

Pathomorphology of Radiation-Induced Changes in Bronchi in the Long Term after Exposure

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Bronchial biopsies were studied in inhabitants from 3 ecologically contrasting regions in the long term after exposure to radiation. It is established that in bronchial biopsies diffuse atrophy of the mucous membrane is prevalent in the bronchial part of the lungs in an ecologically unfavorable region. Under these conditions a marked decrease of metabolic and proliferative reactions is shown in cell populations of the bronchial wall, as is evident from the data of radioautography *in vitro* and stereological analysis.

Key Words: radiation exposure; bronchi; radioautography; morphometry

At present, much attention is being focused on the influence of different anthropogenic factors on the appearance of pathological processes in the lungs. Radiation injury figures prominently in such pathology, the study of which was triggered by the Chernobyl catastrophe. The respiratory organs are one of the main targets of radiation fallout [13]. This recently led to the appearance of the first clinical-morphological studies of this poorly explored lung pathology caused by radionuclides [2-4]. Concurrently, different methods are being used to elaborate criteria for assessment of the ecological risk [3,11].

The aim of the present investigation was a comprehensive morphological analysis of bronchial biotates from inhabitants of ecologically contrasting Altai regions with different levels of radioactive contamination caused by multiannual tests on the Semipalatinsk' atomic test area [3].

MATERIALS AND METHODS

Morphological examinations were performed on 57 biotates of the bronchial mucous membrane ob-

tained from bronchoscopy. For comparative assessment of the state of the bronchi in persons from different Altai regions all observations were divided into 3 groups. The first group consisted of biopsies from 15 rural inhabitants whose region had been subject to the greatest radioactive contamination [1,13]. The second group included broncho-biopsies from 21 urban men, while bronchial biopsies from the same number of rural men of a region which was free of radionuclide contamination made up the third group.

The bulk of each sample was embedded in paraffin and sections were stained with hematoxylin-eosin in combination with Perls' reaction, staining after Van Gieson, and with Schiff-reagent. The lesser part of biotates was fixed in 4% paraformaldehyde followed by postfixation in 1% osmium tetroxide and, after dehydration, embedding in Epon-Araldite. The semithin sections were stained with Azure II and Schiff reagent. Radioautographic analysis was performed on samples with ^3H -uridine (precursor of RNA synthesis) and ^3H -thymidine (precursor of DNA synthesis), as described elsewhere [9] and included calculation of the index of cell labeling on semithin sections [8]. In morphometric and stereological analysis of the tissue semithin sections were also used for estimation of the structural density of

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capillaries and their surface-volume ratio and the height of an epithelial layer [6]. Statistical processing included calculation of the mean values and their errors.

RESULTS

Comprehensive assessment of the endoscopic picture and of the nature of structural alterations in bronchobioptates of all groups studied allowed us to identify the following morphological variations of bronchial mucous membrane reactions: focal bronchitis of the draining bronchus and diffuse injury of the bronchial tree of the atrophic type or bronchopathy of primary dystrophic genesis. Common features in morphology of atrophic bronchitis and bronchopathy were progressive dystrophic-atrophic alterations of bronchial epithelia, marked sclerosis of the lamina propria mucosae (Fig. 1, *a*), and chronic inflammatory cell infiltration of stroma permanent in bronchitis or facultative in bronchopathies.

Comparison of the data from ecologically contrasting regions showed the prevalence of diffuse damage of the bronchial tree (atrophic bronchitis - 67%, bronchopathy - 20%). A high frequency of dystrophy, atrophy (Fig. 1, *b*, *c*), and metaplasia (100, 67, and 60%, respectively) was noted in the bronchial epithelium.

A significant distribution of diffuse dystrophic-atrophic processes in the bronchial tree was found in the 2nd group. In spite of a predominance here of acute pyo-destructive pulmonary diseases with a marked hyperplastic reaction of the mucous membrane in draining bronchi, in 44% of cases acute destructions evolved against the background of diffuse atrophy of the bronchial tree. The frequency of atrophy and metaplasia of the bronchial epithelium (48 and 38%, respectively) engaged our attention. Probably, the great number of the diffuse dystrophic-atrophic processes in the bronchial mucous membrane is due to the residence of the given group in the atmosphere of an industrial center and/or is related to migration processes from the radionuclide-contaminated regions [3].

Ninety percent of the 3rd group exhibited pyo-destructive processes in the lungs, accompanied by focal bronchitis with a hyperplastic reaction of the mucous membrane in draining bronchi (Fig. 1, *d*). Diffuse atrophic bronchitis was found in this group in 24% of cases and bronchopathy of primary dystrophic genesis was revealed in 5%; thus, alterations of bronchial epithelium differentiation occurred more rarely than in the preceding groups (atrophy - 29%, metaplasia - 14%).

The results of the radioautographic analysis of RNA and DNA synthesis in the mucous membrane of bronchi in all groups studied correlated distinctly with the nature of pathological changes. For example, a considerable decrease of the metabolic and proliferative reactions in bronchial epitheliocytes was noted in chronic atrophic bronchitis and in primary dystrophic bronchopathy (Fig. 2, *a*, *b*). The indexes of metabolic activity were relatively low in pyo-destructive processes which evolved against the background of diffuse atrophy of the bronchial tree, such as atrophic bronchitis or bronchopathy. Indexes of ^3H -uridine and ^3H -thymidine labeling in this group had mean values of 64.5% and 1.51%, respectively. In all cases a marked heterogeneity of RNA and DNA synthesis was revealed in epitheliocytes, this reflecting the diversity of the structural-functional state of the epithelium on the preparation (Fig. 2, *c*).

In pyo-destructive processes in the lungs and the focal hyperplastic reaction in the mucous membrane of draining bronchi the index of ^3H -uridine-labeled cells was significantly higher (Fig. 2, *d*) and ranged from 84.5 to 92.5%. The distribution of ^3H -thymidine-labeled cells in the epithelium was extremely nonuniform and grains of silver were revealed in basal and intermediate cells. A strong positive correlation between the levels of protein synthesis was found for bronchial epitheliocytes and endotheliocytes in all groups studied.

A comparative morphometric study was performed in the three groups with respect to the nature of changes in the bronchi: focal bronchitis, diffuse atrophic bronchitis, and bronchopathy. On the whole, a tissue stereologic analysis of bronchial bioptates revealed definite differences in the spatial reorganization of the mucous membrane. The height of the epithelial layer in large bronchi was found to vary widely in bronchopulmonary pathology. The lowest mean value of this index was noted in primary atrophic processes (bronchopathies). A decrease (by 24% in bronchitis and by 17% in bronchopathy) of the volume density index for capillaries in the bronchial mucous membrane was noted in diffuse atrophic processes as opposed to focal disturbances.

The surface density of capillaries had the highest mean value in bronchopathies. As result, the index of the surface-volume ratio of capillaries was highest in this case and diminished in atrophic bronchitis and focal damage of the draining bronchus (as compared with bronchopathy) by 45 and 33%, respectively.

Analysis of the quantitative and qualitative reorganization of capillaries in bronchopathy showed

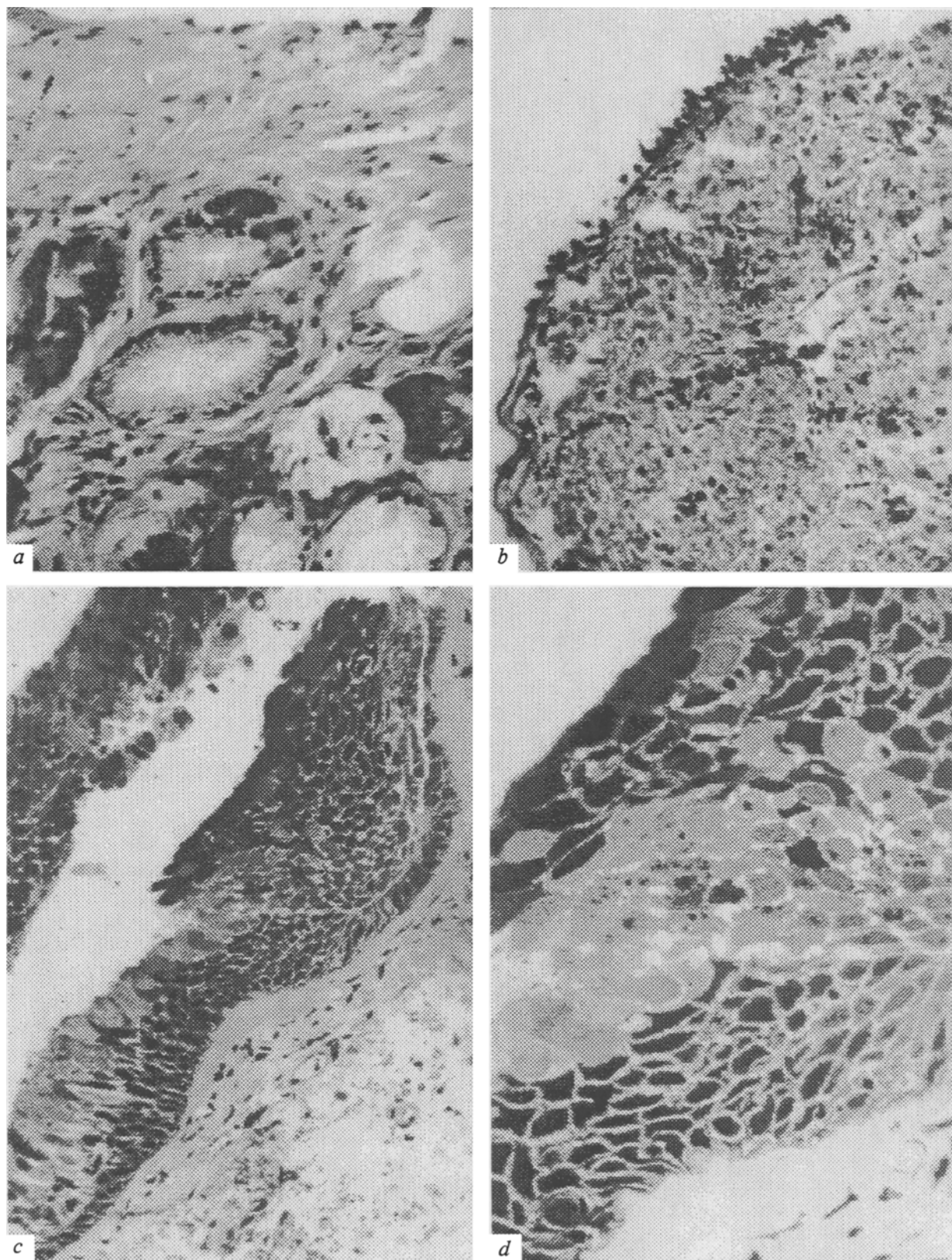


Fig. 1. Light microscopic features of the bronchial mucous membrane in chronic bronchitis and bronchopathies. a) atrophy of bronchial epithelium and thinning and sclerosis of the lamina propria. Hematoxylin-eosin staining, $\times 250$; b) atrophy and partial desquamation of bronchial epithelium and diffuse sclerosis of the mucous membrane in the absence of inflammatory-cellular infiltration. Stained after van Gieson, $\times 160$; c) dystrophy and metaplasia of bronchial epithelium, $\times 400$; d) the same, $\times 1000$.

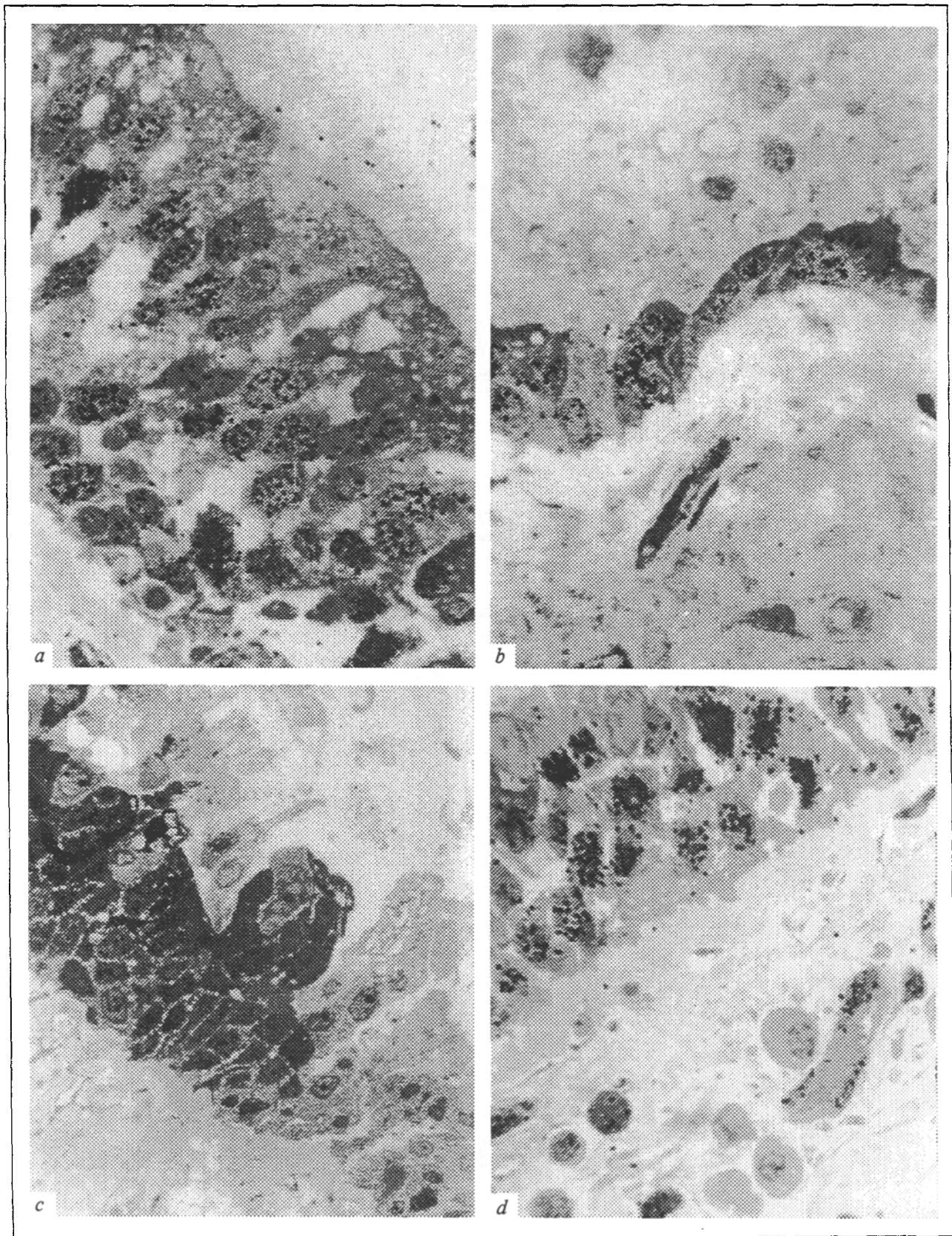


Fig. 2. Radioautographic features of the bronchial epithelium in chronic bronchitis and bronchopathies. Semithin sections stained with Azure II. Incubation with ^3H -uridine. a) high RNA synthesis in the stratified ciliated columnar epithelium; b) low density of ^3H -uridine labeling in the bronchial epithelium in atrophy; c) structural and metabolic heterogeneity of the bronchial epithelium; d) vigorous RNA synthesis in the surface bronchial epithelium. Magnification: a) 1000, b-d) 800.

the high level of surface-volume ratios to be related to abnormal reorganization of microvessels in the bronchial mucous membrane accompanied by significant deformation of the lumen, numerous invaginations of the capillary wall, and marked weakening of biosynthetic reactions in endotheliocytes, this on the whole reflecting the development of plastic unsufficiency of capillaries.

Thus, in the long term after exposure to radiation a diffuse reorganization in the bronchial tree of atrophic phenotype was revealed in persons from ecologically unfavorable regions. Morphological manifestations of atrophy are accompanied by a pronounced decrease of the metabolic and proliferative reactions of bronchial cell populations and by a peculiar spatial reorganization of the mucous membrane structures, on the whole reflecting a state of plastic unsufficiency.

Clinical-morphological aspects of the atrophic changes were described by us previously [10]. Under the conditions studied, disturbances of the processes of differentiation of bronchial epithelium which resulted in atrophy and metaplasia being observed in bronchobiopsies may serve as a morphological criterion of the ecological risk.

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