MORPHOLOGY AND PATHOMORPHOLOGY

Instability of Bronchial Epithelium in Chronic Pulmonary Diseases

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Pathomorphological examination of large bronchi in patients with occupational diseases, lung cancer, and in subjects exposed to radiation revealed structural and functional heterogeneity of the epithelium: the presence of focal atrophy, metaplasia, hyper- and dysplasia in the same biopsy specimen. This phenomenon was termed as instability of the epithelium. Thickness of the epithelium greatly varied, especially, in neoplastic processes. Atrophy and epithelial instability phenomenon are interpreted as morphological markers of ecological and oncological risk.

Key Words: *chronic pulmonary diseases; bronchial epithelium; atrophy; bronchial biopsy; radioautography; electron microscopy*

Atrophy is now a predominant phenotypical modification of the bronchial epithelium under conditions of chronic pulmonary diseases of different origin [4,8, 9,11,13]. New types of structural reactions formed today reflect the interaction between the organism and adverse exo- and endogenous factors [3,14-16]. The role of factors regulating proliferation and apoptosis in lung tumors is analyzed [2]. The study of the bronchial compartment of the lungs helps to reveal specific "behavior" of the bronchial epithelium reflecting changes in the pheno- and genotypical expression in the population of bronchial epithelial cells.

We investigated cell populations of the bronchial wall in various pathological processes in the lungs verified by a complex of clinical and morphological markers.

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MATERIALS AND METHODS

Biopsy specimens from 423 patients with various chronic pulmonary diseases were examined: chronic atrophic bronchitis (CAB, n=53), primary atrophic bronchopathy (PAB, n=50), lung cancer (n=176), radiation-induced processes (n=57), and occupational diseases caused by exposure to coal dust (n=87), including that combined with vibration. Group of patients with radiation-induced diseases consisted of residents of ecologically contrast regions of the Altai territory with different levels of radiation contamination caused by many-year nuclear testing at the Semipalatinsk test fields.

Clinical examination, laboratory tests, bronchoscopy, and biopsy of the lobular or segmented bronchi were performed in all patients. The major portion of each specimen was embedded in paraffin. Sections were stained with hematoxylin and eosin in combination with Perls, Van-Gieson, and Schiff reactions. The lesser portion of each biopsy specimen was fixed in 4% paraformaldehyde and 1% OsO_4, and after stan-

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dard treatment embedded in epon-araldite. Semithin sections were stained with azur II and Schiff reagent. Ultrathin sections were contrasted with uranyl acetate and lead citrate. Autoradiography with ^{3}H-uridine and ^{3}H-thymidine was carried out [12] and the index of labeled cells on semithin sections was estimated. For morphometrical analysis semithin sections were used; the thickness of bronchial epithelium was evaluated by an ocular micrometer and coefficient of variations was calculated.

RESULTS

Comparative analysis showed a tendency to a decrease in epithelium thickness in CAB and PAB. The majority of biopsy specimens had no inflammatory infiltration. Diffuse sclerosis, predominance of vessels with thinned endothelial lining, structural signs of decreased functional activity of endotheliocytes, and inhibition of protein synthesis in the bronchial epithelium and endotheliocytes were detected.

Ultrastructural analysis showed similar changes in specimens of these two groups: reduction of ciliary system and main cytoplasmatic organelles, alteration of nuclei, and progressive disintegration of the epithelium with decreasing number of cell-to-cell contacts. Goblet cells were reduced and contained solitary elements of the Golgi complex and cytoplasmatic reticulum, few dense secretory granules surrounded by numerous lysosomes and autophagosomes were seen in the supranuclear part of the cytoplasm.

In PAB, vessels with thinned endothelial lining predominated among capillaries. Endotheliocytes were characterized by dark electron-dense cytoplasm, high content of heterochromatin in the nuclei, and apical plasmalemma with solitary protrusions. There were virtually no signs of pinocytosis.

Inhibition of protein synthesis in bronchial epitheliocytes correlating with decelerations of biosynthetic processes in the underlying stromal cells were revealed in biopsy specimens from patients with PAB. Metabolic activity of the bronchial epithelium in biopsy specimens from CAB patients was notably higher (Table 1). Autoradiography of the bronchial epithelium revealed no ^{3}H-thymidine incorporation in patients with PAB, while in CAB the index of ^{3}H-thymidine labeling varied within a wide range (Table 1).

The most important is diffuse bilateral atrophy of the bronchial wall in 100% patients in all studied pathological processes. Pathomorphological picture corresponded to PAB in the majority of cases: diffuse sclerosis, reduction of functional activity of capillaries, suppression of biosynthetic reactions in cell populations of bronchial mucosa, and the absence of inflammatory infiltration.

TABLE 1. DNA Synthesis in Bronchial Mucosa and Proliferative Activity of Epithelium in CAB and PAB (*M±m*)

Labeling index, %	CAB	PAB
^{3}H-uridine		
epitheliocytes	69.9±9.9	26.8±12.2
endotheliocytes	72.6±4.4	68.2±9.8
^{3}H-thymidine	1.5±0.8	—

TABLE 2. Thickness of Bronchial Epithelium (*M±m*) and Coefficient of Its Variations in Chronic Pulmonary Diseases

Disease	Thickness of epithelium, μ	Coefficient of variations, %
CAB	39.3±0.17	8
PAB	22.6±6.4	30
Coal dust exposure	47.74±9.69	57.27
+local vibration	41.12±14.13	60.44
Lung cancer	89.99±18.43	68.35
Radiation-induced diseases	98.4±16.6	55

The principal feature of PAB was pronounced structural and functional heterogeneity of the bronchial epithelium. Atrophic epithelium changed its shape from cylindrical to flattened, and in many sites looked like endothelium.

Diffuse atrophy of the bronchial epithelium are accompanied by mosaic changes (Fig. 1): the presence of atrophy, metaplasia, hyper- and dysplasia foci in the same biopsy specimen. We called this phenomenon as epithelial instability. Autoradiography of bronchial biopsy specimens revealed structural and functional heterogeneity associated with low DNA and RNA production in atrophic foci and increased DNA content in proliferating epithelium (Fig. 2). The thickness of the epithelium greatly varied, especially in neoplastic processes (Table 2). Therefore we interpreted atrophy and epithelial instability as morphological markers of ecological and oncological risk.

Our previous pathomorphological study of large bronchi in patients exposed to adverse factors for a long time enabled us to distinguish two typical variants of structural and functional rearrangement in the bronchial epithelium [6,7,10]. The first variant is characterized by decreased metabolic and proliferative activity of epithelial cells (*in vitro* radioautography data) and subsequent atrophy of the epithelium, while and the second variant is characterized by decreased metabolic function of epithelial cells and intensive basal cell proliferation, which was paralleled by metaplasia of the bronchial epithelium into multilayer squamous epithelium [5]. The third variant (mixed) was descri-

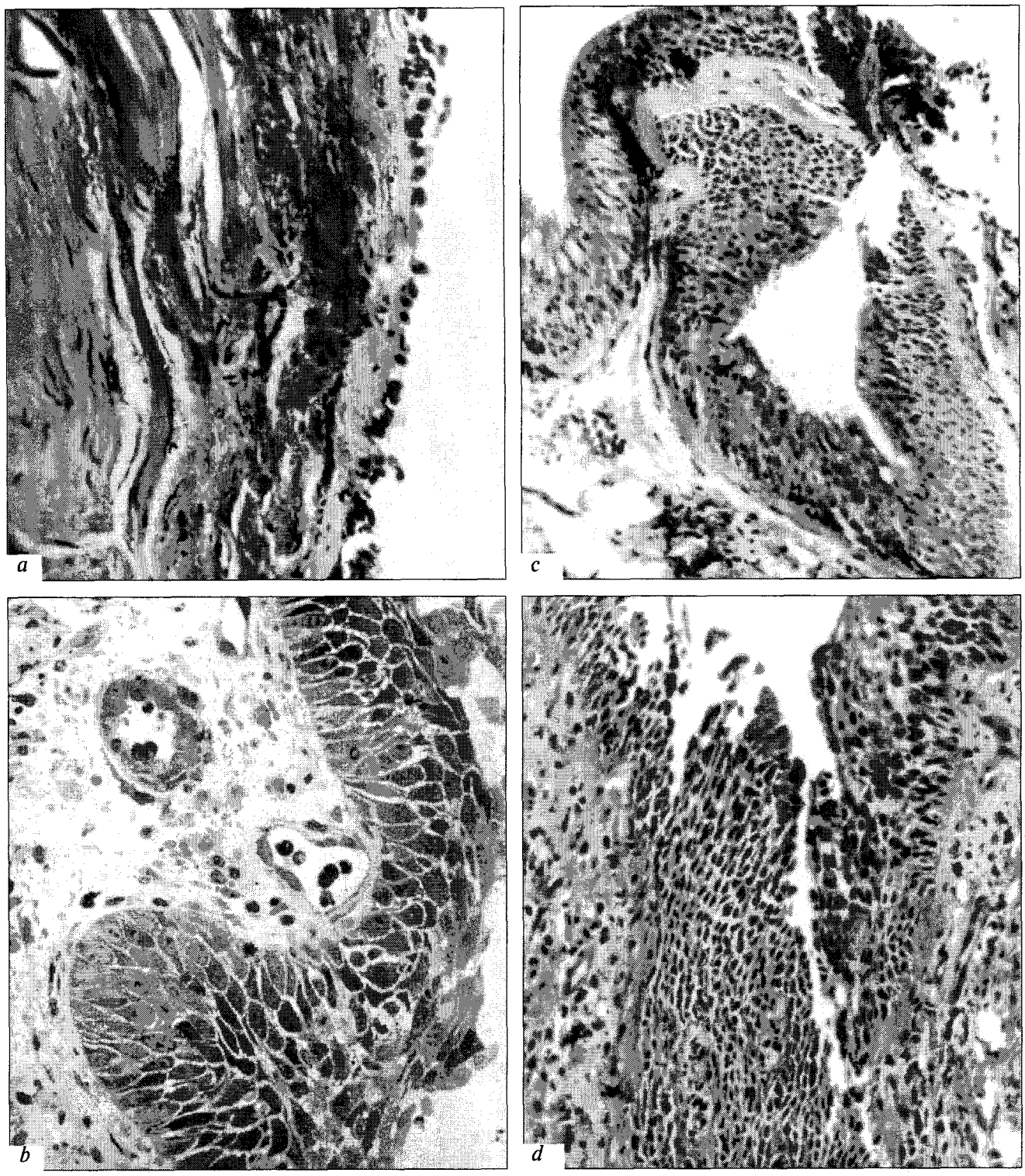

Fig. 1. Light microscopy of large bronchi in chronic pulmonary diseases. *a*) long-term exposure to coal dust and vibration: bronchial epithelium atrophy, sclerosis and hyperelastosis of the lamina propria. Van-Gieson staining, ×250; *b*) exposure to coal dust: bronchial epithelium metaplasia and transformation into multilayer squamous epithelium, uneven thickness of epithelium. Semithin section, azur II staining, ×250; *c*) long-term exposure to radiation: mosaic structure of the bronchial epithelium. Hematoxylin and eosin staining, ×160; *d*) lung cancer: metaplasia and dysplasia of the bronchial epithelium. Hematoxylin and eosin staining, ×250.

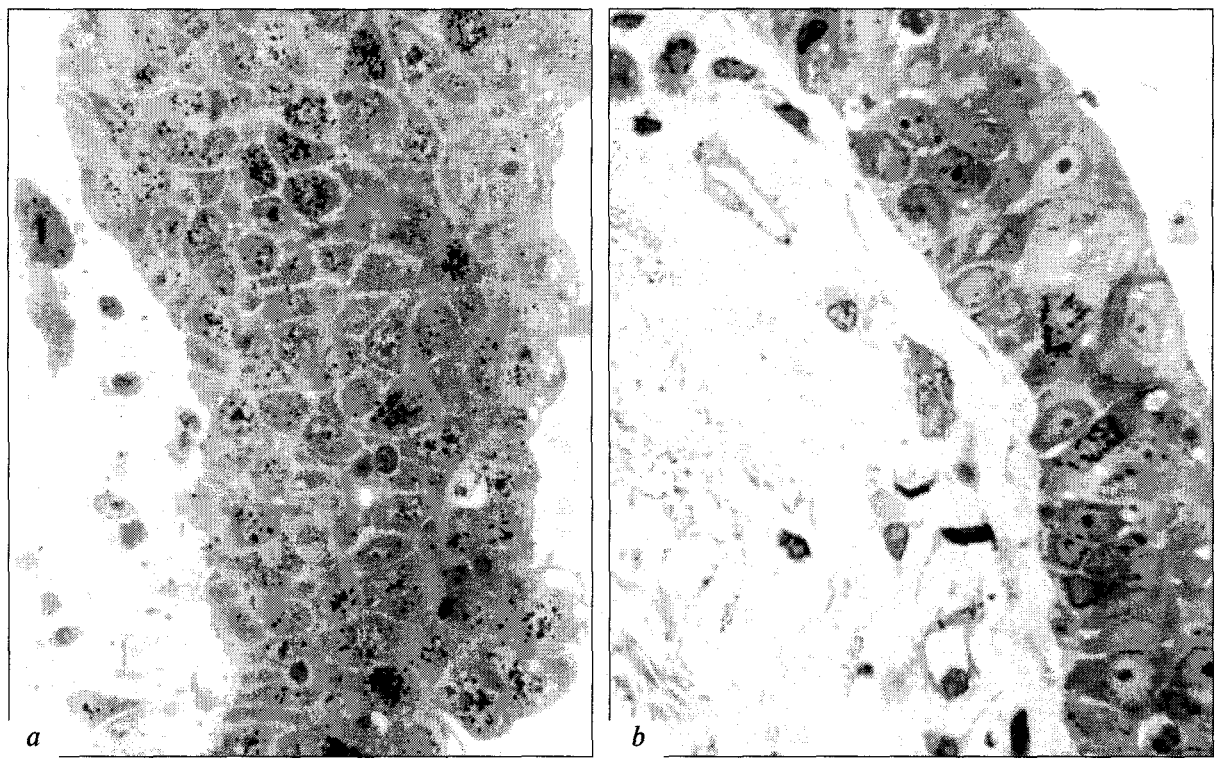

Fig. 2. Autoradiography of biopsy specimens of large bronchi in chronic pulmonary diseases. Semithin sections, incubation with ^{3}H-thymidine, azur II staining. *a*) intensive DNA synthesis in bronchial epitheliocyte proliferation foci, ×400; *b*) low DNA synthesis in atrophy foci, ×600.

bed in this study: it develops in case of essential heterogeneity of structural and biosynthetic reactions of bronchial epitheliocyte population. By their biological essence, all these changes in the bronchial epithelium are manifestations of tissue plasticity and adaptation to various conditions [1].

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