

ACTION OF HYALURONIDASE ON EXPERIMENTAL PLEURAL ADHESION FORMATION

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After injection of hyaluronidase into the pleural cavity of rabbits in which adhesions had been found experimentally, disorganization of the connective tissue of the adhesions took place, as a result of which the adhesions became looser and less dense in structure and underwent partial absorption.

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Experiments on animals [5] have shown that hyaluronidase has a disintegrative action on connective tissue, inhibiting the formation of new scars and breaking up old scars. Hyaluronidase has been used clinically with good results in the treatment of scars of varied etiology [4] and of Dupuytren's contracture [6]. The combined use of hyaluronidase and hormones for treatment of chemical burns of the esophagus has been suggested [1]. Workers studying the action of hyaluronidase on intraabdominal adhesions [2, 7, 8] have found that hyaluronidase has no significant effect on the number of adhesions, but reduces their density.

We set out to study the effect of hyaluronidase on adhesion formation in the pleural cavity.

EXPERIMENTAL METHOD AND RESULTS

Experiments were performed on 42 rabbits. To produce inflammatory changes in the pleural membranes and induce adhesion formation, 0.2 ml of 0.5% iodine solution was injected into the pleural cavity of the animals by D. I. Golovin's method [2] daily for 7 days. As a result, the animals developed aseptic pleural effusions with the formation of adhesions, the presence of which was verified roentgenologically. One month later, injections of hyaluronidase into the same pleural cavity began. The Soviet preparation lidase was used, 1 g of the dry substance being dissolved in 1 ml 0.25% procaine hydrochloride solution, and 0.5 ml of the solution being injected daily into the rabbit's pleural cavity.

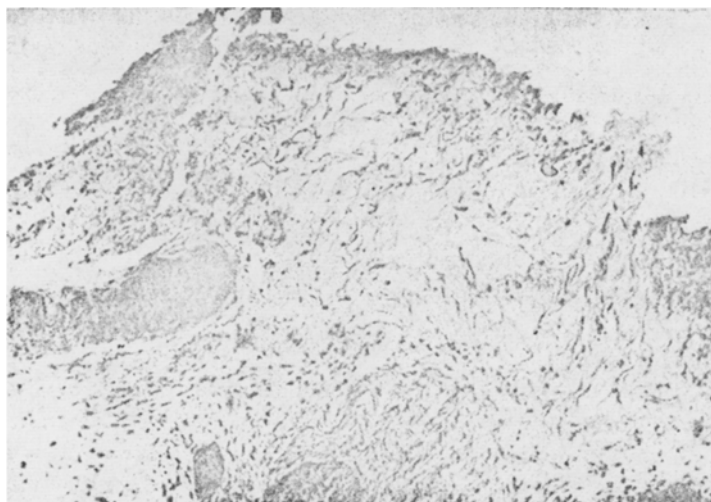


Fig. 1. Tissue of an adhesion consisting of collagen fibers with a few cells. Hematoxylin-eosin. 420 \times .

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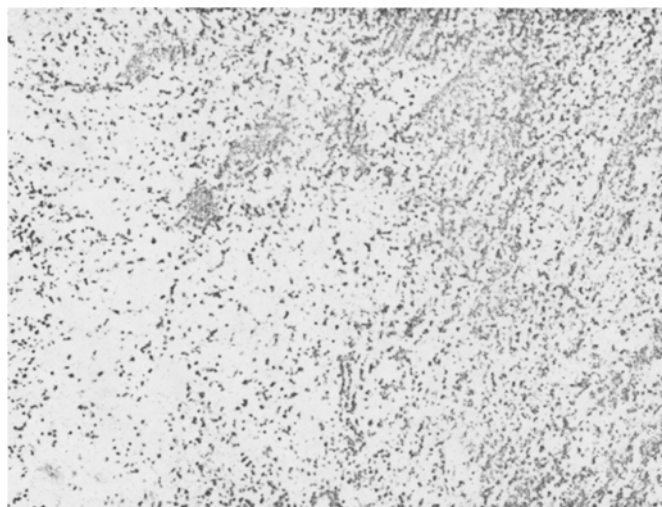


Fig. 2. Tissue of an adhesion with extensive infiltration by lymphocytes and histocytes. Van Gieson. 420 \times .

Four series of experiments were performed: in series I lidase was injected into five animals for 5 days, in series II it was injected into five animals for 10 days, in series III 15 injections were given to 10 animals, and in series IV 20 injections were given to 10 animals. Each group also included three control rabbits, which did not receive lidase.

All the animals were sacrificed at the end of the experiment. Necropsy showed that adhesions were present in the pleural cavity of the experimental and control animals between the parietal and visceral layers of pleura. However, in the animals receiving lidase, fewer adhesions were found, and they were loose in structure, juicy, and highly vascularized. These changes were more marked in the animals receiving the largest dose of lidase. The adhesions in the control animals were coarser and in places they were very dense, with fewer blood vessels.

The layers of pleura and adhesions were examined histologically and histochemically. The material was fixed in 10% formalin and embedded in paraffin wax. Sections were stained with hematoxylin-eosin, and by the methods of Van Gieson and Foot, and tested histochemically for mucopolysaccharides (Hale's reaction for metachromasia with differentiation of acid mucopolysaccharides, PAS reaction).

A study of the histological preparations showed that the adhesions in the control animals consisted of properly formed connective tissue with well defined collagen fibers and a few blood vessels. The cells were mainly fibroblasts with a few lymphocytes (Fig. 1). Argyrophilic fibers were detected by appropriate staining only in certain areas. Staining with toluidine blue revealed well marked metachromasia. With Hale's reagent a positive reaction for hyaluronic acid was obtained.

The tissue of the adhesions in the rabbits receiving hyaluronidase was very edematous and loose in structure, and its blood vessels were engorged with blood. Around the vessels, and sometimes independently of them, extensive zones of infiltration were found, consisting of lymphocytes and histocytes: The fibroblasts were swollen, and here and there solitary mast cells with metachromatically stained granules were found (Fig. 2). The collagen fibers stained unevenly, they were more loosely arranged, and in some places they had broken up into a mass of small granules. Areas of irregular eosinophilia were seen, containing a substance binding colloidal iron. The metachromasia reaction was ill defined. All these changes were very pronounced in the animals receiving the largest dose of lidase. These changes in the connective tissue caused by hyaluronidase lead to loosening of the structure of adhesions, to a decrease in their density, and to their partial absorption.

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