundal specimen, ×320. *b*) luminal-foveal epithelium with signs of active secretion; pyloric specimen, ×800. *c*) elongation of gastric pits, atrophy of glands, and thick polymorphonuclear cellular infiltration of stroma; pyloric specimen, ×320. *d*) manifest dystrophy of luminal-foveal epithelium; fundal specimen, ×800. *a* and *b*) hematoxylin-eosin staining; *c* and *d*) azure II staining.

sclerotic inflammation, and evidently represent stages of the development of a pathological process [5,7].

In chronic catarrh dystrophy of the luminal-foveal and glandular epithelium was observed, frequently attended by increased secretory activity of mucocytes. In the stroma marked vascular disorders were accompanied by a heavy polymorphonuclear cellular infiltration, which was more extensive in the interfoveal layer (Fig. 1, *a* and *b*).

In catarrhal-sclerotic inflammation dystrophy of epithelial structures increased and the gastric pits frequently became deeper and convoluted, giving the impression of an expanded foveal layer (Fig. 1, *c* and *d*). The glands were partly reduced; the gastric epithelium sometimes became transformed into intestinal epithelium. In the lamina propria of the GM, along with inflammatory changes, a tendency toward fibrous matrix hardening was observed, nota-

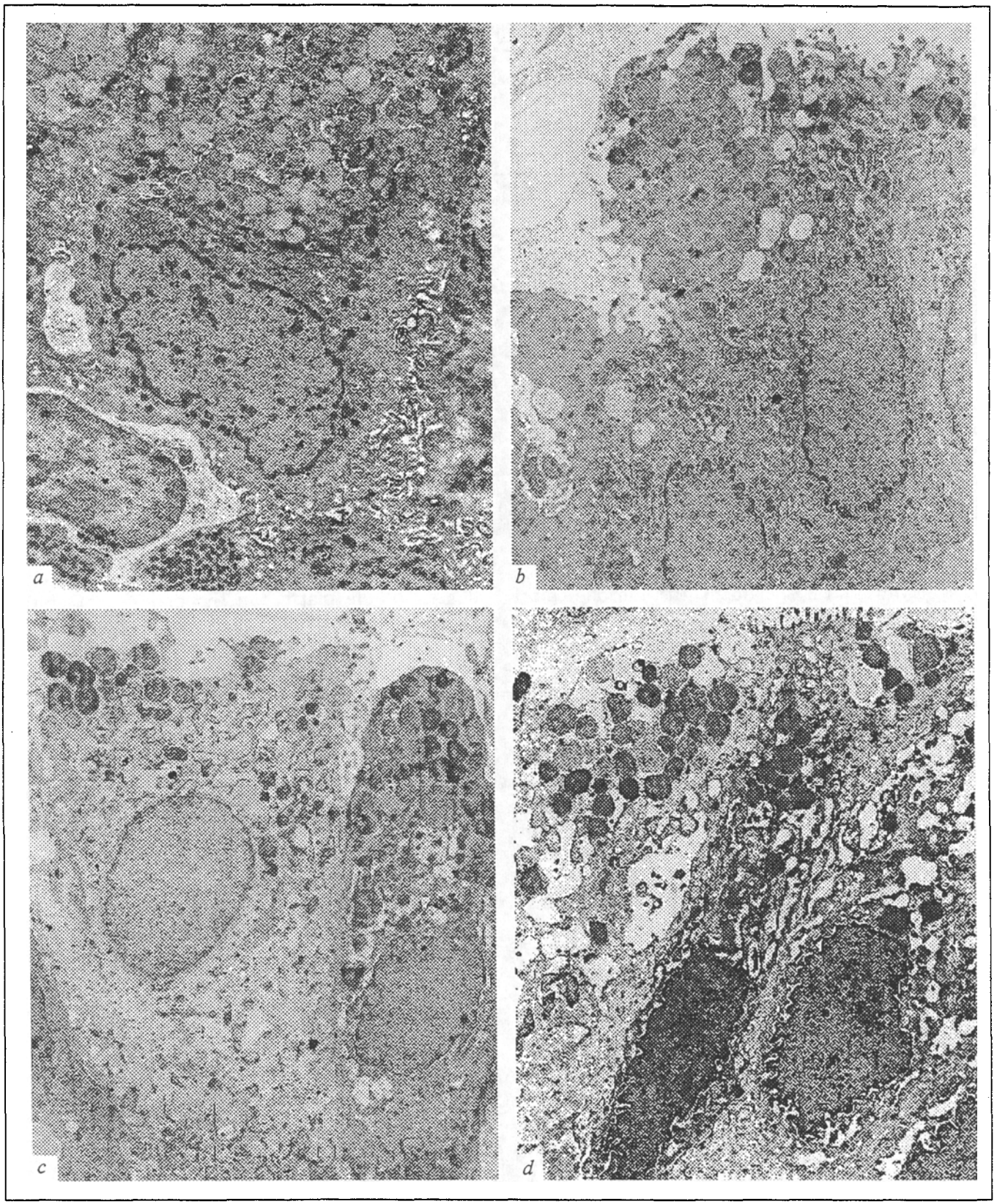

Fig. 2. Electron-microscopic investigation of GM. *a*) luminal epithelium and abundant secretory granules in the cytoplasm; fundal specimen, ×5000. *b*) enlarged cisternae of cytoplasmic reticulum and reduction of microvilli in epitheliocytes; pyloric specimen, ×3300. *c*) epitheliocyte with electron-transparent cytoplasm and destructured organelles; fundal specimen, ×3300. *d*) vacuolized cytoplasmic reticulum and reduced secretory granules in mucocytes; pyloric specimen, ×2600.

TABLE 1. Pattern of Morphological Changes in Gastric Bioptates in Chronic Gastroduodenal Ulcer, %

Chronic inflammation	Fundal portion		Pyloric portion	
	GU	DU	GU	DU
Catarrhal	52.6	61.9	–	31.1
Catarrhal–sclerotic	47.4	38.1	80.9	55.2
Sclerotic	–	–	19.1	13.7

Note. Here and in Table 2: GU: gastric ulcer; DU: duodenal ulcer.

bly around the terminal portions of the glands; sclerotic changes were also found in the muscular layer.

An appreciable thinning of the GM, predominantly at the expense of the lamina propria, is typical of sclerotic inflammation, the number of glands being markedly reduced. The gastric pits in some regions reached the muscular layer, and in the foci of epithelial metaplasia they resembled intestinal crypts. Sclerotic changes predominated in the stroma, this going along with relatively poor exudative manifestations; the muscle layer was thickened and sclerotized.

In chronic gastroduodenal ulcer structural disturbances of the GM are more marked in the distal portions than in the body of the stomach, irrespective of the localization of the peptic defect (Table 1). In pyloroantral specimens the morphological pattern characteristic of catarrhal-sclerotic and sclerotic gastritis predominated, while in fundal specimens signs of catarrh were observed more often.

In view of the importance of the epithelial lining in the formation of protective barrier of the GM, the main attention during electron microscopy was paid to the ultrastructure of luminal epitheliocytes. It was noted that the formation of an ulcer defect in the gastroduodenal zone was frequently attended by disturbances of the submicroscopic organization of the gastric epithelium. Changes in the epitheliocyte ultrastructure in the fundal and pyloric portions were predominantly stereotypic and were largely determined by the pattern of tissue reorganizations.

In chronic catarrh the majority of cells in the epithelial layer preserved the typical structure. The epitheliocyte nuclei were round with a low content of heterochromatin and were distributed over the basal portions of cells; a considerable area of the cytoplasm was filled with densely packed granules of secretion (Fig. 2, *a*). In the perinuclear space, which was devoid of granules, narrow cisternae of the cytoplasmic reticulum, elements of the lamellar apparatus, and small mitochondria with a moderately dense matrix and a few cristae were differentiated. Only a disturbance in the relief of the apical plasmalemma of mucocytes, disappearance of microvilli from their surface, an enlargement of some canaliculi of the cytoplasmic reticulum, and cleared foci in the mitochondria were worthy of note (Fig. 2, *b*).

A considerable heterogeneity of cells in the epithelial layer is characteristic of the sclerotic forms of gastritis. Some epitheliocytes had an optically translucent cytoplasm and destructured organelles (Fig. 2, *c*), in other cells the ultrastructure was poorly distinguishable due to an increased density of the matrix. In the majority of epithelial cells the nuclei had irregular contours, sometimes with deep invaginations; the cytoplasmic reticulum was markedly enlarged and vacuolized; mitochondria had a cleared matrix and destructured cristae (Fig. 2, *d*). In addition, a tendency toward flattening of epithelial cells was observed, which was attended by a decrease in the number of secretory granules in the cytoplasm and a reduction of microvilli.

Autoradiography of gastric biopsy specimens revealed some regularities of the regenerative-plastic reactions of the epithelium in gastroduodenal ulcer. It was established that the proliferative activity of the gastric epithelium, determined as the incorporation of ^{3}H-thymidine in the nuclei, was higher in the pyloroantral zone than in the fundal portion (Table 2). DNA-synthesizing cells were found at the bottom of the pits, and frequently extended over their entire length, including the apex of the ridges (Fig. 3, *a* and *b*).

The majority of cells of the luminal-foveal gastric epithelium exhibited metabolic activity and in-

TABLE 2. Index of Labeled Nuclei in the Luminal–Foveal Gastric Epithelium in Chronic Gastroduodenal Ulcer ($M \pm m$)

Labeled precursor	Fundal portion		Pyloric portion	
	GU	DU	GU	DU
^{3}H–Uridine	80.23±1.46	74.17±4.00	78.81±1.16	69.44±4.35
^{3}H–Thymidine	8.89±0.48	6.27±0.28	12.44±0.62	11.57±0.63

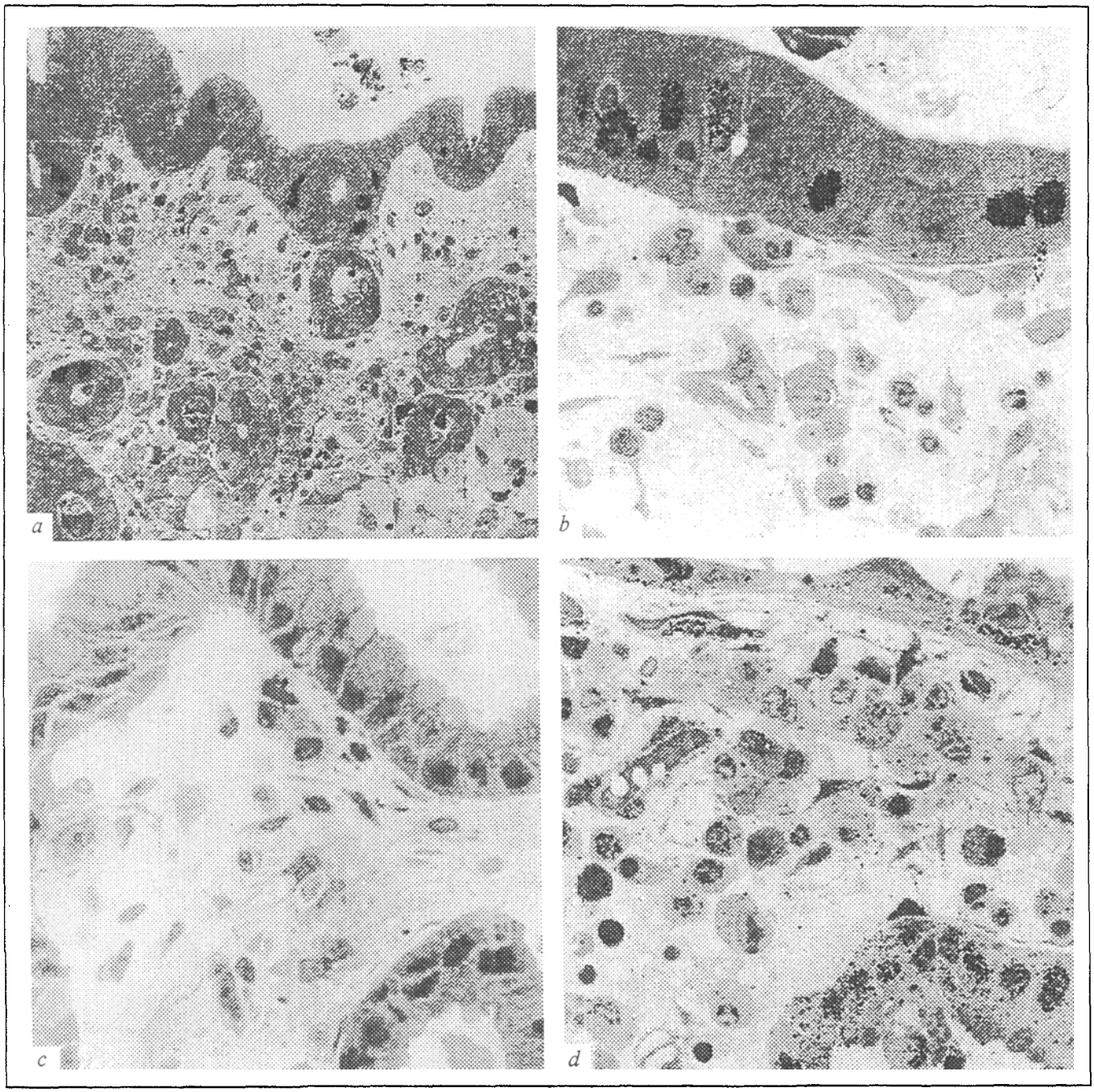

Fig. 3. Autoradiographs of GM. *a*) DNA synthesis in solitary epitheliocytes; fundal specimen, ×800. *b*) active DNA synthesis in luminal epithelium; pyloric specimen, ×800. *c*) active RNA synthesis in luminal–foveal epithelium; fundal specimen ×960. *d*) RNA synthesis in epitheliocytes, ×800. Semithin sections; azure II staining.

tensively incorporated the ^{3}H-uridine label (Fig. 3, *c* and *d*). No marked differences were noted in the level of RNA synthesis between the fundal and pyloric portions; we just observed a tendency toward a reduction of the synthetic activity of epitheliocytes in the distal portion of the stomach. Among the connective-tissue cells it was endotheliocytes of the capillaries which more often incorporated the label.

Thus, the formation of an ulcer defect in the gastroduodenal system is attended by the involvement of the GM as a whole in the pathological process; a specific structural-functional heterogeneity is observed in the fundal and pyloric portions of the stomach. Inflammatory-sclerotic changes in the GM predominate in the pyloroantral portion, as compared to the gastric body; in the same zone an imbalance is observed between the proliferative and metabolic activity of the epithelium. This data are in accord with the concept of the functional morphology of the GM [3,8].

REFERENCES

1. L. N. Aruin and B. Z. Chikunova, *Byull. Eksp. Biol. Med.*, **90**, № 7, 114 (1980).
2. L. N. Aruin, A. B. Shekhter, Z. P. Milovanova, and V. S. Gorodinskaya, *Arkh. Pat.*, № 12, 16 (1989).
3. L. N. Aruin, P. Ya. Grigor'ev, V. A. Isakov, and E. P. Yakovenko, *Chronic Gastritis*, Amsterdam (1993).
4. V. V. Vasilyuk and V. N. Vasilyuk, in: *Proc. Fourth All-Union Congress of Gastroenterologists*, Vol. 1, Moscow-Leningrad (1990), p. 172.
5. G. A. Lapii, L. M. Nepomnyashchikh, and G. V. Panasyuk, *Byull. Sib. Otdel. Akad. Med. Nauk SSSR*, № 5, 82 (1989).
6. L. P. Myagkova, O. A. Sklyanskaya, A. Khorshed, *et al.*, *Probl. Gastroenterol.*, № 1, 41 (1990).
7. G. I. Nepomnyashchikh, V. V. Omigov, L. M. Nepomnyashchikh, *et al.*, *Byull. Sib. Otdel. Akad. Med. Nauk SSSR*, № 4, 53 (1989).
8. V. M. Uspenskii, *Functional Morphology of the Gastric Mucosa* [in Russian], Leningrad (1986).
9. Yu. I. Fishzon-Ryss and E. S. Ryss, Gastroduodenal Ulcers [in Russian], Leningrad (1978).
10. R. Greenlaw, D. G. Sheahan, V. De Luca, *et al.*, *Dig. Dis. Sci.*, **25**, 660 (1980).
11. J. G. Penston, *Scand. J. Gastroenterol.*, **25**, 1 (1990).
12. P. H. Rowe, M. J. Starlinger, E. Kasdon, *et al.*, *Gastroenterology*, **93**, 863 (1987).
13. M. Tatsuta, H. Iishi, and S. Okuda, *Dig. Dis. Sci.*, **31**, 7 (1986).

Morphological Manifestations of Hereditary Hypertrophic Cardiomyopathy in W/SSM Rats

R. I. Salganik, N. A. Solov'eva, L. M. Nepomnyashchikh, and D. E. Semenov

UDC 616.127-007.61-055.5/.7-092.9-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 8, pp. 203-207, August, 1994
Original article submitted May 30, 1994

A W/SSM strain of rats with hereditary hypertrophic cardiomyopathy has been created by inbreeding Wistar rats selected for an increased sensitivity to the cataractogenic effect of high doses of galactose. It is shown that myocardial hypertrophy attended by a diffuse stroma collagenization, focal sclerotic changes, and signs of chronic heart failure spontaneously develops in these animals.

Key Words: *W/SSM rats; hereditary hypertrophic cardiomyopathy; myocardium; cardiomyocyte count*

Hereditary factors play an important role in hereditary hypertrophic cardiomyopathy (HCM) etiology [5]. In this connection the creation of the animal strain with a hereditary pathology of the myocardium similar to HCM in humans is of special interest. A W/SSM rat strain has been created by the inbreeding of Wistar rats selected for an increased sensitivity to the cataractogenic effect of high doses of galactose [8]. In these animals cataracts, hepato- and splenomegaly, and kyphoscoliosis develop spontaneously, and an increased weight of the heart, delayed growth and development, and reduced fertility are observed [2,8,9]. In parallel, we have selected rats resistant to the damaging effect of galactose. In this strain (W/SSM-R) of rats obtained by selection and inbreeding no pathological manifestations have been observed in response to galactose loading [8].

Some biochemical characteristics and their heritability have been studied in W/SSM rats, and

Department of Molecular Genetics, Institute of Cytology and Genetics, Siberian Division of the Russian Academy of Sciences; Laboratory of General Pathological Anatomy, Research Institute of Regional Pathology and Pathomorphology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk

0007-4888/94/0008-0900$12.50