

## PHARMACOLOGY

### THE EFFECT OF EMBIKHINE ON THE COURSE OF EXPERIMENTALLY INDUCED FEVER

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The use of Embikhine as a therapeutic agent in lymphogranulomatosis has shown that Embikhine, as well as acting specifically on the infected ganglia, quickly relieves fever, sweating and itching (sometimes after only 1-2 injections) [3]. The action mechanism of Embikhine has not been studied sufficiently. There are data indicating that the chlorethylamines, even in small doses, disturb the nucleoprotein (especially the nucleic) metabolism. To what extent thermoregulation and other aspects of metabolism are affected by the action of chlorethylamines is not clear from the literature.

We investigated the effect of Embikhine on the development and course of an experimental fever reaction (temperature, gas metabolism — oxygen consumption), using small and medium therapeutic doses of Embikhine (0.3-0.5 ml/kg) and a "shock" dose (1 ml/kg) injected intravenously into the auricular vein.

#### EXPERIMENTAL METHODS

The experiments were done on rabbits. The fever reaction was induced by Vasilyev's method [1] by intravenously injecting an autoclave-processed bouillon culture of *B. mesentericus* in a dose of 2 ml/kg. The temperature (rectal) was taken every half hour with a medical maximum thermometer. The rabbits' oxygen intake was determined hourly for 15 minutes in a closed system according to Prof. P. N. Veselkin's modification [2] of Regnault and Reiset's method.

A total of 50 experiments were done on 12 rabbits. The experiments were divided into two groups as follows: 1) experiments on intact (non-feverish) rabbits to examine the effect of Embikhine on change in temperature and oxygen intake; 2) experiments in which the effect of Embikhine on the development and course of fever was studied (with Embikhine injected before the fever reaction had been induced and at different stages during the development of the fever).

#### EXPERIMENTAL RESULTS

The rabbits' normal daily oxygen intake fluctuated slightly (8%) and, according to our data, was an average 10.9 ml/kg per minute. Embikhine injected once in a dose of 0.3 and 0.5 ml/kg into the intact rabbits caused the body temperature to rise slightly (by up to + 0.8°) and the level of oxygen intake to decrease (by an average of 11%), as did repeated injections of Embikhine (injected for three days and on the day of the experiment).

No decrease in temperature was noticed with one injection of Embikhine in the "shock" dose (1 ml/kg) either (the temperature either remained the same or rose 0.2-0.3°); during the first three hours, the oxygen intake decreased slightly, but returned to the original level five hours after the preparation had been injected.

Having thereby established that Embikhine alone did not lower the body temperature in the control (non-feverish) rabbits, we then tested its effect on rabbits with experimentally induced fever.

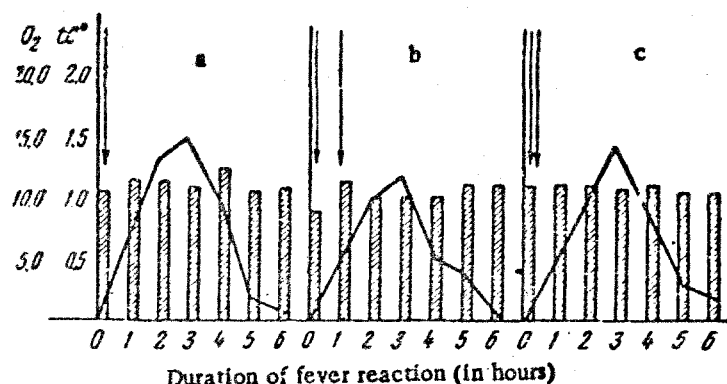
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\* Original Russian pagination. See C.B. Translation.

When comparing the experimental results from this series of experiments, we established:

1. One injection of Embikhine (0.3 and 0.5 ml/kg) given an hour after the pyrogenic injection had no evident effect on either the rate or amount of temperature rise, nor on the character of changes in oxygen intake, although oxygen intake decreased slightly with the 0.5 ml/kg dose of Embikhine.

2. When a "shock" dose of Embikhine was injected simultaneously with the pyrogenic agent, the development and course of the fever reaction was not noticeably affected.



Effect of Embikhine on the course of an experimentally induced fever reaction. (Rabbit 11).

Columns — changes in oxygen intake; curves — changes in temperature.

a) Control fever reaction, arrow shows the culture injection; b) fever reaction with Embikhine injection (0.5 ml/kg intravenously) one hour after the injection of the *B. mesentericus* culture; c) fever reaction with simultaneous injection of *B. mesentericus* culture and Embikhine (1 ml/kg).

3. The maximum temperature of rabbits injected with a "shock" dose of Embikhine an hour after the injection of the pyrogenic agent was 0.2-0.5° lower than that of the rabbits injected with the pyrogenic agent alone; the oxygen intake level was also somewhat lower. We noted that the amount of fluctuation in oxygen intake with fever was somewhat lessened after the Embikhine injection (see Figure).

We therefore propose that the mechanism of Embikhine's antipyretic effect in the treatment of lymphogranulomatosis patients evidently consists primarily of specific action on the pathological process, since Embikhine has no pronounced antipyretic effect.

## SUMMARY

The effect of Embikhine on the body temperature and on the changes of the oxygen intake was studied during various stages of experimentally induced fever. It was established that the introduction of Embikhine to the intact animals does not result in decrease of body temperature. Its effect on the rise of temperature or the character of changes of oxygen intake is immaterial (there is only a certain monotony and fewer variations in the intake of oxygen). The mechanism of the antipyretic effect of Embikhine in treatment of patients with lymphogranuloma evidently consists in the specific effect on the pathological process, since Embikhine by itself has no pronounced antipyretic action.

## LITERATURE CITED

- [1] P. V. Vasilyev, *Byull. Ekspit. Biol. i Med.*, 1949, No. 8, pp. 139-140.
- [2] P. N. Veselkin, *Sechenov Fiziol. Zhur. SSSR*, 1955, No. 1.
- [3] L. F. Larinov, *Embikhine Treatment of Lymphogranulomatosis and Leukemia* (in Russian), Moscow, 1951.