Effect of Incoherent Red Light on the Proliferation and Metabolic Activity of the Gastroduodenal Epithelium

G. I. Nepomnyashchikh, G. A. Lapii, and L. M. Nepomnyashchikh

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

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 8, pp. 194-198, August, 1994
Original article submitted May 30, 1994

It is shown that incoherent red light exerts an antiulcer effect on the mucosa of the duodenum. Some regularities are found in the proliferative-metabolic reactions caused by local irradiation of the gastroduodenal epithelium. Intensified regenerative-plastic processes in the tissue underlie the biostimulating effect of radiation.

Key Words: *incoherent red light; gastroduodenal system; epithelial cells; autoradiography*

Low-intensity laser radiation and incoherent red light are used for the correction of diverse pathological states. The efficacy of laser therapy in gastroduodenal ulcer has been corroborated by many clinical studies [2-4,8,11]. However, the possible mechanisms of the biostimulating effect of radiation have received much less attention [1,6,10]. The morphogenesis of the effect of laser has not been studied in depth. Important information may be obtained using modern methods of structural analysis, one of which is autoradiography [5,10,12,13].

The objective of the present study was to examine, using autoradiography, the state of the regenerative-plastic processes in the gastric and duodenal mucosa for local exposure to incoherent red light.

MATERIALS AND METHODS

Specimens of the stomach and duodenum of 28 patients with chronic duodenal ulcer (men aged 19-55) were investigated. Incoherent red light was produced by the light source of an Olympus GF-B3 gastrofibroscope (Japan) with a special KS-10 light filter. The procedure was performed by placing the fibroscope 0.5-1.0 cm from the ulcer lesion; the number of sessions was from 5 to 8; exposure time was 1-3 min. Sampling was performed before and after irradiation. Specimens were taken from the ulcerated zone of the duodenum, as well as from the fundal and pyloric portions of the stomach.

The larger part of each specimen was used in light microscopy; for this purpose paraffin sections were stained with hematoxylin and eosin in combination with Perls reaction, Schiff reagent, and Van-Gieson staining. Tissue fragments (around 1 mm in diameter) 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 were 200 and 100 μCi/ml, respectively). Specimens were then fixed in a 4% paraformaldehyde solution, treated routinely for electron microscopy, and embedded in Epon-Araldite.

Semithin sections 1 μ thick were coated with photoemulsion M for nuclear investigations and exposed for 5-7 days. After photographic treatment the autoradiographs were stained with azure II. The index of labeled nuclei was counted under a light microscope (×900); the results were statistically processed using Student's t test.

RESULTS

In all examinees exacerbation of duodenal ulcer was observed before exposure to incoherent red light, which was confirmed by the results of laboratory

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)

0007-4888/94/0008-0890$12.50

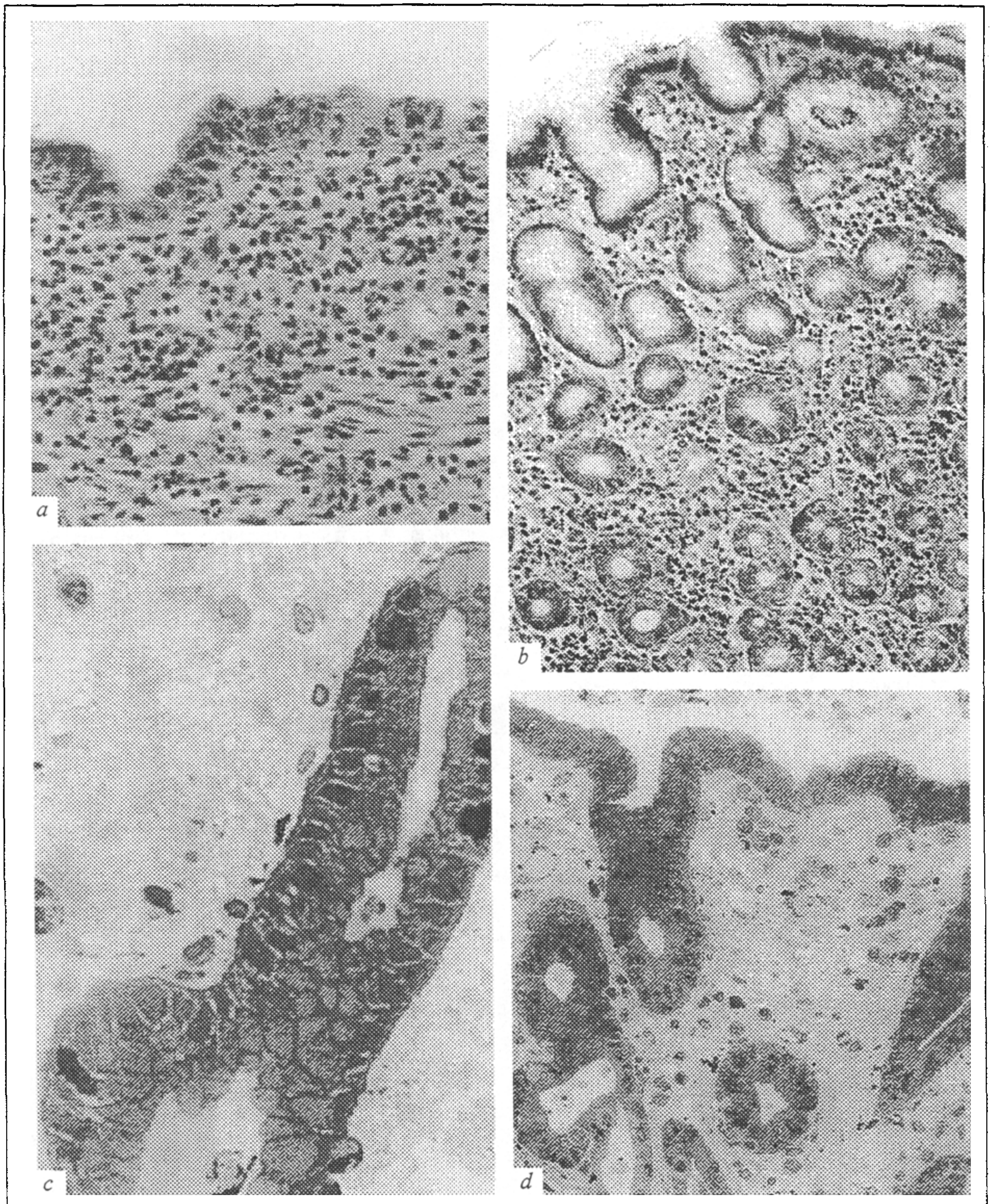

Fig. 1. Morphofunctional changes of gastric and duodenal mucosa prior to exposure to incoherent red light. *a*) pronounced dystrophy of luminal epithelium; extensive inflammatory infiltration of lamina propria; specimen of duodenum, ×800. *b*) dystrophy of luminal–foveal epithelium and glands, diffuse infiltration of lamina propria; specimen from pyloric portion of stomach, ×200. *c*) DNA synthesis in solitary epitheliocytes of gastric pits; specimen from pyloric portion of stomach, ×960. *d*) RNA synthesis in luminal–foveal epithelium; specimen from fundal portion of the stomach, ×800. *a* and *b*) hematoxylin–eosin staining; *c* and *d*) azure II staining.

tests. A large area of necrobiosis was observed in the ulcerated zone. In the surrounding mucous membrane a marked alteration of epithelial structures was accompanied by pronounced disturbances in the microcirculatory bed, massive inflammatory infiltration, and stromal sclerosis (Fig. 1, *a*).

TABLE 1. Autoradiographic Analysis of RNA and DNA Synthesis in Epitheliocytes for Exposure to Incoherent Red Light ($M \pm m$)

Precursor	Biopsy site	Index of labeled nuclei	
		before exposure	after exposure
^3H-Uridine	Boundary of duodenal ulcer	50.68±3.85	66.83±4.24
	Fundal portion of stomach	77.96±2.19	80.11±2.07
	Pyloric portion of stomach	77.65±1.90	85.15±2.13
^3H-Thymidine	Boundary of duodenal ulcer	8.32±0.77	10.86±0.77
	Fundal portion of stomach	7.68±0.81	11.13±1.03
	Pyloric portion of stomach	10.89±0.67	13.83±0.77

Light-microscopic examination of gastric specimens demonstrated that in all cases the gastric mucosa was involved in the pathological process. These changes fit well into the morphological picture of chronic gastritis with the predominance of structural rearrangements in the distal areas (Fig. 1, *b*). Dystrophy of the luminal-foveal and glandular epithelium, polymorphonuclear cellular infiltration, and vascular disturbances of varying severity were characteristic of the fundal portion of the stomach. In addition, foci of epithelial metaplasia were frequently encountered in specimens from the pyloric portion of the stomach; in some cases there was a pronounced atrophy of the glands attended by their replacement with fibrous tissue.

Autoradiography of biopsy specimens before irradiation demonstrated that the proliferative activity of the epithelium at the boundary of the duodenal ulcer was rather high; the index of labeled nuclei varied from 5.8 to 12.9%. In the gastric mucosa this index was from 5.4 to 14.4%, being slightly higher in the pyloroantral portion than in the fundal portion of the stomach (Table 1). DNA-synthesizing cells were situated near the gastric pits and were sometimes observed at the surface of the ridges (Fig. 1, *c*).

The majority of cells in the gastric and duodenal epithelium exhibited metabolic activity with respect to RNA synthesis and incorporated ^3H-uridine (Fig. 1, *d*). Granules of reduced silver were frequently observed above the nuclei of dystrophied epitheliocytes, indicating that they had preserved their synthetic function. Connective-tissue cells, predominantly endotheliocytes of the capillaries, also took up the label.

Local irradiation of the duodenal ulcer with incoherent red light had a rapid sanatory effect. Visual examination showed a reduction of inflammatory infiltration and gradual ridding of fibrous precipitations from the ulcer bottom and its epithelization. Two or three weeks after the start of exposure a tender cicatrix without sclerotic deformation of the surrounding tissues was found in the focus of injury.

Light-optic examination after exposure to incoherent red light demonstrated growth of granulations; a marked diminution of inflammatory-dystrophic disorders was noted in the perifocal zone; the number of goblet cells markedly increased in the regenerating epithelium; mucoidized foci were discovered more rarely (Fig. 2, *a*).

During this period the pattern of structural changes in the gastric mucosa did not change markedly. After local irradiation of the duodenal ulcer with incoherent red light and after cicatrization of the defect, only a slight reduction of epithelial dystrophy and of the severity of inflammatory infiltration of the stroma was observed in specimens from the fundal and pyloric portions of the stomach. On the whole, the morphological pattern did not alter; the signs of chronic gastritis persisted, being more pronounced in the antral portion of the stomach.

Autoradiography of gastroduodenal bioptates after irradiation revealed some regularities of the proliferative-metabolic reactions in the epithelium. It was established that local irradiation of the duodenal ulcer with incoherent red light stimulated the synthetic processes both in the focus of the lesions and in the distant portions of the stomach (Table 1). The most marked changes were found in the zone of lesions, where the index of ^3H-thymidine labeling after irradiation rose 30.5% on

TABLE 2. Autoradiographic Analysis of RNA Synthesis in Endotheliocytes for Exposure to Incoherent Red Light ($M \pm m$)

Precursor	Biopsy site	Index of labeled nuclei	
		before exposure	after exposure
^3H-Uridine	Boundary of duodenal ulcer	64.38±1.86	69.51±1.46
	Fundal portion of stomach	66.55±3.01	73.54±1.91
	Pyloric portion of stomach	72.40±1.82	77.89±1.24

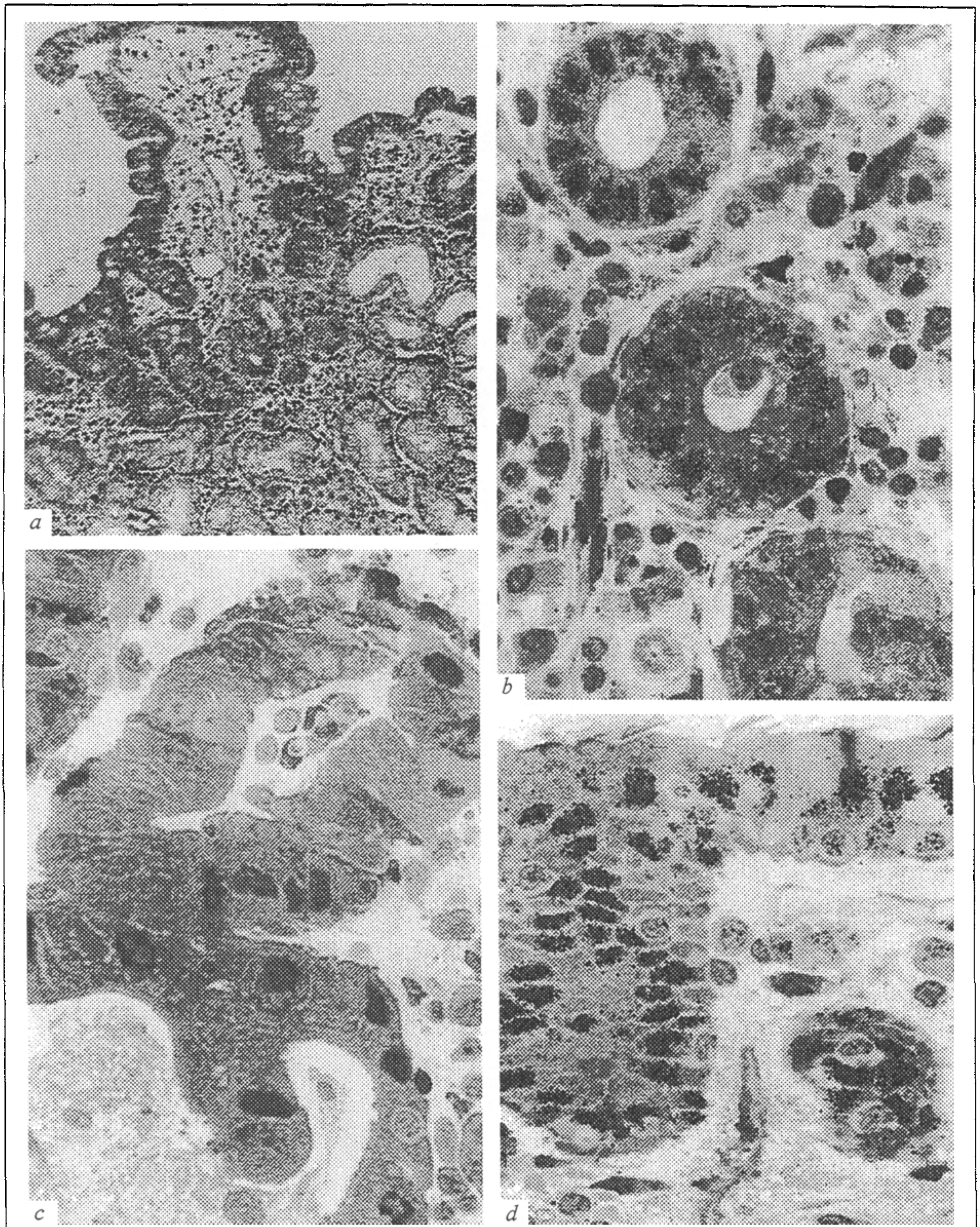

Fig. 2. Morphofunctional changes of gastric and duodenal mucosa after exposure to incoherent red light. *a*) restoration of general structure of mucosa; abundant goblet cells in regenerating epithelium; duodenal specimen. *b*) intensive RNA synthesis in epithelium of intestinal crypts; duodenal specimen. *c*) active DNA synthesis in epitheliocytes; specimen from fundal portion of stomach. *d*) active RNA synthesis in luminal–foveal epithelium; specimen from fundal portion of stomach. *a*) hematoxylin–eosin staining, ×240; *b–d*) azure II staining, ×960.

average, and the number of ^{3}H-uridine-labeled epitheliocytes increased by 31.9% (Fig. 2, *b*).

In the gastric mucosa the degree of regeneration of the epithelium assessed as the number of

DNA-synthesizing cells increased markedly in the fundal portion of the stomach and less markedly in the pyloric portion (Fig. 2, *c*). The change in RNA synthesis was less marked, but a tendency toward its intensification was clearly pronounced. The index of ^{3}H-uridine labeling increased more in the pyloroantral zone than in the body of the stomach (Fig. 2, *d*). It is worthy of note that an enhancement of the plastic reactions in the cells of the microcirculatory bed was paralleled by an augmentation of RNA synthesis (Table 2).

Thus, healing of duodenal ulcer after exposure to incoherent red light was attended by a pronounced stimulation of the proliferative and metabolic functions of the epithelium. In the mucosa of the fundal and pyloric portions of the stomach the intracellular nucleic acid synthesis intensified despite the torpidity of structural changes. Evidently, induction of regenerative-plastic processes in elements of the epithelium and connective tissue underlies the biostimulating effect of irradiation. This is in line with other findings [7,9].

REFERENCES

1. I. M. Baibekov and E. Sh. Musaev, *Byull. Eksp. Biol. Med.*, **111**, № 1, 80-83 (1991).
2. S. B. Barakaev, *Klin. Med.*, № 7, 44-46 (1991).
3. A. E. Dmitriev, S. B. Kashevarov, and N. A. Arapov, *Ibid.*, № 4, 85-87.
4. L. P. Vorob'ev, O. B. Dronova, G. I. Korneev, and A. A. Samsonov, *Ibid.*, № 2, 77-80 (1992).
5. R. I. Kaem and T. S. Ustinova, *Byull. Eksp. Biol. Med.*, **113**, № 6, 667-670 (1992).
6. A. S. Loginov, N. G. Basov, V. R. Ambartsumyan, *et al.*, *Ter. Arkh.*, № 2, 42-46 (1989).
7. A. S. Loginov, G. N. Sokolova, S. V. Sokolova, *et al.*, *Ibid.*, № 2, 58-62 (1990).
8. V. B. Matyushichev, A. I. Soldatov, and V. V. Titov, *Klin. Med.*, № 11, 77-80 (1988).
9. G. I. Nepomnyashchikh, S. M. Egunova, L. M. Nepomnyashchikh, *et al.*, *Byull. Sib. Otdel. Akad. Med. Nauk SSSR*, № 4, 103-110 (1987).
10. L. M. Nepomnyashchikh, V. V. Polosukhin, G. I. Nepomnyashchikh, and V. P. Tumanov, *Byull. Eksp. Biol. Med.*, **104**, № 12, 743-749 (1987).
11. M. I. Rasulov and S. I. Rapoport, *Klin. Med.*, № 2, 28-31 (1992).
12. C. J. Bronson, M. E. Boxer, J. C. Clark, *et al.*, *Scand. J. Gastroenterol.*, **19**, 515-520 (1984).
13. A. Fich, N. Arber, E. Okon, *et al.*, *Arch. Toxicol.*, **61**, 314-317 (1988).