A MODEL OF EXPERIMENTAL LUNG CANCER CAUSED BY
INTRATRACHEAL INTRODUCTION OF RADIOACTIVE CERIUM

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The overwhelming majority of observations on the cancerogenic action of ionizing radiation have been related to tumors of the skeleton, skin, gastrointestinal tract, liver, kidneys, endocrine glands, mammary glands, etc., arising in animals after external irradiation or the introduction of radioactive materials into the organism. As far as lung tumors are concerned, induced by radioactive substances inhaled into the organism, the literature contains only a small amount of data pertaining to the frequency with which these tumors develop, and the dependence of their development on the amount of energy absorbed, the physicochemical properties, character of distribution, and excretion of the radioactive materials from the lungs, and the species of the animals [1,2,4,6-15]. In this case, the morphological investigations are limited to the diagnostics of the tumors.

One of the most frequent routes for access of radioactive substances into the organism is via the organs of respiration. Thus, experimental study of the histogenesis and pathogenesis of lung cancer is of important theoretical and practical interest, this lesion being one of the most possible, primary localizations of malignant tumors in individuals that come into contact with radioactive substances in the course of their work.

The reproduction of lung tumors is associated with great difficulties [3]. The observations noted above, relative to the cancerogenic action of ionizing radiation, were performed mainly on small laboratory animals. However, for complex, multifaceted investigation of the same material, it is more expeditious to develop models of malignant tumors in larger animals.

We set up experiments for the reproduction of lung cancer in rabbits, using a radioactive material.

EXPERIMENTAL METHOD

The basis of the experiments are the data of Cember [9], who produced lung cancer in white rats of the Sprague-Dawley line, after intratracheal introduction of a colloidal solution of cerium-144 fluoride. The experiments were performed on 20 rabbits of the chinchilla family, weighing from 2.5 to 3 kg, and 220 white rats, weighing 180 ± 20 g. The colloidal solution of cerium-144 fluoride (Ce$^{144}$F$_3$) was prepared from cerium-144 chloride.* The dimensions

* Cerium-144 is always found in equilibrium with praseodymium-144. Cerium-144 is a $\beta$-$\gamma$-radiator, with an energy of its $\beta$-particles of 3.1 MeV, and its $\gamma$-quanta, 1.25 MeV. The half-life of cerium-144 is 275 days, and of praseodymium-144, 17½ min. The period of half-excretion of cerium-144 chloride from the lungs, with introduction of inhalation, is 24 h [5], and cerium-144 fluoride, 8 days (our data).
of the particles of this material were equal to 25 millimicra, and the charge (Z-potential) to $2.4 \times 10^{-2}$ microvolts. Intratracheal introduction of the material into the rabbits was carried out with a syringe, by piercing the anterior wall of the trachea without incision of the skin or the use of anaesthesia; in the case of the rats, the animals were narcotized and a skin incision first made. In the first case, each animal was given 0.5 ml of the solution, and, in the second, 0.1 ml. In both cases the activity of the material within the indicated volumes was equal to 25 microcuries. The rabbits were observed up to the time of their natural deaths, in order to ascertain the possibility and frequency of arising of the tumors. The rats were sacrificed at various intervals after introduction of the material for dosimetric and autographic investigations.

**EXPERIMENTAL RESULTS**

In the first few days, the cerium-144 fluoride was more or less equally distributed in one or both lungs; then, it was very rapidly concentrated (4th-6th day) in the root zone of the lungs and in the lymph nodes of the mediastinum, remaining there in large amounts for a long period of time (Fig. 1). Thus, for example, after 128 days, approximately 20% of the material introduced was observed in the lungs. The period required for excreting half the material from the lungs was 8 days. Thus, prolonged ionization of the pulmonary tissue took place, especially in the region around the lung roots.

Microscopic investigation of the lungs from the dead animals showed that, beginning with the first days after introduction of the cerium-144 fluoride, an acute bronchopneumonia could develop, with transition into the chronic form. In this case, we traced all the stages in the development of pneumosclerosis, beginning with the development of granulation tissue and up to the formation of coarse-fibered connective tissue with associated massive bronchiectasis. As a rule, these changes were observed in the lung root zone, and in the interstitial tissue of the mediastinum, corresponding to the localization of the radioactive material. Sometimes the bronchiectases attained huge proportions, forming large abscesses more than 2 cm in diameter. These abscesses, as well as the fine bronchiectatic cavities, always contained purulent exudate. After longer periods of time (100 days or more), it was possible to observe the signs of proliferation and atypical growth of the altered cells in the bronchial epithelium, in addition to metaplasia and proliferation of the alveolar epithelium with formation of the glandular-like structures characteristic for pneumosclerosis of any etiology. At later intervals, these formations took on a highly branching structure. Half the animals died from the lung changes described above in the period from 60 to 238 days after introduction of the material. One rabbit died on the third day, from acute suppurative bronchopneumonia.