HISTOLOGICAL INVESTIGATION OF THE EXPERIMENTALLY AUTOTRANSPLANTED LUNG

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The replanted lung is a classical model for the study of the changes arising after transplantation in conditions when tissue incompatibility is absent. This operation has been used clinically for the treatment of bronchial asthma [9].

The results of the experimental study of the problem show that in the absence of technical faults, the indices of external respiration, which are changed in the early stages after the operation, return toward normal within a few months [12, 13, 18]. Some authors [16, 17, 19] have reported a decrease in the oxygen absorption and an increase in the pressure in the pulmonary artery even in the later stages after the operation (1.5-2.5 years). The histological structure of the transplanted lung, according to most authors, shows no significant change, although in a few cases foci of emphysema appeared [16, 17]. In cases of thrombosis of the veins of the lung and left atrium, the muscle layer of the small arteries of the lung undergoes hypertrophy and they are converted into vessels of "shunt" type [2].

One of the most important aspects of the problem of transplantation of the lung is that of restoring the nervous regulation of the functions of the transplanted organ. It has now been established conclusively that injury to the nervous connections caused by division of the structures at the hilum of the lung is one of the causes of the development of structural and functional changes in the lung. Some investigators who have performed experimental transplantation of the lung in animals have associated the disturbances of the function of the transplanted organ with injuries to the nerve fibers, expecially of the vagus nerve. In this connection the further development of research along the lines of the study of the nerve structures of the lungs after transplantation is of considerable interest. In the present investigation the autotransplanted dog's lung was studied histologically.

EXPERIMENTAL METHOD

Experiments were carried out on dogs. Autotransplantation of the lung was performed by Yu. Ya. Rabinovich [10] by the following method.

Lateral thoractomy on the left side was performed under endotracheal anesthesia. The main bronchial arteries were divided and ligated. The left main bronchus and the pulmonary artery were clamped and divided. A clamp was applied to the left atrium, and the lung was then removed, forming a cuff from part of the wall of the left atrium with the orifices of the pulmonary veins. The lung was withdrawn from the pleural cavity for 5-10 min, after which it was replaced. The wall of the left atrium was joined to the cuff formed from the wall of the left atrium and the orifices of the pulmonary veins by means of a П-shaped everting suture. The divided ends of the pulmonary artery were sutured end-to-end. The clamps were then removed from the atrium and the pulmonary artery and the circulation was restored. The left main bronchus was joined by interrupted sutures, passing through all the layers of the bronchial wall. The lung was inflated and the chest wall closed without drainage. In these experiments the lung was excluded from the circulation for 1.5-2 h.

The replanted lungs in 13 dogs were examined histologically between 1 day and 17 months after the operation. Seven animals died during the first 10 days (2 from hemorrhage, 3 from thrombosis of the venous anastomosis, 2 from pneumonia, complicating stenosis of the bronchi). The remaining 6 dogs

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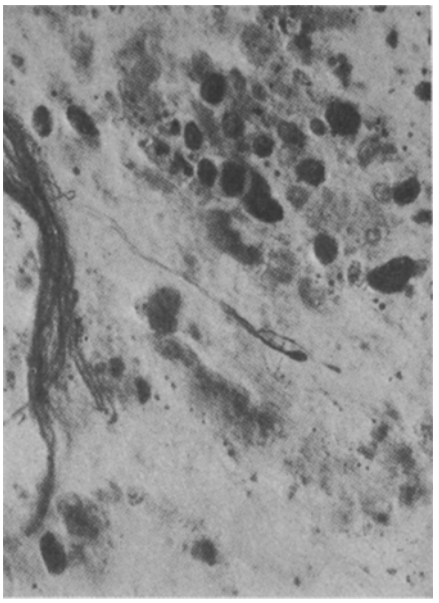

Fig. 1. Regenerating nerve fibers in the wall of the main bronchus of a transplanted lung 8 days after the operation. Bielschowsky–Gros. 280×.

Fig. 2. Degeneration and cystic changes in the mucous glands of the bronchus 44 days after the operation. Hematoxylin–eosin. 120×.

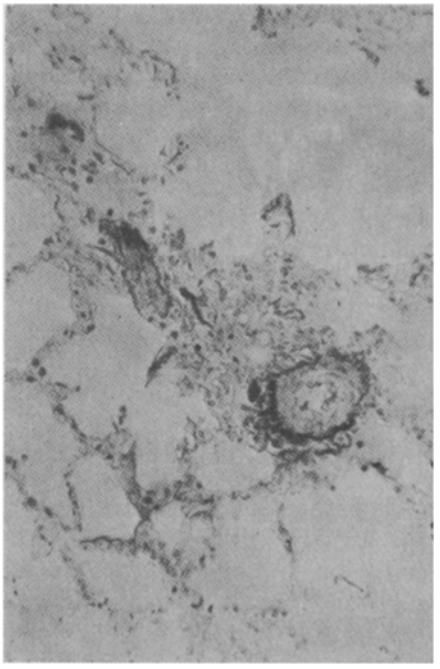

Fig. 3. Gross thickening of the intima of an intralobular vein. Picrofuchsin–fuchselin. 250×.

developed no complications after the operation, and they were sacrificed by intravenous injection of thiopental.

Sections from the various parts of the lungs were stained by the Bielschowsky–Gros method, with picrofuchsin-fuchselin, with toluidine blue, and with hematoxylin-eosin. During the operation the esterase and lipase activity of the lung tissue was investigated. No difference was found in the localization and activity of these enzymes during the period of 1.5-2 h during which the lung was excluded from respiration and the circulation.

The state of the nervous structures in the wall of the main bronchus of the transplanted lung was studied in the first month after the operation on the dogs. Areas of the bronchial wall 1-2 cm distally to the suture were taken for examination.

EXPERIMENTAL RESULTS

Between the 3rd and 5th days after the operation the medullated nerve fibers in the wall of the main bronchus of the transplanted lung degenerated. The absolute majority of the nonmedullated fibers remained intact. The same was true of the nerve cells contained in the nerve plexus of the bronchial wall.

At the beginning of the 2nd week after the operation, numerous thin nonmedullated nerve fibers began to appear in the sections, with pools of neuroplasm at their ends in the form of bulbs of growth (Fig. 1). This was evidence of ingrowth of regenerating nerve fibers and of the gradual restoration of the connections between the transplanted lung and the central nervous system. Between 4 and 17 months after the operation no abnormal nervous structures could be seen in the investigated region.

The authors consider that the concept of "transplanted lung" cannot be identified with that of "completely denervated lung." Many investigators [4, 6, 8] have found that in the wall of the large bronchi and along the course of the branches of the pulmonary artery there are nerve plexuses, containing many nerve cells, some single and others in groups. Connections between the nerve cells of the peripheral autonomic ganglia, responsible for the transmission of local reflex reactions, have been demonstrated morphologically [7]. These findings have been confirmed by the results of physiological investigation [1, 11]. Transplantation of the lung does not therefore disturb the integrity of the nerve cells and of their connections within the lung. The nerve pathways joining the transplanted organ to the central nervous system are, however, injured. This is one of the reasons why marked changes in the bronchial glands were observed in all cases, irrespective of the presence or absence of complications.

Starting on the 2nd-8th day after the operation, mucus was observed to be absent from the lumen of the glands, the glands were dilated to form cysts, and their cells showed necrobiosis. Investigations 8-11 days and 1 month after the operation revealed dedifferentiation, so that the cells contained very dense cytoplasm and were no longer cylindrical in shape, but flattened, like regenerating structures (Fig. 2). The number of glands was considerably reduced 1.5 and 17 months after the operation. Acidophilic masses were visible in their lumen, giving a negative reaction for metachromasia with toluidine blue. Sclerosis of the submucosa of the bronchus could be seen between the small, atrophic vesicles. This phenomenon of the suppression of secretion of the bronchi may be the factor responsible for the beneficial clinical effect of autotransplantation of the lung on the picture of bronchial asthma [9]. However, the results of these investigations revealed severe changes in the blood vessels of the dogs' lung after this operation, so that care is necessary when applying it to clinical conditions. After 1 and 17 months, for instance, despite the absence of thrombosis of the orifices of the pulmonary veins and of the left atrium, obvious signs of venous hypertension were observed in the pulmonary system. In cases not complicated by thrombosis of the veins, the intralobular veins possessed a highly corrugated wall, picrinophilic masses were deposited between the tunica elastica and the endothelium, and muscle fibers appeared, as are characteristically found in the venous hypertension associated with mitral defects. As a result of these changes the lumen of the veins was greatly narrowed (Fig. 3). The study of the region of the venous anastomosis showed that in every case the myocardial structures surrounding the orifice of the pulmonary veins had been divided. Recent investigations [5] have shown that disturbance of the function of these "presses" in man leads to an increase in the resistance of the veins within the lung; this is of compensatory importance in preventing the regurgitation of blood from the left atrium into the capillaries of the lung.

Any autotransplantation, even if free from complications, is accompanied by division of the myocardial presses. The operation may thus be complicated by the development of pulmonary hypertension, for which there is physiological evidence [16, 17].

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