the absence of any organic damage to their motor apparatus. Retesting of the patients (after the end of a course of treatment) revealed cells with motile cilia actually in biopsy material from the bronchial mucosa. Inhibition of ciliary movement can perhaps be explained by the presence of a factor, disturbing ciliary activity [6], in the bronchial secretion of patients with bronchial asthma.

Motile glycerol models of ciliated epithelial cells can thus be obtained from the human bronchial mucosa and used to determine the presence or absence of organic disturbances of structure and function of the ciliary apparatus in various forms of bronchopulmonory pathology.

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REACTION OF FIBROBLASTS OF LOOSE CONNECTIVE TISSUE TO POLY-4-VINYLPYRIDINE

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Loose connective tissue is involved in many processes taking place in the body, and its cells actively respond to the action of both endogenous and exogenous factors. For example, after injection of toxins or of a reacting dose of an antigen into a sensitized recipient, intensive vacuolation of the cytoplasm and enlargement of the processes of fibroblasts and macrophages are observed [3, 8]. However, it is virtually impossible to detect all the cells and to estimate the size of their processes in histological tissue sections. For this purpose total (film) preparations of loose connective tissue are required [1]. By means of histological stains it is difficult to identify electively the boundaries of the cytoplasm of fibroblasts, and to do this it is possible to use animal sera containing antibodies against cytoplasmic components of fibroblasts; if these are used, the immunofluorscence method can reveal the outlines of the cells, including processes and fragments of cytoplasm isolated as a result of clasmacytosis. Human or animal sera containing natural antibodies or antibodies appearing as the result of development of a pathological process can be used. Such antibodies as a rule possess high tissue specificity and are often used in immunomorphological research as a tool [12, 13, 15]. Antibodies to fibroblast antigens have been found in human and animal sera [4, 7, 15]. Since the character of action of polymers, including poly-4-vinyl-pyridine (PVP), which has been used experimentally to stimulate the immune response [6, 9, 11], on different cells has been inadequately studied, it is interesting to investigate, in particular,

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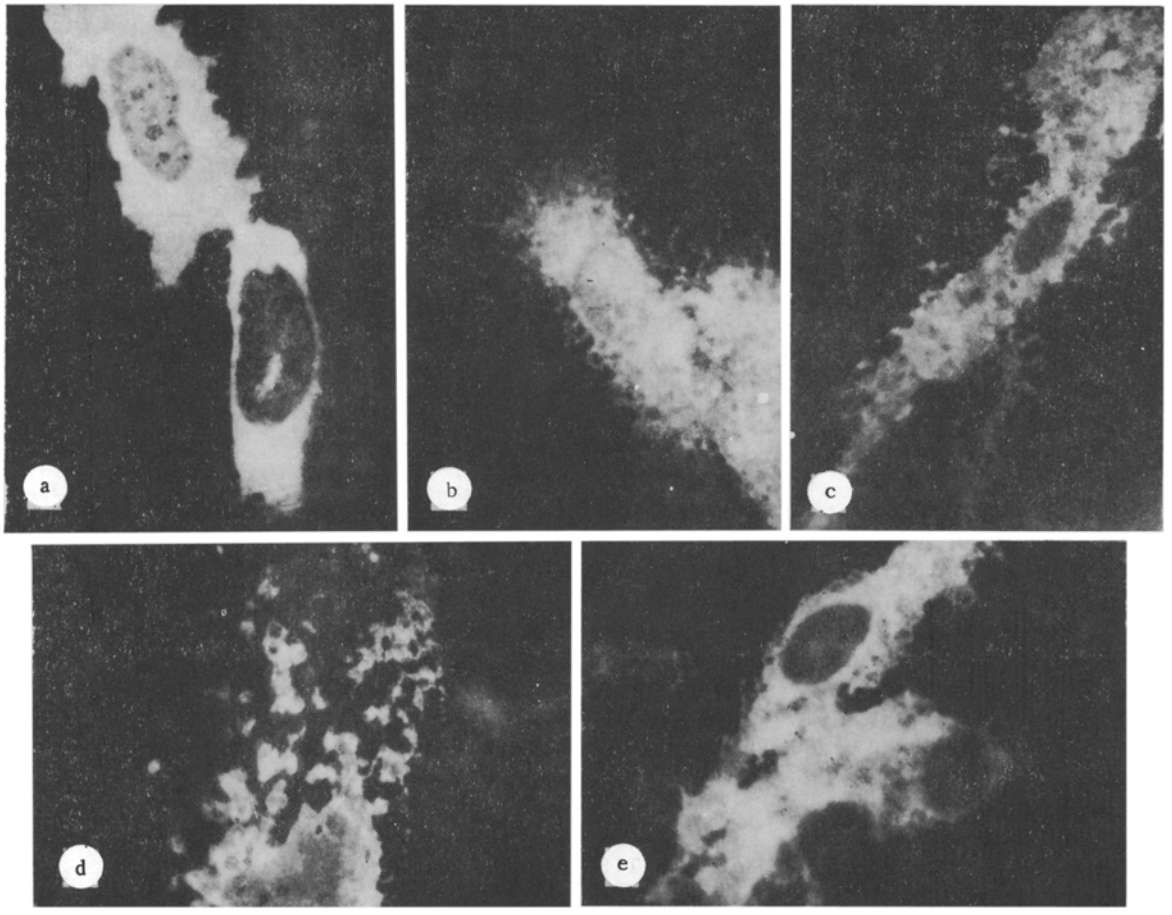

Fig. 1. Loose connective tissue of a mouse: a) fibroblast of intact mouse, b) fibroblast 1 h after injection of PVP; cell outlines became more tortuous, vacuoles appeared in cytoplasm, c) fibroblast 3 h after injection of polymer: cytoplasmic processes are larger, clasmacytosis appears, d) fibroblast 5 h after injection: clasmacytosis sharply intensified, e) cells 48 h after injection of polymer: reaction of fibroblast surface absent, a few vacuoles remain in cytoplasm. Total preparation. Treatment with rabbit serum containing antibodies reacting with cytoplasmic antigens of fibroblasts. Indirect immunofluorescence test. Objective 90× (oil immersion), ocular homal 3.

the state of the tissue cells of the interstitial medium of the body in response to administration of this polymer. The aim of the present investigation was an immunofluorescence study of the reaction of fibroblasts in loose connective tissue to administration of PVP.

EXPERIMENTAL METHOD

Noninbred albino mice and CBA mice weighing 16-18 g were used. A solution of PVP was prepared by the addition of 0.5% acetic acid. The mice were given a single intravenous injection of 0.2 ml of a 1% solution of PVP in a dose of 100 mg/kg body weight. As the control, animals were given an injection of 0.2 ml of 0.5% acetic acid solution. The mice were killed 1, 2, 4, 6, 18, and 24 h and 2-5 days after the injection by ether anesthesia. Total preparations of subcutaneous loose connective tissue were prepared by the method described previously [1]. Rabbit sera containing natural antibodies against fibroblast cytoplasmic antigens were used. Pure antibodies to rabbit immunoglobulins, labeled with fluorescein isothiocyanate, were used for the immunofluorescence tests. The method of isolation and labeling of the antibodies was described previously [2]. After preparation of the total preparations they were air-dried for 10 min, after which rabbit serum was applied to them in a dilution of 1:5-1:10. The preparations were placed in a humid chamber for 45 min at room temperature, washed in buffered physiological saline (BPS), pH 7.2, for 10 min, and treated for 30 min with labeled antibodies against rabbit immunoglobulins. After washing in BPS the preparations were mounted in 60% neutral glycerol and examined in the LYUMAM-2 luminescence microscope with 5× ocular and

40× (water immersion) and 90× (oil immersion) objectives. Photographs were taken on RF-3 film with homal 3 ocular. Some preparations were fixed and stained with Weigert's iron-hematoxyline as the morphological control.

EXPERIMENTAL RESULTS

When total preparations of subcutaneous loose connective tissue from intact mice were treated with serum containing natural antibodies, the majority of tissue cells were discovered: fibroblasts, histiocytes, mast cells, etc. The most numerous group consisted of cells with morphological features of fibroblasts, as was clearly visible after staining with hematoxylin and by immunofluorescence. In the immunofluorescence test they appeared elongated, their cytoplasm gave off numerous short processes, but these could not be detected after staining with hematoxylin. The borders of the cytoplasm gave bright green fluorescence, the outlines of which stood out against the dark background of the ground substance. Components of the nucleus did not take part in the reaction, and for that reason the territory of the nucleus appeared to be darker than the cytoplasm (Fig. 1a). The boundaries between the ectoplasm and endoplasm were not always observable. Macrophages preserved their morphology in the immunofluorescence test and could be identified sufficiently easily. They were round in shape and had a few short pseudopodia. The mast cells are not numerous in mice, and in the preparations they were distinguished by the stronger fluorescence than that of other cells, and sometimes typical granules could be seen alongside them. Changes in outlines of the fibroblasts were observed 1 h after injection of the polymer. Their outlines became more tortuous, the number of their processes increased, as also did the number of vacuoles in their cytoplasm (Fig. 1b). Later (after 2-3 h) the cytoplasm of the fibroblasts appeared frothy, and small fragments began to detach themselves from it (clasmacytosis), which also reacted positively with serum (Fig. 1c). After another 2-3 h, clasmacytosis was more marked (Fig. 1d). Later these changes gradually disappeared. After 2-3 h the structure of the fibroblasts in the loose connective tissue of the mice was restored (Fig. 1e). After injection of the polymer, the macrophages showed less severe changes. Mainly only the number of cytoplasmic processes was increased. The mast cells showed active degranulation, accompanied by the spread of a large number of brightly luminescent granules around the cell. Intravenous injection of 0.2 ml of 0.5% acetic acid solution into mice in the control experiment caused no visible reaction of the connective-tissue cells.

A single intravenous injection of PVP solution into mice in the dose used experimentally to stimulate immunogenesis in mice [6, 9] was thus accompanied on the 1st day by a marked reaction of fibroblasts of the loose connective tissue, in the form of the appearance of numerous cytoplasmic processes, vacuolation of the cytoplasm, and clasmacytosis. These phenomena were demonstrated more electively by immunofluorescence than by staining with hematoxylin. The structure of the cytoplasm of the fibroblasts 2-3 days after injection of the polymer was completely restored. Some workers suggest [5] that the mechanism of action of the polymer on the body cells is associated with its ability to combine with proteins of the cytoplasmic membrane. Such interaction in lymphoid organs, which has a mitogenic effect, is accompanied in particular by increased proliferation and differentiation of B cells [6]. The same mechanism evidently lies at the basis of the reaction of fibroblasts also to injection of PVP. Interaction of polymer with membrane is accompanied by stimulation of the numerous cell surface receptors. The nonspecific stimulus of the receptors induces inappropriately violent metabolic reactions, which are expressed morphologically as a rapid change in size of the cell surface. The response of loose connective tissue fibroblasts may perhaps be used to assess the degree of biological activity of polymers.

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MINUTE RHYTHMS OF HALOPERIDOL-INDUCED CATALEPSY IN RATS

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Processes taking place in the brain have a precise temporal organization, and in turn, this affects fluctuations of activity of various neurotropic drugs. This state of affairs is confirmed by analysis of the as yet limited information in the literature on the role of the circadian rhythm of work of the brain in the action of psychotropic drugs [2]. During recent years shorter fluctuations, measured in minutes and tens of minutes, in the behavior and brain activity have assumed great functional importance [1, 3]. It is also important to take these fluctuations into consideration when the properties of psychotropic drugs and, in particular, the cataleptogenic effect of neuroleptics, are evaluated.

The aim of this investigation was to study rhythmic fluctuations of catalepsy after administration of haloperidol (HP).

EXPERIMENTAL METHOD

Experiments were carried out on 16 noninbred male albino rats weighing 200-300 g. For visual and graphic recording of the intensity of neuroleptic-induced catalepsy, we used our own modification of the holding onto a horizontal rod test [5]. The time during which the rat held on to the rod, hanging down from it and grasping the rod with its forelimbs, was counted. These determinations were carried out every minute for 2-4 h. HP was injected intraperitoneally in doses of 0.25 to 2 mg/kg. There were two series of experiments: In one of them the animals were given the same cataleptogenic dose of the neuroleptic in repeated tests. In the other series the effect of increasing doses of the drug was assessed after different times. In both series the interval between injections was not less than 4 days. Observations on each rat were repeated on average 5 times. In some investigations progressive accumulation of the drug took place in the course of one experimental day. The anticataleptogenic action of dopa (levodopa in a dose of 25, 50, or 100 mg/kg) was determined against the background of HP. The animals were kept in the animal house and allowed food and water *ad lib*. Natural illumination was provided and the experiments were carried out at the same time of day. There were altogether 70 experiments on two groups of rats: 42 experiments in winter (January-February) and 28 in spring (March-May).

The results of individual experiments were analyzed by the sliding means method [6]. To discover a periodic process the data were subjected to autocorrelation and spectral analysis on the Nairi-2 computer.

EXPERIMENTAL RESULTS

Under the influence of a cataleptogenic dose of HP (starting with a dose of 0.25 mg/kg)

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