EXPERIMENTAL PULMONARY DYSTROPHY

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The experimental pharmacological treatment of pathological processes inevitably encounters the difficulty of finding an appropriate model. Although numerous and varied methods for reproducing various pathological processes have been worked out, because of features of the development and course of these processes, they are not always suitable for experimental therapeutic studies.

In order to reproduce pulmonary damage experimentally, frequent use has been made of acute toxic pulmonary edema induced by the injection of adrenalin, ammonium chloride, phosgene, or other chemical substances. Such damage is usually extremely severe, and causes rapid death.

The difficulty of using the models referred to above for pharmacological treatment of impaired pulmonary function has been the stimulus to a search for other models.

In working out this method of impairment of pulmonary function, we were guided first by the work of A. V. Tonkikh [4,5], who found that stimulation of the superior cervical sympathetic ganglion of cats causes death within 7 days from pneumonia; a second source of ideas for us was contributed by our own experimental observations of 1955 and 1956, in which we found that death of the animals from these causes could be prevented by the injection of certain drugs.

For the present investigations we used white rats. They were convenient because in them the superior cervical sympathetic ganglion innervates the m. orbitalis (in the same way as it does the third eyelid in the cat). Stimulation of this ganglion causes contraction of the m. orbitalis and hence exophthalmos [7,8]. The exophthalmos may be used to indicate the functional condition of the superior cervical sympathetic ganglion.

METHOD

The studies were carried out on sexually mature rats weighing 150-250 g; according to Kaller [5], older or younger rats are not suitable on account of functional changes in the condition of the superior cervical sympathetic ganglion (lability in the first case, and inertia in the second). A midline incision of the neck was made aseptically on rats which were either unanesthetized or, in some experiments, kept under light ether anesthesia. The fibers of the sternocleidomastoid muscle were bluntly dissected to reveal the superior cervical sympathetic ganglion lying near the point at which the common carotid divides. The ganglion was seized with forceps and lightly compressed for 3 min. The wound was sewn up, and for the next 6 days observations were made on the general condition, weight, and changes in the position of the eyeball.

On the 7th day, the animals were killed and the lungs investigated. The trophic condition of the lungs was assessed from the macro- and microscopical appearance, and also from the index K:

$$K = \frac{\text{weight of lungs} \cdot 100}{\text{weight of body}}.$$

RESULTS

In the first set of experiments, mechanical stimulation was applied to the superior cervical sympathetic ganglion of 20 rats. This interference caused a change in the functional condition of the ganglion, and the early appearance of exophthalmos on the operated side 2 days after stimulation. In some experiments there was a ptosis on the stimulated side, which we interpreted as being due to death of certain cells of the ganglion [1]. Usually, from the 2nd day

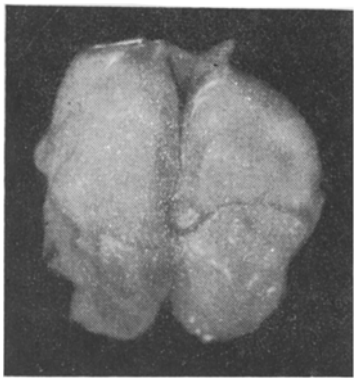

Fig. 1. Lungs of an intact rat.

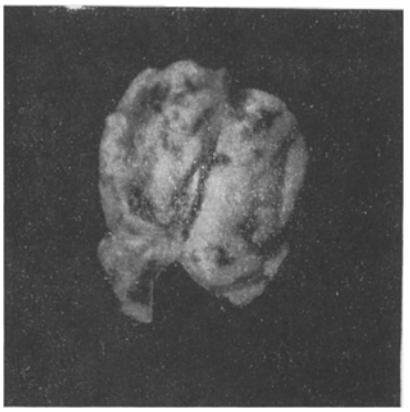

Fig. 2. Lungs of a rat on the 7th day after stimulation of the left superior cervical sympathetic ganglion.

onwards there was also a deterioration in the animals' general condition, they were lethargic, and lost weight.

A comparison of sections of the lungs made on the 7th day with sections of the lungs of control rats (Figs. 1 and 2) revealed considerable changes. In 3 of the rats the damage was only on the operated side, and in 14 of the rats on both sides; in 3 of the rats the damage was on the opposite side.

The lungs were bloody and spotted, and dark brown spots alternated with paler areas so as to present a "marble" appearance. The changes in the lungs frequently resembled those due to "red hepatization." In section, the pulmonary tissue failed to show the normal outline of the organ, and a brown fluid oozed from the cut surface.

Pathological investigation revealed acute pulmonary dystrophy, including severe circulatory disturbances, emphysametous changes, and breakdown of the interalveolar partitions. There was also a mild focal process and an exudate of lymphoid and histoid cells containing a few neutrophils. The index K was increased from its value in the control rats of 0.72 (±0.034) to 1.01 (±0.025).

Thus, in rats, just as in cats, the changes induced by stimulation of the superior cervical sympathetic ganglion cause marked pulmonary disturbances to develop by the 7th day. This degree of damage did not cause death; in the different experiments, the observations were continued until the rats were killed, 21, 42, and 80 days after the operation. Weight had recovered to normal, and the general condition had improved, exophthalmos had become reduced, and at post-mortem examination it was found that there was some residual pulmonary damage and some increase in the index K as compared with the control animals (0.83-0.87).

The development of pulmonary damage on both the ipsi- and contralateral sides may be due to reflex mechanisms [2], and to the fact that the superior cervical sympathetic ganglion contributes to the pulmonary innervation of both sides [6].

The constancy of the observed pulmonary changes which can be evaluated quantitatively will enable this method to be used subsequently as a model for therapeutic studies.

In the second set of experiments, 10 rats received 10 mg/kg of hexamethonium intramuscularly 30 min before stimulation of the ganglion. Otherwise, the experiment was carried out in the same way as before. Post-mortem examination showed less pulmonary damage in this group; the index K was 0.93 (±0.04).

The same dose of hexamethonium was far more effective when given daily for 6 days. Of the 20 rats used in this way, in 8 of them there was no exophthalmos. After the operation the animals were active, and lost no weight. It was found post-mortem that pulmonary damage which was visible microscopically occurred in a smaller number of the animals; the mean value of K was 0.76 (±0.026).

In this way, we have shown that the prolonged injection of hexamethonium, i.e., blocking the transmission of impulses at the autonomic ganglia, greatly reduces the development of pulmonary damage, so that the index K approximates to its value in the intact animals.

SUMMARY

Mechanical stimulation of the superior cervical sympathetic ganglion in rats caused trophic pulmonary disturbances to develop by the 7th day. The changes could be diagnosed both macro- and microscopically, and took the form of acute circulatory disturbances and microfocal inflammatory processes. The changes were not always confined to the site of stimulation. A rise of the index K served as a criterion of the degree of pulmonary damage ($K = \frac{\text{weight of lungs} \cdot 100}{\text{body weight}}$) in the intact animals K = 0.72 ± 0.034, and in the experimental group the value was

1.01 ± 0.025. Intramuscular injection of 10 mg per kg of hexamethonium daily for the whole observation period reduced the severity and incidence of pulmonary damage. In this group, K = 0.76 ± 0.026.

LITERATURE CITED

1. A. G. Ginetsinskii and A. V. Lebedinskii, Course on Normal Physiology [in Russian] (Moscow, 1956).
2. I. P. Dolgachev, Byull. éksper. biol., No. 5, 16 (1953).
3. E. C. Pozovskaya and M. M. Kholodenko, Collection: Report of the Eighth All-Union Conference on Pharmacologists (Abstracts of Reports). [in Russian] (Tbilisi, 1960), p. 130.
4. A. V. Tonkikh, Collection: Military Medical Collection [in Russian] (Moscow-Leningrad, 1946), Collection 3, p. 161.
5. A. V. Tonkikh, Collection: Problems of Soviet Physiology, Biochemistry, and Pharmacology [in Russian] (Moscow, 1949), p. 283.
6. B. de Daly, quoted by M. B. Visscher, F. J. Haddy, and G. Stephens, Pharmacol. Rev., 8, 389 (1956).
7. H. Kaller, Arch. exp. Path. Pharmak. No. 225, 104 (1955).
8. H. Kaller, Arch. exp. Path. Pharmak., No. 228, 361 (1956).
9. H. Kaller, Arch. int. Pharmacodyn., 105, 337 (1956).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
