ELECTRON-MICROSCOPIC INVESTIGATION OF THE INITIAL CHANGES IN EXPERIMENTAL BERYLLIOSIS

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The morphological changes in the respiratory organs caused by beryllium compounds have received inadequate study, especially in the early stage of the process.

Optical microscopic studies have shown that during the first days after intratracheal injection of beryllium oxide into the lungs, its toxic effects are the most pronounced. Severe congestion and edema are observed, and many degenerating cells of the alveolar epithelium are found in the lumen of the alveoli. At the same time intensive proliferation of the cells takes place, with the appearance of "pneumonitis" (the lumen of the alveoli is filled with desquamated cells of the alveolar epithelium, protein, and cells of lymphoid type, with the almost complete absence of polymorphonuclear leukocytes) [1, 2].

The object of this investigation was to study by means of the electron microscope the mechanism of development of the initial changes in berylliosis.

EXPERIMENTAL METHOD

Beryllium oxide at a high degree of dispersion (80% of particles under 2μ in diameter) was injected intratracheally into male albino mice in a dose of 5 mg/ml neutral physiological saline. The animals were sacrificed by decapitation 1-4 days after injection of the compound. Pieces of the lungs were fixed in 1% osmium tetroxide solution buffered with veronal-acetate buffer (pH 7.4) and embedded in a mixture of methyl and butyl methacrylates. The material was stained with phosphotungstic acid and uranyl acetate.

EXPERIMENTAL RESULTS

Electron micrographs of the particles of beryllium oxide showed that they measured 0.25-4.5 μ. In their external appearance they were amorphous, of different density at the center and periphery, and with uneven edges.

The localization of the particles of beryllium oxide in the lung varied: they were found in the lumen of the alveoli and among the ground substance of the basement membrane of the alveolar septum, beyond which they did not penetrate. Everywhere in the tissues, the particles of beryllium oxide were surrounded by protein, with which they formed a protein-beryllium complex (Fig. 1). The protein of the complexes was evidently formed by breakdown of the cells from the toxic action of beryllium oxide on them, by removal of proteins from the blood as a result of the toxic action of this compound on the capillary walls, and also by contact between the beryllium oxide and the ground substance of the connective tissue. On the first day the protein of the complex appeared homogeneous. On the fourth day, it acquired a definite structure, i.e., ill-defined fibrils appeared in it. Evidently, these structural changes in the protein were associated with changes in the large quantities of polymerized mucopolysaccharides contained in the ground substance of the connective tissue surrounding the beryllium. Depolymerization of the mucopolysaccharides led to the appearance of the fibrillary structures [3].

At the times of observation the basement membrane of the alveolar walls showed considerable changes: it was swollen (in some places its thickness was 0.4 μ compared with a normal 0.05-0.1 μ), and depolymerized and dissolved in the abundant edema fluid filling the septal space (Fig. 2).

The conditions were thus created for free migration of the cells, as a result of which alveolar cells measuring 5-15 μ in diameter appeared in the lumen of the alveoli along with the protein-containing fluid. These cells had

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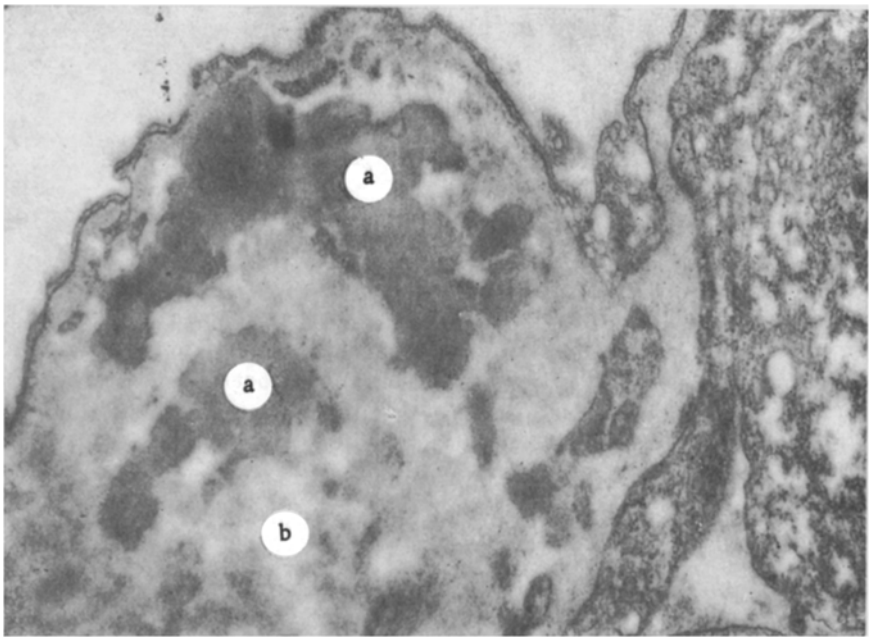

Fig. 1. Beryllium-protein complex during the first day after injection of the compound. a) Particles of beryllium oxide, b) homogeneous protein. Magnification 37,000×.

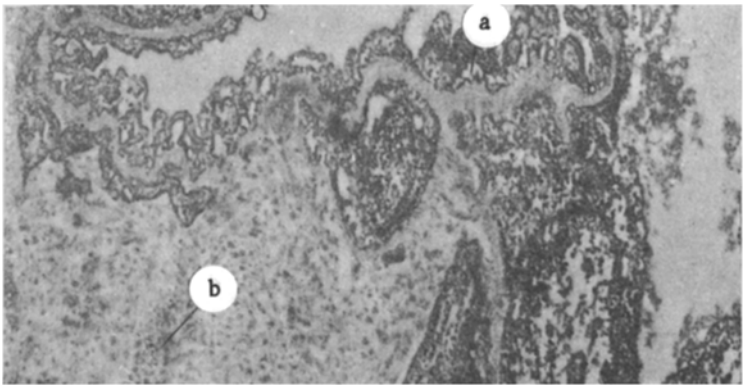

Fig. 2. Basement membrane of alveolar septum. a) Marked swelling of basement membrane; b) basement membrane dissolving in edema fluid. Magnification 17,500×.

many microvilli, pseudopodia, and vacuoles with light and dark contents, consisting of lipid granules and fragments of phagocytized and partially destroyed erythrocytes and foreign particles [4]. These cells were evidently large alveolar and free cells. The presence of pseudopodia and vacuoles, arising mainly by pinocytosis, demonstrates the phagocytic activity of these cells, directed toward the removal of the foreign substance—beryllium oxide.

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