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Ultrastructural Characteristics of Cell Populations in the Gastric and Duodenal Mucosa during Psoriasis

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In biopsy specimens of the gastric and duodenal mucosa from patients with psoriasis we revealed severe degenerative and dystrophic changes in cells of the surface and glandular epithelium with destruction of functionally important cytoplasmic organelles. The stroma of the gastric mucosa was characterized by hyperplasia of the lymphoid tissue, formation of numerous lymphoid follicles, and destruction of the endothelium in microvessels. These changes are interpreted as the syndrome of regenerative and plastic insufficiency.

Key Words: *psoriasis; stomach; duodenum; biopsy; electron microscopy*

Psoriasis is a systemic disease accompanied by damage to the skin, musculosceletal system, and internal organs [6,7,11,14]. Therefore, various internal organs are involved in the pathological process during psoriasis [2]. In recent years the constantly increasing morbidity makes psoriasis an urgent problem. The number of patients with severe and atypical forms of this disease resistant to standard therapy markedly increased [4,12,13,15].

Despite detailed investigations of pathomorphological characteristics in the skin [1,8] and structural changes in the synovial membrane of joints during psoriasis [3], damage to the internal organs received little attention. Usually these observations are performed on autopsy specimens [10]. It should be emphasized that 28% patients with psoriasis have gastrointestinal disorders [4]. Modern notions about the morphogenesis of this disease are focused on skin lesions. The major phenotypic characteristics of psoriasis are hyperplasia of epidermal cells and disturbances in their differentiation [9].

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Here we studied structural changes in cells of the gastric and duodenal mucosa during psoriasis.

MATERIALS AND METHODS

We examined 20 patients with psoriasis (11 men and 9 women, 18-50 years). The duration of psoriasis varied from 1 to 40 years. The diagnosis was made after clinical examination, diagnostic tests specific for dermatosis, laboratory tests and instrumental assays for the stage, type, and severity of psoriasis. The patients were subjected to fibrogastroduodenoscopy and target biopsy of fundal and antral portions of the stomach (38 samples) and duodenal bulb (22 samples).

For light microscopy the specimens were fixed in 10% neutral formalin, paraffin sections were stained with hematoxylin and eosin in combination with Perls reaction and after van Gieson with poststaining of elastic fibers with Weigert resorcin fuchsin. Periodic acid-Schiff reaction in combination with azure-eosin staining was performed. Preparations stained by the method of Giemsa were used for bacterioscopy. Specimens for electron microscopy were fixed in 4% paraformaldehyde, postfixed in 1% OsO_4, and embedded in Epon-araldite mixture. Semithin sections

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were stained with Schiff reagent and azure II. Ultrathin sections were contrasted with uranyl acetate and lead citrate and examined under a JEM 1010 electron microscope.

RESULTS

Endoscopic examination revealed signs of superficial gastritis. Some patients had erosions in the antral portion of the stomach. We revealed atrophy of the gastric mucosa (n=4) and chronic duodenitis (n=5). In 2 patients chronic duodenitis was accompanied by scary deformation of the duodenal bulb and duodenogastral reflux.

Light and electron microscopy revealed structural changes in the mucosa of the fundus, pylorus, and duodenal bulb. In most specimens the surface epithelium of the gastric mucosa was characterized by diffuse degeneration and atrophy. Pathological changes extended to the cambial epithelial region. It should be emphasized that intestinal metaplasia of the epithelium was not observed. Only in 2 patients we revealed focuses of insignificant dysplasia. These data indicate that proliferation of epithelial cells in the stomach remained unchanged.

Structural changes in the mucosa of fundal and antral portions in the stomach were manifested in the reduction of crypts and irregular enlargement of folds. The height of the epithelial layer varied due to different count of secretory granules in apical zones of epitheliocytes. Foveolar cells had a cylindrical shape. However, we found regions of pseudomulticellularity with pronounced polymorphism, which was associated with flattening of cells and horizontal orientation of nuclei. In the epithelial layer close intercellular contacts were preserved only at the level of apical regions. Integration of epitheliocytes was associated with multiple interdigitations of lateral plasmalemmas. They were visualized due to enlarged intercellular spaces. The basal cytolemma of foveolar cells formed numerous long processes along the basal membrane.

Surface and cryptal mucocytes were characterized by high electron density (Fig. 1, *a*, Fig. 2, *a*) and hypoplasia of cytoplasmic organelles. We revealed single profiles of the granular endoplasmic reticulum, small mitochondria, elements of the Golgi apparatus, polymorphic lysosomes, phagosomes, and residual bodies. Rounded heterogeneous secretory granules with high electron density were localized in the supranuclear cytoplasmic zone. These signs indicate that processes of exocytosis were impaired. In individual flattened epitheliocytes secretory granules were localized not only in the apical, but also in the basal region.

Individual curved electronically dense rods of *Helicobacter pylori* were found near the apical cytolemma of epitheliocytes in both portions of the stomach. They were localized in the near-wall mucus and sometimes approached microvilli of epitheliocyte (Fig. 1, *a*). However, microorganisms were not incorporated into the epithelial layer (intercellularly or intracellularly). It should be emphasized that ultrastructural characteristics of epitheliocytes did not depend on the presence of bacteria near the surface. Moreover, we did not observe intensification of leukodiapedesis and cytotoxic or cellular reactions.

The degree of damage to fundal glands attracted attention. Most epitheliocytes were characterized by pronounced degeneration. The cytoplasm was vacuolized and loosened and had fuzzy contours. Glandular cells were poorly differentiated into main types (chief, accessory, and parietal cells) due to dystrophic transformation. A large number of degenerating cells were localized in the lumen of glands. Atrophy and death of cells played an important role in the pathogenesis of gland lesions. These changes were associated with the distribution of cellular infiltrates primarily containing lymphocytes in the mucosa and development of fibrosis. Pyloric glands also underwent degeneration, which was not accompanied by their considerable reduction.

Parietal cells in fundal glands of different localization were characterized by suppressed functional activity due to degradation of the specialized cytoplasmic organelle (secretory tubule). Its lumen was narrowed, reduced, and filled with large residual bodies (Fig. 1, *b*). Most parietal cells in secretory tubules contained single or numerous mucous granules (mixt-cells). These changes reflected abnormal differentiation of highly specialized fundal glandular cells. Although parietal cells included a large number of mitochondria, some organelles were altered and characterized by reduction and destruction of cristae, degeneration, and formation of residual bodies.

The count of protein-synthesizing organelles decreased in chief cells. Epitheliocytes contained heterogeneous secretory granules with high and irregular electron density. In many cells secretory granules underwent degradation with the formation of secondary phagolysosomes and large myelin figures (Fig. 1, *c*). These changes reflect disturbances in the secretory cycle of chief cells and blockade of excretion.

In the duodenal mucosa structural changes were less pronounced than in fundal and pyloric portions of the stomach. We found mild or moderate degeneration of the epithelium in intestinal villi and crypts. Hypoplasia of goblet cells was accompanied by their focal hyperplasia. Brunner's glands were characterized by moderate degeneration, but retained secretory activity. Electron microscopy revealed stereotypic dystrophic changes in duodenal enterocytes that were observed even near intestinal crypts. Reduction of ultrastruc-

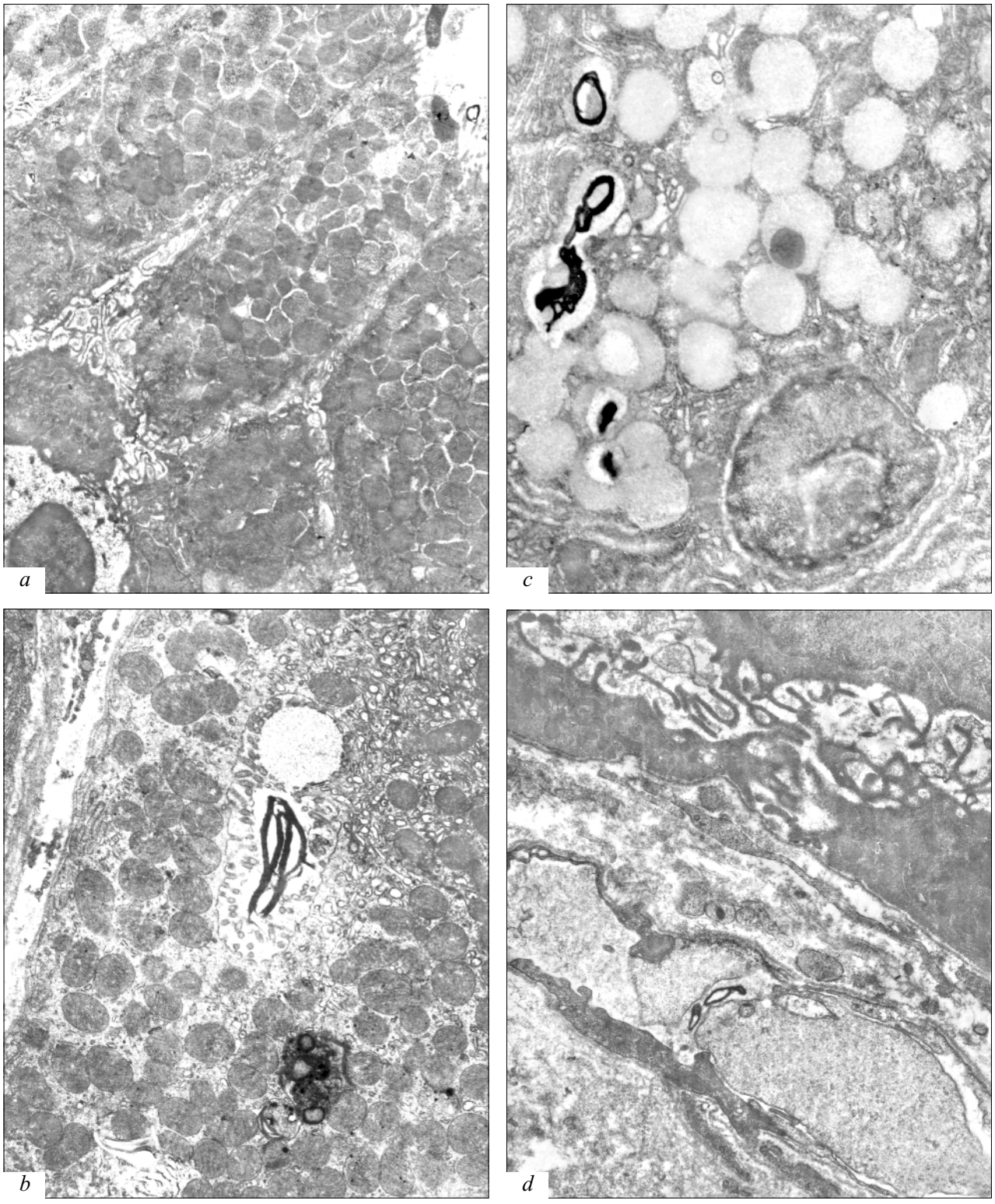

Fig. 1. Degenerative and dystrophic changes in gastric fundus mucosa cells in patients with psoriasis: degeneration of surface and cryptal epitheliocytes, high density of the cytoplasm and secretory granules above microvilli (*H. pylori*, ×3000, *a*); myelin figure and mucous granules in narrowed secretory tubules in the parietal cell (×12,000, *b*); formation of large bodies in the cytoplasm of chief cells (×5000, *c*); myelin figures and fragments of died cells in the lumen of subepithelial microvessels (×8000, *d*).

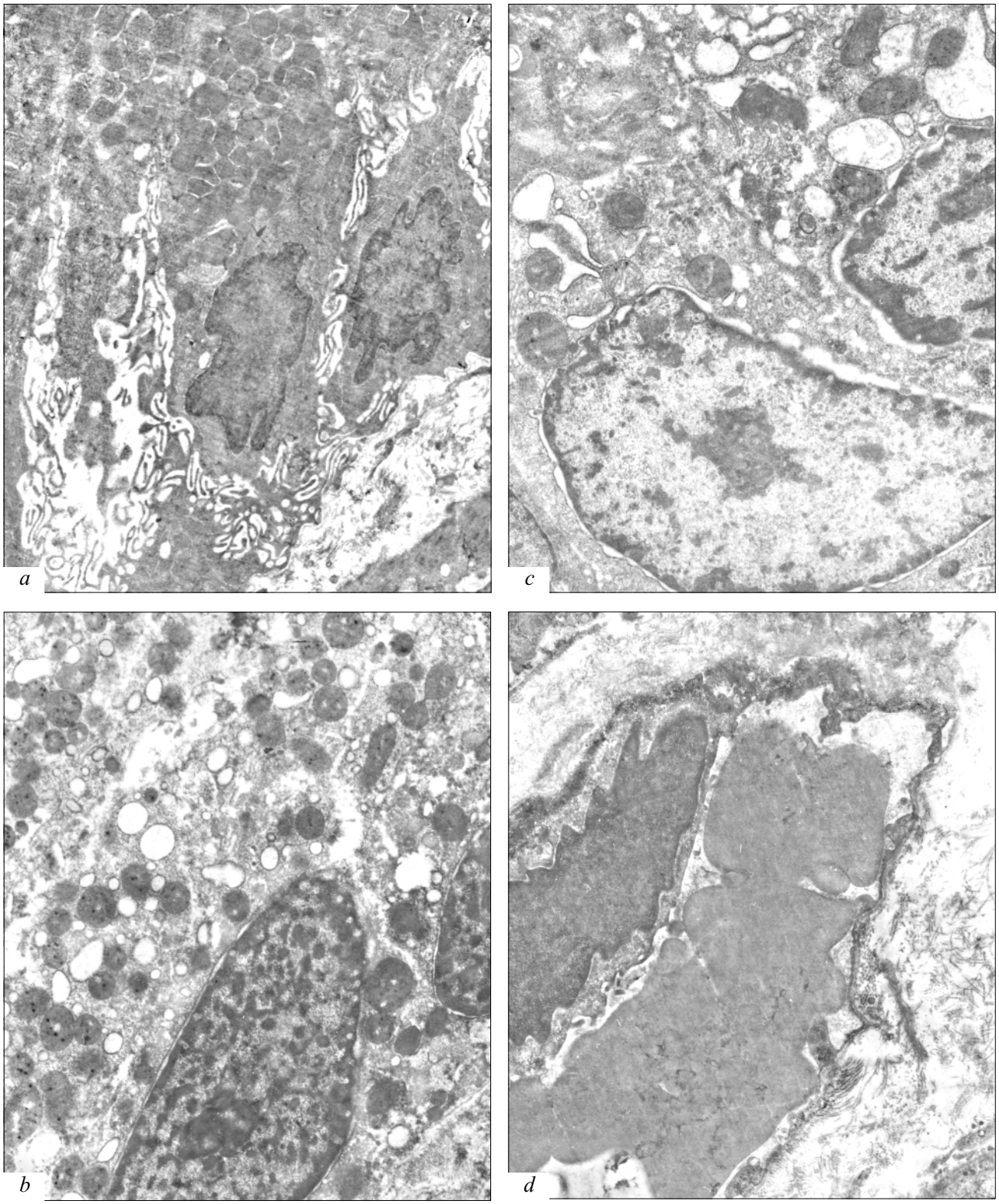

Fig. 2. Degenerative and dystrophic changes in pyloric and duodenal mucosa cells from patients with psoriasis: degeneration of surface and cryptal epitheliocytes, enlargement of intercellular spaces, edema of the basal membrane (×3000, *a*); fragments of enterocytes, vacuolization of the smooth cytoplasmic reticulum, formation of secondary lysosomes (×8000, *b*; ×12,000, *c*); degenerative changes in endotheliocytes of microvessels, sludge syndrome, perivascular edema (×12,500, *d*).

tures responsible for biosynthesis and degeneration of membrane cytoplasmic organelles (vacuolization) were found in most epitheliocytes. Polymorphic multivesicular and osmiophilic residual bodies appeared in many cells (Fig. 2, *b*, *c*). The number, size, and electron density of specific granules in the supranuclear zone of Paneth cells decreased. Goblet cells were characterized by high density of the cytoplasmic matrix and mucous granules. These granules underwent fusion and formed heterogeneous conglomerates. Fusion of these conglomerates with lysosomes led to the formation of large phagolysosomes. The excretory cycle was impaired.

Microcirculatory disturbances in the gastric and duodenal mucosa were accompanied by polymorphocellular infiltration (lymphocytes, plasmocytes, macrophages, eosinophils, and neutrophils). These changes were most pronounced in the gastric mucosa. Transepithelial leukodiapedesis was observed in some regions. The lymphoid tissue in the gastric mucosa was characterized by hyperplasia. Lymphoid follicles were revealed in most specimens of the pylorus and 50% specimens of the fundus. Their number varied from 2 to 4. Lymphoid follicles were found only in 1 specimen of the duodenum.

Pronounced microcirculatory disturbances were revealed in the stroma of the gastric and duodenal mucosa. Endotheliocytes were hypertrophic and had large perikarya and spindle-like nuclei. The signs of degeneration included focal blurring and thinning of the cytoplasm, destruction of cytoplasmic organelles (Fig. 1, *d*), reduction of pinocytotic vesicles, loosening and edema of the basal membrane, perivascular edema, activation of fibroblasts, and formation of numerous collagen fibrils (Fig. 2, *d*).

Our results indicate that epitheliocytes in the gastric and duodenal mucosa are characterized by degenerative and dystrophic changes. At the electron microscopic level these changes are manifested in the reduction and destruction of functionally important cytoplasmic organelles and formation of numerous polymorphic residual bodies. Parietal cells undergo most pronounced degeneration, which probably contributes to severe disturbances in secretory function of the stomach in patients with psoriasis.

The stroma of the gastric and duodenal mucosa is characterized by hyperplasia of lymphoid tissues with the formation of lymphoid follicles and polymorphocellular infiltration. These changes are interpreted as the compensatory and adaptive reaction. The microcirculatory bed plays an important role in the pathogenesis of systemic changes during psoriasis. Considerable changes in endotheliocytes and basal membrane of microvessels in the subepithelial layer of the mucosa are of considerable importance in this respect. Degenerative and dystrophic changes in parenchymal cells of the mucosa can be considered as the syndrome of regeneration and plastic insufficiency [5]. Various factors, including deficiency of plastic reserves in the organism, cytopathic effect of therapy with cytostatic preparations, and severe microcirculatory disturbances, play a role in the pathogenesis of this syndrome.

REFERENCES

1. S. I. Dovzhanskii, G. I. Nepomnyashchikh, Yu. M. Samoteikina, *et al*., *Byull. Sib. Otd. Akad. Med. Nauk SSR*, No. 4, 48-55 (1988).
2. S. I. Dovzhanskii and S. R. Utts, *Psoriasis or Psoriatic Disease* [in Russian], Saratov (1992).
3. T. N. Kop'eva, E. R. Agababova, O. V. Makarova, *et al*., *Arkh. Pat*., No. 6, 36-44 (1985).
4. Yu. M. Krinitsina, *Morphogenesis, Clinical Signs, and Several Aspects for Correction of Psoriasis in Modern Ecological Situation*, Abstract of Doct. Med. Sci. Dissertation, Novosibirsk (1998).
5. G. I. Nepomnyashchikh, *Boundary Tissues (Mucosa and Skin) in the Morphogenesis of General Pathological Processes* [in Russian], Novosibirsk (1996).
6. Yu. K. Skripkin, *Skin and Venereal Diseases. Manual for Physicians* [in Russian], Moscow (1995).
7. S. A. Khardikova, E. I. Beloborodova, and P. N. Pesterev, *Psoriasis and Intestinal Absorption* [in Russian], Tomsk (2000).
8. G. M. Tsvetkova and V. N. Mordovtsev, *Pathomorphological Diagnostics of Skin Diseases* [in Russian], Moscow (1986).
9. V. N. Shilov and V. I. Sergienko, *Byull. Eksp. Biol. Med*., **129**, No. 4, 364-369 (2000).
10. V. G. Shlopov and T. I. Shevchenko, *Arkh. Pat*., No. 9, 32-38 (1987).
11. A. Hannuksela-Svahn, E. Pukkala, E. Laara, *et al*., *J. Invest. Dermatol*., **114**, 587-590 (2000).
12. U.-F. Haustein, *Dermatol. Online J*., **8**, No. 1, 3 (2002).
13. T. P. Millard, K. E. Birch, and E. R. Young, *N. Engl. J. Med*., **345**, No. 25, 1853-1855 (2001).
14. H. H. Roenigk and H. I. Maibach, *Psoriasis*, New York (1990).
15. C. Taylor, D. A. Burns, and M. J. Wiselka, *Postgrad. Med. J*., **76**, 365-367 (2000).